Gene Expression Profiling of Peripheral Tissues in Amyotrophic Lateral Sclerosis

by

Joanna J Bury, MSc

Academic Unit of Neurology
Sheffield Institute for Translational Neuroscience (SITraN)
University of Sheffield

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ABSTRACT

Background: Amyotrophic Lateral Sclerosis, in which cortical and spinal MN's degenerate, is a late onset neurodegenerative condition that accounts for ~1 in 400 UK deaths, typically within 3-5 years from the initial manifestations of disease. It forms part of a broad spectrum of clinically, genetically as well as pathologically hetergeneous disorders that include behavioural variant frontotemporal lobar degeneration (bvFTLD). A large intronic hexanucleotide G_4C_2 repeat expansion of >30 copies was recently identified, in 2011, in the previously uncharacterised chromosome 9 open reading frame 72 (*C9ORF72*) gene which is now thought to explain up to 43% of familial ALS (~20-30% of familial FTLD) and around 7% of sporadic cases. **Rationale & Hypothesis:** The principle aim of the PhD was to perform gene expression profiling of peripheral tissues in ALS. In the first instance whole blood was trialled. However, this proved unreliable, owing to the sheer abundance of erythrocyte derived alpha and beta haemoglobin transcripts that are contained within the sample and the variability in the efficiency of its removal using the Ambion® GLOBINClear™ or NuGEN Ovation® WB reduction strategies. Instead disease related changes in transcription/ alternative splicing were detected in a large bank (n=820) of patient and control lymphoblastoid cell lines (LCL's) with the main purpose of: 1) elucidating further the mechanism(s) of neurotoxicity associated with the *C9ORF72* G_4C_2 repeat expansion and, 2) establishing within this specific genetic subtype, modifiers of a fast (<2yrs) versus slow (≥4yrs) disease progression in order to identify potential new areas of therapeutic research. **Methodology:** Biotinylated, sense-strand cDNA targets of ~40-70nt were hybridized onto Human Exon 1.0ST GeneChip® Arrays. A GC-RMA normalisation procedure was carried out in Partek® Genomics Suite™ and differentially expressed or alternatively spliced transcripts were detected at the 5% significance level ($p<0.05$) with a fold-change threshold of ≥ ±1.20 applied. **Findings:** Overall a marginal increase in gene transcription was observed with respect to *C9ORF72* (59.3%, n=650/1,096) and non*C9ORF72*-related_SALS patients (63.9%, n=1,148/1,796) compared to neurologically healthy controls. DAVID enriched gene ontology terms included translation, which was specific to carriers of the G_4C_2 repeat, in addition to RNA processing, DNA metabolism, RNP complex biogenesis and the cell cycle which reflect more common features of the broader ALS phenotype. A number of key validation targets, including several RNA binding partners of the G_4C_2 repeat (*FUS, RPL 22, NUDT2, PURA, EIF4H* and *HNRNPA0/F*) were subsequently confirmed in a qRT-PCR assay. Isoform A/B specific transcripts of the *C9ORF72* gene, itself, were found not to be differentially expressed across the LCL's in the ECACC discovery and replication cohorts. **Conclusions:** Whether pathogenicity of the G_4C_2 expanded allele arises as a consequence of haploinsufficiency or through an aberrant gain of function mechanism has yet to be determined; although emerging evidence favours a role of RNA toxicity. In light of this model, an up-regulation in the expression of *C9ORF72* binding partners and other, RNA processing & splicing related transcripts fits with the hypothesis that the cells are attempting to compensate for the sequestration of these proteins into toxic RNA foci in the cytoplasm which leads to disruption of their normal physiological function. Small sample sizes meant limited conclusions could be drawn from the analysis of *C9ORF72* specific modifiers of survival in ALS. Clinical data points towards a possible effect of gender which is supported in the literature but other factors such as correlations with expansion length would need to be considered in conducting future work.

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LIST OF ABBREVIATIONS

Aβ	amyloid, beta
Ab	antibody
ABI	Applied Biosystems
ACD-B	acid citrate dextrose solution B
ACTB	actin, beta
AD	autosomal dominant
ADM	adrenomedullin
ADP	adenosine diphosphate
AHC	anterior horn cell
ALS	Amyotrophic Lateral Sclerosis
ALSoD	ALS Online Database
ALT-SPLICE	alternative splicing
ALZ	Alzheimer's disease
AMP	adenosine monophosphate
AMPA	alpha-Amino-3-hydroxyl-5-methyl-4-isoxazolepropionic acid
ANCOVA	analysis of covariance
ANOVA	analysis of variance
ANG	angiogenin
AOA2	ataxia oculomotor apraxia type 2
AR	autosomal recessive
AS	alternative splicing
as	antisense
ATP	adenosine triphosphate
ATPase	adenosine triphosphatase
ATXN2	Ataxin 2
AUC	area under the curve
bac	bacterial
BC	Birmingham control
BD	Becton, Dickinson and Company
BDNF	brain-derived neurotrophic factor
Be	Belfast
bgrd	background
BLDCON	blood control
BLDPAT	blood patient
BP	Birmingham patient
BPD	bipolar disorder
Br	Bristol Frenchay Hospital
BSA	bovine serum albumin
bvFTLD	behavioural variant FTLD
C9ORF72	chromosome 9 open reading frame 72
Ca	Cambridge
Ca^{2+}	calcium ions
cAMP	cyclic AMP
CBS	Corticobasal syndrome
cDNA	complementary DNA
CEL	cell intensity
CEU	Utah residents with ancestry from Northern and Western Europe
CHB	Han Chinese, Beijing
CHMP2B	chromatin modifying protein 2b
CI	confidence interval
Cl	chloride
CLNS1A	chloride channel, nucleotide-sensitive, 1A
CMT	Charcot Marie Tooth
CMT4J	Charcot Marie Tooth type 4J
CNS	central nervous system

CO$_2$	carbon dioxide
cRNA	copy RNA
CSF	cerebrospinal fluid
CST	corticospinal tracts
Ct	cycle threshold
⇩$_{\text{reg}}$	down-regulated
DAVID	Database for Annotation, Visualisation and Integrated Discovery
db	database
dd	double-distilled
DE	differentially expressed
DENR	density-regulated protein
DMSO	dimethyl sulfoxide
DN	dystrophic neurite
DNA	deoxyribonucleic acid
DNase	deoxyribonuclease
DPR	dipeptide repeat
ds	double-stranded
DSB	double-strand break
Du	Durham
DUSP16	dual specific phosphatase 16
dUTP	deoxyuridine triphosphate
EAAT2	excitatory amino acid transporter 2
EASE	enrichment score
EBV	Epstein-Barr virus
ECACC	European Collection of Cell Cultures
EDTA	ethylenediaminetetraacetic acid
EEC	El Escorial Rating Criteria
eEF	eukaryotic translation elongation factor
EGFP	enhanced green fluorescence protein
eIF	eukaryotic translation initiation factor
EIF4H	eukaryotic translation initiation factor 4H
EL	emotional lability
EMG	electromyography
EMSA	electrophoretic mobility shift assay
ER	endoplasmic reticulum
ERBB4	V-Erb-B2 Avian Erythroblastic Leukemia Viral Oncogene Homolog 4
eRF	eukaryotic translation release factor
EST	expressed sequence tag
Euk	eukaryotic
EuroMOTOR	European multidisciplinary ALS network identification to cure motor neurone degeneration
F	female
F’	forward primer sequence
F-actin	filamentous actin
FA	flail arm
FALS	familial ALS
Fas	first apoptosis signal
FasL	Fas ligand
FBS	foetal bovine serum
FC	fold-change
FDR	false discovery rate
Fe^{2+}	iron ions
FIG4	FIG4 homolog, SAC1 lipid phosphatase domain containing (*S. cerevisiae*)
FISH	fluorescent *in situ* hybridization
FL	Flail Leg
FRS-R	Functional Rating Scale Revised
FS	fluidics station
FTLD	frontotemporal lobar degeneration
FTLD-U	FTLD with ubiquitin and TDP-43 positive inclusions

FUS	fused in sarcoma
G-actin	globular actin
GAPDH	glyceraldehyde 3-phosphate dehydrogenase
GCOS	GeneChip® Operating Software
GDP	guanosine diphosphate
GE	gene expression
GEF	guanosine exchange factor
GEMIN6	gem (nuclear organelle) associated protein 6
GEP	gene expression profiling
GluR2	glutamate receptor 2
GmbH	Gesellschaft mit beschränkter Haftung
GO	gene ontology
GRB2	growth factor receptor-bound protein 2
GTF	general transcription factor
GTP	guanosine triphosphate
GTPase	guanosine triphosphatase
GWAS	genome-wide association study
H^+	hydrogen ions
H_2	molecular hydrogen
H_2O	water
H_2O_2	hydrogen peroxide
$\cdot HO$	hydroxyl free radical
HBA2	haemoglobin, alpha 2
HCl	hydrogen chloride
HD	Huntington disease
HG	human genome
hnRNP	heterogeneous RNP
HNRNPA0	heterogeneous nuclear ribonucleoprotein A0
HNRNPA1	heterogeneous nuclear ribonucleoprotein A1
HNRNPA2B1	heterogeneous nuclear ribonucleoprotein A2/B1
HNRNPF	heterogeneous nuclear ribonucleoprotein F
HNRNPH1	heterogeneous nuclear ribonucleoprotein H1 (H)
HNRNPH2	heterogeneous nuclear ribonucleoprotein H2 (H’)
HPA	Health Protection Agency
HSP	hereditary spastic paraplegia
HTT	huntingtin
IAHSP	infantile-onset ascending HSP
IBM	inclusion body myopathy
IDT	Integrated DNA Technologies®
IgG	immunoglobulin G
iPSC	induced pluripotent stem cell
IVT	*in vitro* transcription
JB	Joanna Bury
JNK	c-Jun N-terminal kinase
JPT	Japanese, Tokyo
KARS	lysyl-tRNA synthetase
KEGG	Kyoto Encyclopaedia of Genes and Genomes
LB	Lewy body
LC	London control
LCL	lymphoblastoid cell line
Li	Liverpool
LiC	lithium carbonate
LMN	lower motor neurone
lncRNA	long ncRNA
LNh	London National Hospital
LP	London patient
LWK	Luhya Webuye, Kenya
M	male
Ma	Manchester

MAPK	mitogen-activated protein (MAP) kinase
MAPT	microtubule associated protein tau
MAS	Microarray Suite
MATR3	matrin 3
MEK	mitogen-activated ERK kinase
MES	2-(*N*-morpholino)ethanesulfonic acid
miRNA	microRNA
MM	mismatch
MN	motor neurone
MND	Motor Neurone Disease
MNDA	MND Association
MRI	magnetic resonance imaging
mRNA	messenger RNA
mRNP	messenger RNP
MS	Multiple Sclerosis
MSP	multisystem proteinopathy
mt	mutant
MW	Dr Matthew Walsh
MZ	monozygotic
N	number
n/a	not available
NADE	p75NTR associated cell death executor
NaH_2PO_4	monosodium phosphate
Nc	Newcastle
NCBI	National Centre for Biotechnology Information
NCBP2	nuclear cap binding protein subunit 2, 20kDa
NCI	neuronal cytoplasmic inclusion
ncRNA	non-coding RNA
NF	nuclease free
NF-κB	nuclear factor kappa-light-chain-enhancer of activated B cells
NGF	nerve growth factor
NGS	next generation sequencing
NII	neuronal intranuclear inclusion
NIPPV	non-invasive positive pressure ventilation
NRG1	neuregulin-1
Nt	Nottingham
NTC	no template control
NTF	nuclear transcription factor
NTP	nucleotide triphosphate
NUDT21	nudix (nucleoside diphosphate linked moiety X)-type motif 21
O_2	molecular oxygen
$O_2^{\cdot -}$	superoxide anions
OPTN	optineurin
OR	odds ratio
OS	oxidative stress
Ox	Oxford
P	present calls
PBMC	peripheral blood mononuclear cell
PBP	Progressive Bulbar Palsy
PBS	phosphate buffered saline
PCA	principal component analysis
PCR	polymerase chain reaction
PD	Parkinson's disease
PDB	Paget's disease of bone
PEG	percutaneous endoscopic gastrostomy
PFN1	profilin 1
PGRN	progranulin
PHAX	phosphorylated adaptor for RNA export
P_i	inorganic phosphate

PIC	pre-initiation complex
PIK3R2	PI3K (phosphoinositide 3 kinase) regulatory subunit 2, beta
PLIER	probe logarithmic intensity error
PLS	Primary Lateral Sclerosis
PM	perfect match
PMA	Progressive Muscular Atrophy
PNFA	progressive non-fluent aphasia
Po	Poole General Hospital
POAG	primary open angle glaucoma
Pol II	RNA polymerase II
POLR2G	polymerase (RNA) II (DNA directed) polypeptide G
poly(A)	polyadenylated
PPMCC	Pearson's product-moment correlation coefficient
Pr	Preston
pre-mRNA	precursor mRNA
PrLD	prion like domain
PSEN	presenilin
PTPRC	protein tyrosine phosphatase, receptor type, C
PURA	purine-rich element binding protein A
Py	Plymouth's Derriford Hospital
QC	quality control
qPCR	quantitative PCR
qRT-PCR	quantitative Real-Time PCR
#	rank
R'	reverse primer sequence
R^2	coefficient of correlation
RAN	repeat-associated non-ATG
RBM3	RNA binding motif (RNP1, RRM) protein 3
Rf	Royal Free Hospital
RIN	RNA integrity number
RLE	relative log expression
RMA	robust multi-array average
RNase	ribonuclease
RNA-seq	RNA sequencing
RNP	ribonucleoprotein
Ro	Royal London Hospital
ROC	receiver operating characteristic
ROS	reactive oxygen species
ROX	5(6)-Carboxy-X-Rhodamine
RPL22	ribosomal protein L22
RPMI	Roswell Park Memorial Institute
RR	Dr Rohini Raman
RRM	RNA recognition motif
rRNA	ribosomal RNA
RT	room temperature
SALS	sporadic ALS
SAM	significance analysis of microarrays
SAPE	Streptavidin Phycoerythrin
SC	Sheffield control
SC	spinal cord
SCA	spinocerebellar ataxia
SCHIZ	Schizophrenia
SD	semantic dementia
Se^{2-}	selenium ions
SEM	standard error of the mean
SETX	senataxin
SF	scaling factor
SFPQ	splicing factor proline/glutamine-rich
SFRS	splicing factor arginine/serine-rich

SG	stress granule
SGNP	SG and nucleolar protein
Sh	Southampton General Hospital
SIGMAR1	sigma non-opioid intracellular receptor 1
SMA	Spinal Muscular Atrophy
SMN	survival motor neurone
SNP	single nucleotide polymorphism
snRNA	small nuclear RNA
snRNP	small nuclear RNP
SNV	single nucleotide variation
SOD1	copper/zinc superoxide dismutase 1
SOS	son of sevenless
SP	Sheffield patient
SPG11	spatacsin
SPIA™	single primer isothermal amplification
ss	single-stranded
SS	sense strand
SSPE	saline-sodium phosphate EDTA
ST	sense target
STRAP	serine/threonine kinase receptor associated protein
TAF	TATA-binding protein (TBP) associated factor
TAF13	TAF13 RNA polymerase II, TBP-associated factor, 18kDa
Taq	*Thermus aquaticus*
TARDBP	transactive response (TAR) DNA binding protein
TBE	Tris Borate EDTA
TDP-43	TAR DNA binding protein 43kDa
TE	Tris-EDTA
TLS	translocated in liposarcoma
T_m	melting temperature
TNF	tumor necrosis factor
Tris	tris(hydroxymethyl)aminomethane
tRNA	transfer RNA
$tRNA_i^{met}$	initiator methionine tRNA
⇧$_{reg}$	up-regulated
UBQLN2	ubiquilin 2
UMN	upper motor neurone
UNC13A	Unc-13 homolog A
UNRIP	UNR-interacting protein
UPR	unfolded protein response
UPS	ubiquitin-proteasome system
UTP15	U3, small nucleolar ribonucleoprotein, homolog (*S. cerevisiae*)
UTR	untranslated region
VAPB	VAMP (vesicle associated membrane protein) associated protein B and C
VCP	valosin-containing protein
VCPDM	vocal cord and pharyngeal weakness with distal myopathy
VEGF	vascular endothelial growth factor
WES	Whole Exome Sequencing
wt	wild-type
WT	whole transcriptome
YRI	Yoruba Ibadan, Nigeria
ZCRB1	zinc finger CCHC-type and RNA binding motif 1

CHAPTER 1: INTRODUCTION

1.1 Motor Neurone Disease Spectrum

1.1.1 Background

Motor Neurone Disease (MND), originally coined by Brain in 1933, is a term used to encompass a broad clinical spectrum of rapidly progressive (Hardiman et al 2011) and invariably fatal (Dion et al 2009), late onset neurodegenerative disorders which include: Amyotrophic Lateral Sclerosis (ALS) (~60%) (Section 1.2.1); ALS with concomitant frontotemporal lobar degeneration (ALS+FTLD) (~5-10%) or Parkinson's disease (ALS+PD) (~5%) (Lomen-Hoerth et al 2003, Manno et al 2013); Progressive Bulbar Palsy (PBP) (~20%) (Section 1.2.2.1); Progressive Muscular Atrophy (PMA) (~10%) (Section 1.2.2.3) and Primary Lateral Sclerosis (PLS) (~2-5%) (Section 2.2. 2.2).

1.1.2 Epidemiology

MND has a prevalence of 3.4 or 5.2 (range 4-8) per 100,000 of the North American and European Caucasian populations, respectively (Traynor et al 1999). Incidence rates vary, but are reported to occur within the region of 0.6 (Sicily) (De Domenico et al 1988, Rosati et al 1977) and 2.4 (Finland) (Murros & Fogelholm 1983) with an average of 1 or 2 individuals per 100,000/year (Chio et al 2013a, Logroscino et al 2008, Werneck et al 2007). This confers a relative lifetime risk of ~1 in 400 by the age of 70 (Johnston et al 2006). In non-European countries the frequency has been estimated to be higher in the Chamorro tribe, of the Western Pacific island of Guam (22 per 100,000/year) (Plato et al 2002, Waring et al 2004), and in several regions of the Kii peninsula of the Japanese island, Honshu (9.5 per 100,000/year) (Kaji et al 2012, Okamoto et al 2009) where there have been reports of a ALS/Parkinsonism -dementia complex; but is, however, considerably lower across the Far East (1.3 per 100,000/year) (Kihira et al 2005, Yoshida et al 1998), Africa (0.9 per 100,000/year) (Marin et al 2012, Radhakrishnan et al 1986) and Asia (0.3 per 100,000/year) (Fong et al 1996). A slight trend towards a male preponderance is evident (Leblond et al 2014) with male to female (M:F) ratios ranging between 1.2 and 1.5:1 (Logroscino et al 2010, McCombe & Henderson 2010). Prognostic factors that have been found to correlate negatively with survival include poor nutritional status, signs of bulbar or respiratory muscle involvement, early age at symptom onset, a short diagnostic delay and evidence of cognitive dysfunction (Logroscino & Bennett 2014, Scotton et al 2012).

1.1.3 Diagnosis

A single definitive diagnostic test for MND does not currently exist (Hardiman et al 2011). Clinical evaluations, based upon a detailed history and physical examination of the patient, are supported by electrophysiological testing [e.g. electromyography (EMG) as well as sensory and motor nerve conduction velocities], neuropsychiatric evaluation, imaging [e.g. magnetic resonance imaging (MRI) of the brain and spinal cord (SC)], genetic consultation and neuropathological information (McDermott & Shaw 2008). Other laboratory investigations, such as muscle biopsy, cerebrospinal fluid (CSF) analysis, serum creatine kinase measurements, thyroid function tests, a full blood count, erythrocyte sedimentation rate and urine protein electrophoresis, may also aid in the exclusion of other neuromuscular disorders that can mimic MN degeneration (Hardiman et al 2011, Sathasivam 2010, Turner & Talbot 2013). The World Federation of Neurology introduced the El Escorial Rating Criteria (EEC) in 1994, later amended in 1998, to ensure standardization in the diagnosis of MND, for the purposes of clinical research (Figure 1.1) (Brooks 1994, Brooks et al 2000). According to this system, patients are assigned to one of four diagnostic categories, namely definite, probable, possible or suspected ALS, as determined by the various levels of certainty with which clinical and laboratory assessments are made. Signs of upper MN (UMN) dysfunction include increased muscle tone, hyperreflexia and spasticity, whereas lower MN (LMN) dysfunction is characterised by severe muscle wasting & weakness, as well as hyporeflexia, fasciculations and cramping (Kinsley & Siddique 2001). Often, however, the initial manifestations of the disease are mild and relatively non-descript (McDermott & Shaw 2008). Its insidious nature means that a period of observation, lasting 12 months or longer, may be required (Paganoni et al

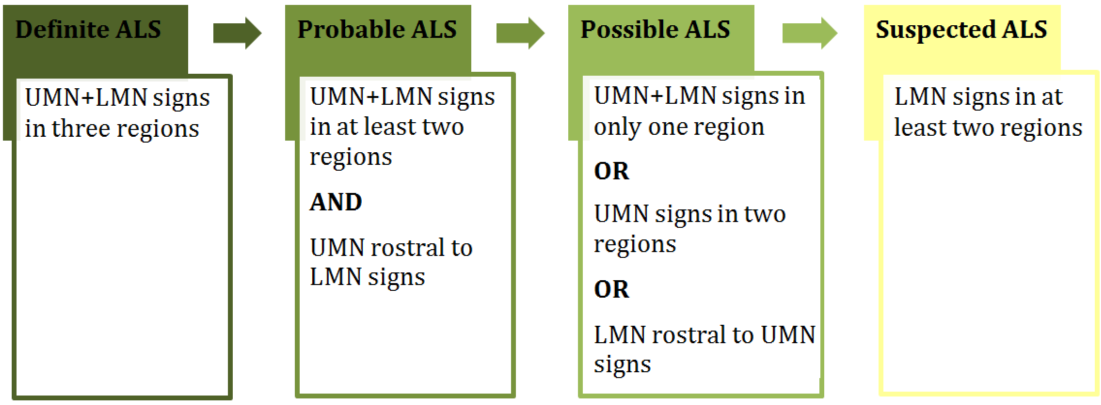


Figure 1.1 El Escorial Rating Criteria (EEC) for the Diagnosis of MND

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, LMN - lower motor neurone, MND - Motor Neurone Disease and UMN - upper motor neurone.

2014) before a patient is referred to a specialist neurologist and a diagnosis of MND can be confirmed (Nzwalo et al 2014). Hence, an urgent need exists for the identification of specific biological markers or biomarkers that can facilitate an earlier diagnosis and more accurate monitoring of disease progression, as well as offering the potential to better predict individual responses to novel therapeutic agents and/or treatment strategies (Frank & Hargreaves 2003, Lehnert et al 2014, Mendez & Sattler 2014, Silani et al 2011, Su et al 2013).

1.1.4 Clinical Management

As yet there is no known cure for MND. Clinical management is based on guidelines which have been published by the American Academy of Neurology® (AAN) and the European Federation of Neurological Societies (EFNS). Over the years there have been more than thirty phase II and phase III clinical trials of promising therapeutic agents identified from various *in vitro* and *in vivo* studies, including lithium carbonate (LiCALS), brain derived neurotrophic factor (BDNF), Novartis (Ozanezumab), ONO-2506 (Arundic acid), minocycline and Copaxone® (glatiramer acetate) which relate to patient LCL samples in the National MNDA DNA Bank, held at the Health Protection Agency (Public Health England, UK), that were subsequently recruited into the ECACC discovery (Section 4.1.1) and replication (Section 4.1.2) cohorts [REVIEWED BRIEFLY IN APPENDIX TABLE B4]. Disappointingly, however, these have yielded little success, with the glutamate antagonist, Riluzole (Bensimon et al 1994) remaining the only Food and Drug Administration (FDA) approved drug for the treatment of MND in the UK (Hardiman et al 2011). Individual responses vary with a modest increase in survival of ~2-3 months (Miller et al 2007, Riviere et al 1998) reported in some sufferers, but not others. Current efforts, therefore, are largely focused on symptom management and alleviating pain and discomfort in order to maintain as good a quality of life for as long as possible (McDermott & Shaw 2008).

The provision of palliative care is heavily reliant upon a multidisciplinary approach that requires a specialist neurologist and a team of trained nursing staff supported by additional healthcare professionals including a psychiatrist, genetic counsellor, nutritionist, pulmonologist, social worker and speech/occupational therapist (Bede et al 2011, Kinsley & Siddique 2001). Muscle relaxants such as benzodiazepine and baclofen may be administered to relieve spasticity and cramping (Ashworth et al 2004). Oral secretions can be controlled with the use of a saline nebulizer in combination with a beta (β)-receptor antagonist (e.g. metoprolol/propranolol), tricyclic antidepressant compounds, mucolytic agents and mechanical suctioning devices (Andersen et al 2007, Miller et al 2009b). Complications associated with increased metabolic activities and difficulties in swallowing (dysphagia) (Miller et al 2009a) such as weight loss and malnutrition can be overcome by modifying the consistency of food and fluid intake initially, or in more advanced cases, through the insertion of a percutaneous endoscopic gastrostomy (PEG) feeding tube. If tolerated, non-invasive positive pressure ventilation (NIPPV) assistance is highly recommended for patients with a forced vital capacity (FVC) lung function test <50% (Miller et al 1999). It has proven a particularly beneficial intervention in instances where it is used for a minimum of five hours daily and can be implemented before the onset of severe bulbar dysfunction, with reports of median survival times being extended by approximately 7 months (Bourke et al 2006, Farrero et al 2005, Hannan et al 2014). Several studies have also evaluated the use of Vitamin C/E or multivitamin supplements, herbal preparations such as Gingko biloba and Ginseng, coenzyme Q10, antioxidant therapies and zinc but sample sizes have been small and the effects of these agents remain controversial (Cameron & Rosenfeld 2002, Galbussera et al 2006, Kaufmann et al 2009, Orrell et al 2007).

1.2 Amyotrophic Lateral Sclerosis

1.2.1 ALS

Amyotrophic meaning atrophy of the muscles and **L**ateral **S**clerosis referring to the hardened tissues and scarring of the lateral spinal cord (ALS) was first reported by French physician and neurologist, Jean-Martin Charcot over a century ago (Charcot & Joffroy 1869) (Leblond et al 2014). It represents by far the most common form of MND accounting for up to two-thirds (~60%) of cases (Ekbom 1992, Gomes Mda & Engelhardt 2013, Kumar et al 2011). In America it is more commonly referred to as Lou Gehrig's disease in memory of the famous New York Yankees baseball player of the same name (Lewis & Gordon 2007), who died prematurely from the condition in 1941, aged just 37 years. ALS is characterised by the rapid degeneration and progressive loss of both UMN's, consisting of giant Betz, as well as, other large pyramidal cells of the primary motor cortex and LMN's which include the cranial motor nerve nuclei and anterior horn cells (AHC's) of the brainstem and SC (Hardiman et al 2011, McDermott & Shaw 2008) (Section 1.2.3). Denervation results in muscle weakness, atrophy and spasticity that leads to a failure in initiating and controlling voluntary movements (Gordon et al 2003, Kinsley & Siddique 2001, Sathasivam 2010). Onset usually occurs focally and is asymmetric (Korner et al 2011) with symptoms initially restricted to the upper or lower extremities (~66%) (limb or spinal onset), bulbar region (~30%) or, more infrequently, the respiratory muscles, which account for ≤ 5% of cases (Gautier et al 2010, Ravits et al 2007, Sekiguchi et al 2014). Contiguous advancement and eventual widespread paralysis culminates in respiratory failure, typically within 3-5yrs from the initial point of diagnosis (Cluskey & Ramsden 2001). Although some patients will progress more rapidly, dying inside a year, it is anticipated that only around one in twenty cases will survive beyond a decade (Gordon 2011, McDermott & Shaw 2008, Preux et al 1996). Additionally, executive and memory deficits also afflict between 25 and 50% of cases (Goldstein & Abrahams 2013); with 10 to 20% of these meeting the diagnostic criteria for frontotemporal lobar degeneration (FTLD) (Barson et al 2000, Massman et al 1996, Phukan et al 2012, Ringholz et al 2005, Strong et al 2009) by the time they have reached their terminal stages of disease progression and *vice versa*, ~15% of FTLD patients (Burrell et al 2011, Lomen-Hoerth et al 2002, Strong et al 1999) have reportedly presented with some degree of motor dysfunction. After Alzheimer's disease (ALZ), FTLD is recognised as the second most frequent cause of presenile dementia, accounting for between five and fifteen percent of cases occurring in individuals before the age of 65 (Cooper-Knock et al 2014a). It is characterised by a progressive phenotype in which severe frontal and temporal lobe atrophy leads to alterations in personality and behaviour as well as impaired cognitive functioning and language difficulties (Neumann 2013, Riedl et al 2014). According to the Neary defined consensus criteria of 1998, three clinically distinct subtypes are thought to exist: a) behavioural variant FTLD (bvFTLD) most commonly associated with ALS; b) progressive non-fluent aphasia (PNFA) including word retrieval problems and loss of speech and c) semantic dementia (SD) producing deficits in word comprehension and memory (Mignarri et al 2014, Morimoto et al 2012). Evidence of a family history of MND or dementia is usually apparent in around 25 to 50% of cases, with mutations having been identified in the microtubule associated protein, tau (*MAPT*), progranulin (*PGRN*) and presenilin (*PSEN*) [Briefly reviewed in Section 1.2.5.3], in addition to a number of ALS causative genes, namely transactive response (TAR) DNA binding protein (*TARDBP*), fused in sarcoma (*FUS*), angiogenin (*ANG*), ataxin 2 (*ATXN2*), ubiquilin 2 (*UBQLN2*), profilin 1 (*PFN1*), sigma non-opioid intracellular receptor 1 (*SIGMAR1*), charged multivesicular body protein 2b (*CHMP2B*), valosin-containing protein (*VCP*), heterogeneous nuclear ribonucleoprotein A1 (*HNRNPA1*) (Section 1.2.5.1) (Ferrari et al 2012, Mackenzie et al 2014) and chromosome 9 open reading frame 72 (*C9ORF72*) (Section 1.2.5.4) which is the focus of this project. A long established clinical, neuropathological and genetic overlap between ALS and bvFTLD is suggestive of these two heterogeneous disorders of the brain and central nervous system (CNS) lying on a continuum rather than forming distinct and entirely separate disease entities (Pliner et al 2014). In some instances, ~4% of ALS and around 20-30% of FTLD patients, Parkinsonian features may also be apparent including poor response to Levodopa (L-dopa), rigidity, bradykinesia without resting tremor and a vertical gaze palsy (Karageorgiou & Miller 2014, Park & Chung 2013, Seelaar et al 2008).

The rarer and more benign brachial amyotrophic diplegia variant or Flail Arm (FA) syndrome was originally described by Alfred Vulpian in 1886 and accounts for ~11

% of cases. It is a condition of predominant LMN dysfunction, characterised by proximal wasting and progressive weakness of the upper limbs. Traditionally, it is thought of as having a higher predisposition in men versus women, with a M:F ratio of 9:1 (Hu et al 1998). Age at symptom onset does not differ from that of "classical ALS" which has a peak in the mid-60's and 70's for sporadic (SALS) patients and a second in the early 40's or 50's for instances where there is known to be at least one other first or second degree relative who is affected (Calvo et al 2014b, Kinsley & Siddique 2001). One distinguishing feature, however, is disease duration with 52% exceeding 5 years survival and 17.4% extending beyond 10 years (Chio et al 2011a, Wijesekera et al 2009). Furthermore, FTLD which is typically diagnosed in 5 to 10% of "classical ALS" patients is found to be distinctly lacking in cases associated with the FA syndrome (~1.4%) (Wolf et al 2014)

The rarer still pseudopolyneuritic variant or Flail Leg (FL) syndrome was first identified in 1918 by a student of Pierre Marie, namely Jean Patrikios (Patrikios 1918), and accounts for a further 6% of cases. It is a condition of predominant LMN dysfunction characterised, in the absence of overt pyramidal signs, by distal wasting and progressive weakness of the lower limbs, abnormal tendon reflexes and extensive demyelination of the corticospinal tracts (CST). The median age of symptom onset is reported to be 55 (range 31-79yrs) with roughly equal numbers of male and female patients affected. Disease progression is typically slower than that of "classical ALS" with a mean duration of 71 versus 36 months, respectively (Wijesekera et al 2009).

1.2.2 Other Rare Variants of MND

1.2.2.1 PBP

Progressive bulbar palsy (PBP) was originally described in 1860 by Guillaume Benjamin Amand Duchenne as labioglossopharyngeal paralysis (Broussolle et al 2012), which was later renamed by Wachsmuth in 1864. It is a condition of both UMN and LMN involvement that primarily affects the muscles controlling speech and swallowing (Hughes & Wiles 1998, Rocha et al 2005). Symptoms include weak palatal movement, an excessive/uncontrollable production of saliva, reduced gag reflexes, tongue fasciculations and emotional lability (EL), in addition to, dysarthria (speech impairment) and dysphagia (Cerero Lapiedra et al 2002, Talacko & Reade 1990). PBP has a higher prevalence in women than men (Kuhnlein et al 2008a, McDermott & Shaw 2008) and is associated with an especially poor prognosis in which the majority of patients will succumb to the onset of pulmonary pneumonia, 1-3yrs after the initial manifestations of disease. Although initially thought to be a distinct phenotypic entity, accounting for up to a fifth of MND cases, recent evidence has emerged to suggest that as many of 87% will progress to fulfil the diagnostic criteria of definite ALS (Figure 1.1) and in much of the current literature many of these cases have been reclassified accordingly as having bulbar-onset ALS (Karam et al 2010).

1.2.2.2 PLS

Primary Lateral Sclerosis (PLS) is a relatively rare, atypical form of MND which accounts for between 2 and 5% of cases (Kuipers-Upmeijer et al 2001, Le Forestier et al 2001, Pringle et al 1992, Singer et al 2005, Zhai et al 2003). It was initially described by Wilhelm Heinrich Erb in 1902 as a condition of pure UMN involvement that typically has a slower disease course of up to 17 years (Almeida et al 2013b, Hardiman et al 2011) and is almost exclusively idiopathic in nature (Tartaglia et al 2007). PLS presents clinically from CST degeneration, and in the absence of pronounced muscular atrophy, as a triad of hyperreflexia, mild to moderate lower limb weakness and spasticity with patients often reporting stiffness, clumsiness/reduced coordination and occasional bladder symptoms (Gordon et al 2006, Singer et al 2007).

1.2.2.3 PMA

Progressive Muscular Atrophy (PMA) was originally described in 1850 by François-Amilcar Aran as a condition of pure LMN involvement that accounts for around 10% of the total number of MND cases (Kim et al 2009, Riku et al 2014). It is virtually always sporadic, although a few incidences involving a prior family history have been recorded (Rowland 2010). Progressive degeneration of the AHC's within the brainstem and SC are known to bring about fasciculations that ultimately lead to severe muscle weakness and atrophy (Cervenakova et al 2000, Jansen et al 1986). In comparison to those diagnosed with "classical ALS", PMA patients exhibit a greater male preponderance with a slightly older than anticipated age of symptom onset and a longer disease duration [median survival 48 versus 36 months (Tsuchiya et al 2004, Visser et al 2008)].

1.2.3 ALS Pathology

At autopsy, specimens derived from familial ALS (FALS) and SALS patients are largely indistinguishable. Both are characterised by: a) degeneration of the CST carrying axonal nerve fibres, which project from the primary motor cortex to the LMN's and extensive loss of LMN's within the brainstem and SC (Ghatak et al 1986, Hughes 1982); b) degeneration and loss of UMN's including giant Betz and other, large pyramidal cells of the primary motor cortex (Hammer et al 1979, Maekawa et al 2004, Udaka et al 1986) and c) widespread reactive gliosis which is a more generic feature of CNS injury and inflammation (Ekblom et al 1994, Kawamata et al 1992, Murayama et al 1991, Schiffer et al 1996). Residual, atrophied MN's are classically hallmarked by the presence of ubiquitinated intracellular proteinaceous Lewy body (LB) (20-40%) or skein-like inclusions (90%) that are immunoreactive for TDP-43 or FUS (Arai et al 2006, Deng et al 2010, Ling et al 2010, Neumann et al 2006). Additional crescent shaped inclusions (SCI's) (infrequent) may be seen in the upper cortical layers II to IV and dentate gyrus of MND patients with dementia (Al-Sarraj et al 2002). Moreover, there have also been reports of cystatin C containing Bunina bodies (70-80%) (Okamoto et al 1993, Sasaki & Maruyama 1994) and axonal spheroids (frequent) occurring in MN's of the SC (Corbo & Hays 1992, Millecamps et al 2006). Hyaline conglomerate inclusions (HCI's) that are composed of hyperphosphorylated accumulations of neurofilament subunits and peripherin are a much rarer occurrence and usually restricted to cases involving mutant SOD1 (mtSOD1) (Ince et al 1998, Leblond et al 2014, Munoz et al 1988, Sobue et al 1990).

In addition to the classic ubiquitinated, p62 and TDP-43 positive, neuronal and glial cytoplasmic inclusions described above in the motor cortex and AHC's of the brainstem and SC (Cooper-Knock et al 2015a), *C9ORF72+* ALS and ALS-FTLD related cases can also be characterised by the superimposition of extra-motor features which are observed in the hippocampus, frontal neocortex and cerebellum (Al-Sarraj et al 2011, Cooper-Knock et al 2012b, Murray et al 2011, Stewart et al 2012). These include further ubiquitinated, p62 positive but TDP-43 negative, neuronal cytoplasmic (NCI) and intranuclear (NII) inclusion bodies which are immunoreactive for both sense as well as antisense dipeptide repeat proteins (DPR's) (poly-GA, GR and GP) produced from non-ATG mediated or RAN translation of the aberrantly expanded G_4C_2 repeat (Section 1.2.5.4) (Gendron et al 2013a, Mann et al 2013, Mori et al 2013c).

1.2.4 Mechanisms Underlying MN Degeneration in ALS

Most of our current understanding of the mechanisms which underlie MN degeneration in ALS has come from the study of transgenic SOD1^{G93A} mice (Ferraiuolo et al 2007) with particular emphasis on the importance of glutamate excitotoxicity (Section 1.2.4.2), mitochondrial dysfunction (Section 1.2.4.3) and oxidative stress (Section 1.2.4.1). Mutations, however, in the antioxidant gene copper/zinc superoxide dismutase 1 (*SOD1*) are responsible for only a minority, (~2%) of the total number of ALS cases (Rosen et al 1993) (Section 1.2.5.1.1). With the emergence of many new genetic subtypes (Table 1.1), most notably *C9ORF72*; accounting for up to 43% of F ALS and around 7% of SALS cases (Section 1.2.5.4) (Cooper-Knock et al 2012b), and the identification of TDP-43 as well as other mutated proteins as major constituents of NCI's (Section 1.2.3) (Neumann et al 2006) a complex interplay between multiple disease causative mechanisms is now thought to exist which supports diverse roles such as axonal transport defects (Section 1.2.4.4), intracellular protein aggregation (Section 1.2.4.5), non-cell autonomous glia and inflammation (Section 1.2.4.6), autophagy (Section 1.2.4.7), apoptosis (Section 1.2.4.8) and, perhaps most significantly RNA processing (Section 1. 2.4.9) (Ferraiuolo et al 2011).

1.2.4.1 Oxidative Stress

Oxidative stress (OS) is a phenomenon which arises as a consequence of a cytosolic imbalance between the production of reactive oxygen species (ROS), a consequence of aerobic respiration, and their subsequent neutralisation, degradation or removal, to affect the prevailing reducing environment inside the cell (Barber & Shaw 2010); together with the system's inability to overcome or repair ROS damage to structural constituents of lipids, proteins and nucleic acids. The leakage of electrons from the mitochondrial respiratory electron transport chain, along with xanthine oxidase and cytochrome P450, contribute to incomplete oxidative phosphorylation of molecular oxygen (O_2). This leads to the generation of superoxide anions ($O_2^{\cdot -}$) and hydrogen peroxide (H_2O_2) which are themselves relatively unstable and may undergo further downstream reactions to produce even more potent oxidizing species e.g. hydroxyl free radicals ($^{\cdot}HO$) and peroxynitrite ($ONOO^-$); molecules which subsequently cause protein carbonyls to form, nitrosylation of tyrosine residues, lipid peroxidation and oxidative damage to DNA and RNA (Turner et al 2013).

1.2.4.2 Glutamate Excitotoxicity

A state of excitotoxicity arises from an increased or prolonged stimulation of post-synaptic, sodium-dependent inotropic AMPA (alpha-Amino-3-hydroxyl-5-methyl-4-isoxazolepropionic acid) or NMDA (N-methyl-D-aspartate) receptors by glutamate which triggers a large influx of calcium ions (Ca^{2+}) (Corona et al 2007, Turner et al 2013). Elevated levels of this excitatory neurotransmitter compound are detectable in patient CSF which is found to correlate with disease severity (Spreux-Varoquaux et al 2002). The permeability of AMPA receptors is determined in a large part by the GluR2 (glutamate receptor 2) subunit which is relatively lowly expressed in MN's. This, in combination with the fact that these cells have a smaller calcium buffering capacity compared to other neuronal populations (e.g. oculomotor neurons which are generally spared in ALS), offers an insight as to the reasons why it is perhaps the MN's which are most susceptible to excitotoxic injury & death in neurodegeneration (Robberecht & Philips 2013). A substantial rise in intracellular Ca^{2+} concentrations results in the production of ROS from the mitochondrion that establishes a negative feedback loop involving impaired EAAT2 (glial excitatory amino acid transporter 2) function and reduced re-uptake of glutamate from the synaptic cleft (Grosskreutz et al 2010, Kong et al 2014). Significant decreases in the level of EAAT2 protein expression have been observed in around 80% of human autopsy derived brain and SC tissue (Rothstein et al 1995); whereas overexpressing endogenous forms in the transgenic SOD1^{G93A} mouse has been shown to delay the onset of motor deficits (Guo et al 2003). The minor allele of SNP rs12608932 (Table 1.3) (Section 1.2.5.1.11) in the unc-13 homolog A (*UNC13A*) gene (Diekstra et al 2012, van Es et al 2009c), an important regulator of synaptic glutamate release, is associated with an increased risk of developing ALS (OR 1.33, $p<0.005$) which correlates negatively with survival. Ultimately, activation of the calpain and/or cathepsin protease enzymes regulate the cleavage of apoptosis inducing factor (AIF) and its subsequent translocation into the nucleus where it elicits large scale DNA fragmentation and programmed cell death in a caspase independent manner (Cande et al 2002, Oh et al 2006, Shibata et al 2009).

1.2.4.3 Mitochondrial Dysfunction

Mitochondria are critical for the survival of eukaryotic cells, acting as a powerhouse which drives adenosine 5'-triphosphate (ATP) production. In addition to providing the cell with a source of energy, these organelles are also required for the regulation of apoptosis and calcium ion homeostasis (Kasahara & Scorrano 2014) (Section 1.2. 4.2). Morphological, ultra-structural and biochemical abnormalities have been observed in both FALS and SALS cases in the form of enlarged, vacuolated mitochondria with inner membrane defects and aberrantly arranged cristae (Hirano et al 1984). There is also evidence to suggest that transportation of mitochondria along microtubles in ALS may be impaired, which supports a "dying-back" axonopathy model of the disease (Shi et al 2010). Several mitochondrial modulators with neuroprotective properties in mammalian cell and animal systems are currently under investigation including the immunosuppressant cyclosporine (CsA) which prevents formation of the mitochondrial permeability transition pore complex (Karlsson et al 2004, Keep et al 2001) and the cholesterol-like compound, Olesoxime, that stabilizes the outer-membrane, through its association with voltage-dependent anion-selective channel (VDAC) and benzodiazepine receptors (Bordet et al 2007, Martin 2010, Sunyach et al 2012).

1.2.4.4 Axonal Transport

MN's are reliant upon mechanisms of anterograde and retrograde axonal transport to maintain cellular homeostasis and for communication between the cell body and distant nerve terminals (Chevalier-Larsen & Holzbaur 2006). Genetic alterations in a number of cytoskeletal components, adaptor molecules and motor proteins have been associated with the disease including dynactin (*DCTN1*), neurofilament heavy chain (*NEFH*) (Section 1.2.5.1.10), profilin 1 (*PFN1*) (Section 1.2.5.2.9) and kinesin-associated protein 3 (*KIFAP3*) (Section 1.2.5.1.11). Reduced messenger RNA (mRNA) transcript levels pertaining to neurofilament light chain (*NEFL*), a causative gene of Charcot Marie Tooth (CMT) disease, have also been observed in the AHC's of SALS patients (Bergeron et al 1994). RNA processing proteins TDP-43 (Section 1.2.5.2.1) and FUS (Section 1.2.5.2.2) bind NFL (Lagier-Tourenne et al 2012, Polymenidou et al 2011, Strong et al 2007) to disrupt its normal physiological function by resulting in its aberrant sequestration into stress granules (SG's) (Volkening et al 2009).

1.2.4.5 Intracellular Protein Aggregation

A major pathological feature of ALS, as discussed previously in Section 1.2.3, is the presence of p62 positive, ubiquitinated intracellular proteinaceous inclusion bodies which accumulate in the cytoplasm of residual, atrophied MN's and glia of the CNS. Many have been shown to be immunoreactive for C9ORF72, TDP-43, FUS or SOD1; among several other translated products of ALS causative genes, depending on the underlying genetic cause of the disease. For example, whilst *FUS* and *SOD1* mutation carriers contain aggregates of these proteins, they are found to be negative for TDP-43, unlike *TARDBP* and most other ALS cases. The precise manner in which protein aggregation contributes to MN degeneration is unclear with experimental evidence pointing towards both loss of function and gain of function mechanisms (Blokhuis et al 2013).

1.2.4.6 The Role of Non-Cell Autonomous Glia and Inflammation

Evidence which suggests that the astrocytes and microglia surrounding MN's in the CNS are determinants of disease onset and progression (Boillee et al 2006, Wang et al 2011, Wang et al 2009, Yamanaka et al 2008, Zhu et al 2014) implicates a role for non-cell autonomous neurodegeneration in the pathogenesis of ALS (Appel et al 20 11, Ilieva et al 2009). The increasing activation and proliferation of these cells produces a neuroinflammatory response (Glass et al 2010, McGeer & McGeer 2002, Philips & Robberecht 2011) with elevated levels of proinflammatory cytokines and other markers of inflammation including tumor necrosis factor alpha (TNFα) and Fas ligand (FasL); a potent inducer of apoptosis (Section 1.2.4.8) (Petri et al 2006, Kuhle et al 2009, Meissner et al 2010, Mitchell et al 2009, Sekizawa et al 1998). Treatment with anti-inflammatory compounds such as Celastrol, a triterpene which is extracted from the roots of the traditional Chinese herb, *Tripterygium wilfordii* (Thunder god vine), or Thalidomide and its derivative REVLIMID® (lenalidomide) have proved beneficial in prolonging the lifespan of ALS rodents with reports of a significant dose-dependent increase in survival, reduced weight loss, improved rota-rod performance, higher neuronal cell counts and a delay in the onset of symptoms (Kiaei et al 2005, Kiaei et al 2006, Neymotin et al 2009).

1.2.4.7 Autophagy

In ALS aggregates of misfolded mutant (mt) or wild-type (WT) proteins (Section 1.2.4.5) accumulate in the cytosol which overwhelms the ubiquitin-proteasome system (UPS) and causes it to become impaired. The cells attempt to compensate, in order to maintain a homeostatic environment, by activating the autophagosome-lysosome clearance pathway (Li et al 2008b, Sasaki 2011). This along with several autophagy inducing compounds such as lithium, resveratrol and trehalose (Albani et al 2010, Fornai et al 2008, Gomes et al 2010) have proven beneficial in promoting survival of MN's and delaying disease progression in the SOD1^{G93A} mouse model (Ghavami et al 2014).

1.2.4.8 Apoptosis

Activation of cell surface death receptors (e.g. Fas) by extrinsic factors such as TNFα and TNF-related apoptosis-inducing ligand (TRAIL), or endoplasmic reticulum (ER) stress and mitochondrial release of cytochrome c caused by intrinsic factors such as DNA damage and OS triggers a cascade of caspase (**c**ysteine-**asp**artic **a**cid protea**se**) enzymes that initiate apoptosis or programmed cell death. Morphological features associated with this process include cell rounding, chromatin condensation, nuclear fragmentation, shrinking cell volume, cytoskeletal disassembly and blebbing of the plasma membrane prior to phagocytosis by macrophages, which have been seen in

ALS (Ghavami et al 2014).

1.2.4.9 RNA Processing

The identification of RNA binding proteins TDP-43 and FUS as constituents of NCI's in up to 90% of non-SOD1 linked FALS and SALS cases (Arai et al 2006, Neumann et al 2006) and the segregation of a number of pathological changes with the disease in these as well as other related genes (Table 1.1), including *C9ORF72* (Section 1.2.5.4) is strong evidence in support of a role of RNA toxicity in causing MN's to degenerate in ALS (Baumer et al 2010, Polymenidou et al 2012).

1.2.5 Genetic Factors

MND and its clinical variants (Sections 1.1.1) represent a genetically heterogeneous group of neurological disorders with more than twenty different chromosomal loci (Table 1.1) having been identified through linkage analysis [ALS1-8, 10, 15, 17, 19 and ALS-FTLD1-2], candidate gene association (CGA) studies [ALS9], homozygosity mapping [ALS12 and 16], targeted sequencing [ALS11], repeat association studies [ALS13] and next generation sequencing (NGS) approaches including exome/whole genome analyses [ALS14, 18 and 20-21] (Goodall et al 2012, Renton et al 2014).

Between 5 and 10% of cases are reported to have a family history in which there is at least one other first or second degree relative who is known to be affected (Byrne et al 2011). Mutations in *SOD1* (Section 1.2.5.1.1), *TARDBP* (Section 1.2.5.2.1), *FUS* (Section 1.2.5.2.2) and *C9ORF72* (Section 1.2.5.4), among others listed in Table 1.1, are now thought to explain up to two-thirds of pedigrees (Ravits 2014, Renton et al 2014). The mode of transmission follows a Mendelian pattern of inheritance that is largely autosomal dominant (AD); although autosomal recessive (AR) and X-linked forms have been described. In the majority of instances disease onset is expected to occur during mid-late adulthood, however, juvenile onset (<25yrs) and young onset ALS (<45yrs) are also known to account for ~1 or 10% of cases, respectively (Calvo et al 2014b, Leblond et al 2014, Logroscino et al 2010).

In the following sections, ALS (Section 1.2.5.1), ALS-FTLD (Section 1.2.5.2 and 1.2.5.

Locus	**Chr.**	**Gene**	**Function**	**Mode**	**Onset**	**Mutation**	**Diagnosis**	**Ref.(s)**
ALS1	21q22.11	*SOD1*	oxidative stress	AD/AR	adult	SNV	ALS, PMA	(Rosen et al 1993)
ALS2	2q33.2	*ALSIN*	guanine nucleotide exchange factor	AR	juvenile	SNV	ALS, PLS, HSP	(Hand et al 2003)
ALS3	18q21	unknown	unknown	AD	adult	unknown	ALS	(Hand et al 2002)
ALS4	9q34.13	*SETX*	DNA/RNA helicase	AD	juvenile	SNV	ALS, AOA2	(Chen et al 2004)
ALS5	15q21.1	*SPG11*	transmembrane protein	AR	juvenile	SNV	ALS, HSP	(Daoud et al 2012b)
ALS6	16p11.2	*FUS*	pre-mRNA splicing and export	AD	adult	SNV	ALS, FTLD	(Chio et al 2009a)
ALS7	20p13	unknown	unknown	AD	adult	unknown	ALS	(Sapp et al 2003)
ALS8	20q13.33	*VAPB*	vesicular trafficking	AD	adult	SNV	ALS, SMA	(Nishimura et al 2004)
ALS9	14q11.1	*ANG*	blood vessel formation	AD	adult	SNV	ALS, FTLD, PD	(Greenway et al 2006)
ALS10	1p36.22	*TARDBP*	regulator of transcription/splicing	AD	adult	SNV	ALS, FTLD, PD	(Sreedharan et al 2008)
ALS11	6q21	*FIG4*	phosphoinositide phosphatase activity	AD	adult	SNV	ALS, PLS, CMT	(Chow et al 2009)
ALS12	10p13	*OPTN*	ocular tension, vesicular trafficking	AD/AR	adult	SNV	ALS, POAG	(Maruyama et al 2010)
ALS13	12q24.12	*ATXN2*	unknown	AD	adult	CAG repeat	ALS, FTLD, SCA2	(Elden et al 2010)
ALS14	9p13.3	*VCP*	ATP-binding, vesicle transport/fusion	AD	adult	SNV	IBMPFD/ALS, FTLD, CMT, HSP	(Johnson et al 2010)
ALS15	Xp11.2.1	*UBQLN2*	ubiquitination, protein degradation	X-linked	adult, juvenile	SNV	ALS-FTLD	(Deng et al 2011)
ALS16	9p13.3	*SIGMAR1*	endoplasmic reticulum chaperone	AR	juvenile	SNV	ALS-FTLD	(Luty et al 2010)
ALS17	3p12.1	*CHMP2B*	vesicular trafficking	AD	adult	SNV	ALS, PMA, FTLD	(Parkinson et al 2006)
ALS18	17p13.3	*PFN1*	cytoskeletal dynamics	AD	adult	SNV	ALS, FTLD	(Wu et al 2012a)
ALS19	2q33-q34	*ERBB4*	epidermal growth factor receptor	AD	adult	SNV	ALS	(Takahashi et al 2013)
ALS20	12q13.1	*HNRNPA1*	RNA metabolism	AD	adult	SNV	IBMPFD/ALS	(Kim et al 2013)
ALS21	5q31.2	*MATR3*	RNA metabolism	AD	adult	SNV	ALS, VCPDM	(Johnson et al 2014)
ALS-FTLD1	9q21-q22	unknown	unknown	AD	adult	SNV	ALS-FTLD	(Hosler et al 2000)
ALS-FTLD2	9p21.2	*C9ORF72*	unknown	AD	adult	G_4C_2 repeat	ALS-FTLD	(DeJesus-Hernandez et al 2011, Renton et al 2011)

Table 1.1 Summary of Genetic Loci and ALS Causative Genes in ALSoD (alsod.iop.kcl.ac.uk) [Adapted from Leblond et al (2014)].

.4) and FTLD (Section 1.2.5.3) loci are discussed with a focus on those genes which have been designated an ALS number according to information attained from ALSoD, the Amyotrophic Lateral Sclerosis Online Genetics Database that is freely available at alsod.iop.kcl.ac.uk (Abel et al 2013).

1.2.5.1 ALS Loci

1.2.5.1.1 SOD1

The free radical scavenging enzyme copper/zinc superoxide dismutase 1 (*SOD1*), situated at the chromosome 21q22.11 locus (Table 1.1), was discovered by Rosen et al (1993) more than twenty years ago as the first causative gene linked to the pathogenesis of AD and, across parts of Scandinavia, AR inherited forms of adult-onset ALS (ALS1). Since then >170 missense mutations of variable penetrance have been identified, spanning the gene's five coding exons (Al-Chalabi et al 2012, Su et al 2014). These account for between 12 and 23% of FALS cases and a further 2 to 7% of SALS cases (Ajroud-Driss & Siddique 2014, Battistini et al 2005, Chio et al 2008, Gros-Louis et al 2006, Ling et al 2013, Shaw et al 1998). Almost half of all carriers will become symptomatic by the time they have reached their fifth decade with around 90% becoming symptomatic before the age of 70 (Siddique et al 1991). Patients present with predominantly lower limb weakness and in the absence of impaired executive functioning (Millecamps et al 2010, Turner et al 2005). Median survival mirrors that of "classical ALS" (Section 1.2.1) which ranges between 2 and 4 years from the initial manifestation of disease symptoms until the onset of respiratory failure; although considerable phenotypic variability has been observed with respect to SOD1-linked ALS (Renton et al 2014, Su et al 2014). For example a dominant p.A4V substitution that arose twice from a single common ancestor in Europe and North America, where it accounts for 50% of FALS cases, is associated with a particularly aggressive disease course of ~12 months (Cudkowicz et al 1997, Saeed et al 2009). Homozygous carriers of the p.D90A mutation, on the other hand, develop a much milder phenotype that is characterised by a long disease duration extending beyond 10 years (Al-Chalabi et al 1998, Andersen et al 1996). A distinct neuropathological profile apparent in FALS patients with a SOD1 mutation or the transgenic SOD1^{G93A} mouse model has been described (Bruijn et al 2004, Mackenzie et al 2007, Pickles & Vande Velde 2012) which is found to be absent in the majority of SALS cases (Brotherton et al 2012, Kerman et al 2010, Liu et al 2009). Aggregates of mutant or misfolded WT protein are observed in the cytoplasm of residual MN's and glia of the brain and CNS (Banci et al 2008). These inclusions are found to be immunoreactive against antibodies for ubiquitin but stain negative for TDP-43 (Section 1.2.5.3.1) and FUS (Section 1.2.5.3.2) (Ling et al 2013).

SOD1 is a ubiquitously expressed metalloenzyme with antioxidant properties that normally functions to protect cells against elevated levels of ROS (Section 1.2.4.1). Specifically, it has been shown to act as a catalyst for the conversion of superoxide anions (O_2^-) into molecular oxygen (O_2) and hydrogen peroxide (H_2O_2) (Therrien & Parker 2014). A correlation between reduced enzyme activity and disease severity is not evident (Borchelt et al 1994, Saccon et al 2013) pointing towards a toxic gain of function mechanism in which pathogenicity arises from both cell autonomous as well as non-cell autonomous processes (Ajroud-Driss & Siddique 2014, Ling et al 2013).

1.2.5.1.2 ALSIN

Mutations (n=23) in the gene encoding alsin (*ALSIN*), situated at the chromosome 2q33.2 locus (Table 1.1), are the cause of a rare spectrum of AR inherited disorders including a juvenile onset form of ALS (ALS2) (Hadano et al 2001, Yang et al 2001), PLS with oculomotor signs (Section 1.2.2.2) (Pringle et al 1992) and infantile-onset ascending spastic paraplegia (IAHSP) (Eymard-Pierre et al 2002, Eymard-Pierre et al 2006, Gros-Louis et al 2003, Wakil et al 2014). The latter are both conditions of primary UMN involvement with IAHSP characterised by progressive degeneration of the corticospinal and corticobulbar (CBT) tracts that usually begins in the distal extremities of the lower limbs and slowly advances to affect the upper limbs and bulbar muscles (Devon et al 2003, Herzfeld et al 2009, Racis et al 2014, Sztriha et al 2008, Verschuuren-Bemelmans et al 2008). Alsin is a ubiquitously expressed protein of undetermined function. Its structure contains three putative guanosine exchange factor (GEF) motifs including: a) the N-terminal Ran GTPase (guanosine triphosphatase) regulator of chromatin condensation 1 (RCC1) domain; b) the Rho GTPase diffuse B cell lymphoma/Pleckstrin homology (Db1/PH) domain and c) the

C-terminal Rab5-GTPase vacuolar protein sorting 9 (VPS9) domain. There are also seven membrane occupation and recognition nexus (MORN) repeats which span a region between the Db1/PH and VPS9 domains that have since been recognised as key modulators of Rab5-GTPase activity (Chandran et al 2007, Hadano et al 2007, Wakil et al 2014). So far most of the pathological changes that have been identified to date result in a frameshift/nonsense mutation. The introduction of a premature stop codon promoting early termination of translation leads to the production of a truncated protein that is inherently unstable (Yamanaka et al 2003). Of interest is the observation that genetic abnormalities of both long (6.5kb) and short (2.6kb) form *ALSIN* mRNA transcripts are apparent in cases of ALS2 whereas those which only affect the long form tend to be associated with UMN variants PLS and ISHAP (Panzeri et al 2006, Yang et al 2001). Chandran et al (2007) have since proposed a neuroprotective role for the short form product in LMNs as a possible explanation for the clinical diversity observed in the presence of these mutations. Furthermore, Alsin deficient MN's are shown to have impaired AMPA receptor mediated trafficking which increases their susceptibility to glutamate excitotoxicity (Section 1.2.4.2) (Lai et al 2006). In addition, the WT protein has been found to interact with mtSOD1 to attenuate Nox2-dependent endosomal ROS damage (Section 1.2.5.1.1) (Kanekura et al 2004, Li et al 2011).

1.2.5.1.3 SETX

Senataxin (*SETX*), a DNA/RNA helicase situated at the chromosome 9q34.13 locus, (Table 1.1) is a rare cause of ataxia oculomotor apraxia type 2 (AOA2) (Asaka et al 2006, Duquette et al 2005, Moreira et al 2004) and an AD inherited juvenile onset form of ALS (ALS4) (Avemaria et al 2011, Chance et al 1998, Chen et al 2004, Zhao et al 2009). The latter is a condition which is characterised by a distal hereditary motor neuropathy (dHMN) with progressive weakness and severe muscle wasting of all four limbs, a prolonged survival and extensive pyramidal features (Rabin et al 1999). The precise function of senataxin is not known. However, its structure is predicted to contain a P-loop adenosine triphosphate and guanosine triphosphate (ATP-GTP) binding site which is highly conserved across yeast and mammalian systems and has been shown to play a critical role in nucleotide unwinding (Chen et al 2004, Molnar et al 1997); a process that is required for gene transcription in addition to mechanisms of DNA replication, recombination & repair (Su et al 2014, Tanner & Linder 2001).

1.2.5.1.4 SPG11

Spatacsin (*SPG11*) which is situated at the chromosome 15q21.1 locus (Table 1.1) is the most common cause of hereditary spastic paraplegia (HSP) with occasional Parkinsonian features and pronounced thinning of the corpus callosum (Anheim et al 2009, Guidubaldi et al 2011, Liao et al 2008, Rajakulendran et al 2011, Stevanin et al 2008, Winner et al 2004, Zhao et al 2013). In recent years it has also been associated with a rare AR inherited juvenile onset form of ALS (ALS5) (Orlacchio et al 2010) characterised by a disease onset of less than 25yrs and a median survival spanning three and a half decades (Daoud et al 2012b). Clinical manifestations vary with the majority of patients experiencing distal muscle weakness, spasticity and atrophy accompanied by a bulbar phenotype, abnormal gait and signs of pyramidal involvement which occur in the absence of overt cognitive or sensory impairment (Su et al 2014). Truncating loss of function, nonsense or frameshift mutations have been identified as well as a small number of splice site alterations and insertions or deletions which promote early termination of translation through the introduction of a premature UAG/UAA/UGA stop codon (Iguchi et al 2013, Orlacchio et al 2010). Although spatacsin has not yet been fully characterised in the mammalian system, it is shown to be an essential requirement for neuromuscular junction connectivity and axonal outgrowth in the developing zebrafish (Martin et al 2012, Southgate et al 2010).

1.2.5.1.5 VAPB

Two single base substitutions in the VAMP (vesicle-associated membrane protein) associated protein B (*VAPB*) gene, situated at the chromosome 20q13.33 locus, have been associated with <1% of familial cases of AD inherited adult-onset ALS (ALS8) (Table 1.1) (Chen et al 2010, Millecamps et al 2010). Phenotypic heterogeneity has been observed, with a wide variety of clinical presentations ranging from cases with "classical ALS" and a faster than anticipated disease course to delayed onset forms of PMA (Section 1.2.2.3) or ALS with essential tremor (Nishimura et al 2004). The mtVAPB protein sequesters its WT counterpart into ubiquitin, p62 and TDP-43 positive inclusion bodies within the cytoplasm of residual MNs and glia of the CNS (Teuling et al 2007). Aggregation in this manner has been shown to elicit the UPR which is expected to lead to an increase in vulnerability to ER stress (Gkogkas et al 2008, Ling et al 2013, Su et al 2014, Suzuki et al 2009). Another implication of a loss of function of WT VAPB is the disruption of ephrin (Eph) receptor mediated signalling via a reduction in ligand availability from the cleavage and secretion of VAPB amino-terminal domains that would ordinarily serve to protect the cells against glutamate excitotoxicity (Section 1.2.4.2) (Tsuda et al 2008).

1.2.5.1.6 FIG4

The *FIG4* gene encoding the phosphoinositide 5-phosphatase enzyme, situated at the chromosome 6q21 locus (Table 1.1), is reported to account for around 2% of AD inherited adult onset ALS (ALS11) and PLS (Section 1.2.2.2) cases in addition to having been identified as a cause of the AR inherited juvenile onset CMT4J (Charcot Marie Tooth type 4J); a severe and rapidly progressive sensory & motor peripheral neuropathy (Chow et al 2009, Chow et al 2007, Verdiani et al 2013). Its function is to regulate the cellular abundance of the signalling lipid phosphatidylinositol 3, 5-bisphosphate [PI(3,5)2] which has been implicated in aspects of autophagy as well as retrograde membrane transport through the *trans*-Golgi network (Ferguson et al 2010, Iguchi et al 2013, Rutherford et al 2006, Zhang et al 2007).

1.2.5.1.7 OPTN

The optineurin (*OPTN*) gene, situated at the chromosome 10p13 locus (Table 1.1), was originally identified as a major cause of primary open angle glaucoma (POAG) (Fuse et al 2004, Huang et al 2014, Rezaie et al 2002, Xiao et al 2009) and more recently Paget's disease of bone (PDB) (Albagha et al 2010, Chung et al 2010). In 2010, Maruyama and colleagues described a deleterious heterozygous c.1743A>G (p.E478G) missense substitution, c.1502C>T (p.Q398X) truncation and an exon five deletion in three Japanese consanguineous families which co-segregated with an AD/AR inherited form of adult-onset ALS (ALS12). Subsequent studies reported mutations in *OPTN* to be a relatively rare occurrence in Caucasian populations of North European or Scandinavian descent (~0.2%) (Chio et al 2012b, Kenna et al 2013, Tumer et al 2012, van Blitterswijk et al 2012c, Weishaupt et al 2013). The gene itself encodes the ubiquitously expressed 67kDa cytosolic **opt**ic **neur**opathy **in**ducing protein that has been shown to play a key role in cellular morphogenesis, membrane trafficking and transcriptional activation in addition to vasoconstriction and host defence against viral pathogens (Kachaner et al 2012, Renton et al 2014). So far, two plausible mechanisms of action have been proposed in order to explain the neurotoxicity of mutant optineurin towards MN's in ALS: 1) Loss of function of the WT protein lifts inhibition of activation of the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) transcriptional regulator complex to induce mitochondrial apoptotic signalling cascades and programmed cell death or 2) Gain of function mediated by an impaired autophagosome system and the subsequent accumulation of toxic intracellular protein aggregates (Akizuki et al 2013, Korac et al 2013).

1.2.5.1.8 ERBB4

Recently, two single nucleotide variants (SNV's) of reduced penetrance in the v-erb -b2 avian erythroblastic leukemia viral oncogene homolog 4 (*ERBB4*) gene, situated at the chromosome 2q33-q34 locus (Table 1.1), have been identified through whole genome sequencing (WGS) and linkage analysis as a rare cause of AD inherited adult onset ALS (ALS19) in three pedigrees of Japanese or Canadian descent. Signs of UMN and LMN involvement (Section 1.1.3) were prominent in all affected family members with a distinct lack of overt cognitive dysfunction (Takahashi et al 2013). The disease course was relatively slow, with a median survival of greater than five years. The c.2780G>A (p.R927Q) alteration occurring within the protein's tyrosine kinase domain is associated with an older than anticipated age of symptom onset peaking in the mid-sixties or early seventies, whereas the less common c.3823C>T (p.R1275W) substitution at the highly conserved C-terminal region is associated with a younger onset ALS of around 45 years. ERBB4 is a member of the epidermal growth factor (EGF) receptor family and is one of four structurally related proteins which are modulated through autophosphorylation upon neuregulin-1 (NRG1) binding (Takahashi et al 2013). *ERBB4* knock-down in mice is demonstrated to be embryonically lethal (Gassmann et al 1995) and in the residual MN's of autopsy derived human post-mortem SC tissue depleted levels of the cysteine-rich domain (CRD) containing isoforms of NRG1 have been detected (Song et al 2012), further implicating the NRG1-ERBB signalling pathway as another plausible mechanism of pathogenicity in ALS (Takahashi et al 2013).

1.2.5.1.9 MATR3

NGS approaches have identified several missense substitutions (n=4) in the matrin 3 (*MATR3*) gene, situated at the chromosome 5q32.2 locus (Table 1.1), as a cause of AD inherited adult onset ALS (ALS21) (Johnson et al 2014, Millecamps et al 2014) or vocal cord and pharyngeal weakness with distal myopathy (VCPDM) (Muller et al 2014, Senderek et al 2009, Yamashita et al 2014) in four large, multigenerational pedigrees of North European descent. Sequencing data obtained from an additional 204 UK patients suggest that mutations occur at a frequency of 2.75% for FALS and <1% of SALS cases. Clinical manifestations include widespread UMN and LMN signs with evidence of a 'split-hand' pattern of weakness, brisk tendon reflexes, extensor plantar responses, increased jaw jerk with clonus, fasciculations, severe wasting of the tongue and respiratory dysfunction with normal cognition and a relatively slow disease course of up to 15 years. Neuropathological evaluations of human derived post-mortem SC tissue from patient carriers and non-carriers of a *MATR3* mutation revealed universal matrin-3 proteinopathy in residual MN's with intense nuclear staining and occasional, more diffuse cytoplasmic staining (Johnson et al 2014). The gene encodes an RNA and DNA binding domain containing nuclear matrix protein of 125kDa that has been shown to interact with TDP-43 (Section 1.2.5.2.1) (Salton et al 2011). Its importance in the neurodegenerative disease process is not yet well understood, although it is known to function in aspects of RNA processing including the nuclear retention of hyper-edited RNA's and mRNA transport, DNA repair and gene silencing/chromatin remodelling (Hock et al 2007, Zhang & Carmichael 2001).

1.2.5.1.10 Other Rare Genetic Causes of FALS

Additional loci that have been implicated in the pathogenesis of AD inherited forms of the disease, for which a designated ALS number has not yet been assigned in the ALSoD (alsod.iop.kcl.ac.uk) (Abel et al 2013) either due to lack of evidence regarding transmission (i.e. low penetrance) or its rarity, are summarised in Table 1.2.

Gene	Name	Locus	Reference
ARHGEF28	Rho guanine nucleotide exchange factor (GEF) 28	5q13	(Droppelmann et al 2013)
CHCHD10	coiled-coil-helix-coiled-coil-helix domain containing 10	22q11	(Bannwarth et al 2014)
DAO	D-amino-acid oxidase	12q24	(Mitchell et al 2010)
DCTN1	dynactin 1	2p13	(Puls et al 2003)
EWSR1	Ewing's sarcoma breakpoint region 1	22q12.2	(Couthouis et al 2012)
HNRNPA2B1	heterogeneous nuclear ribonucleoprotein A2/B1	7p15	(Kim et al 2013)
LMNB1	lamin B1	5q23	(Johnson et al 2014)
NEFH	neurofilament, heavy polypeptide	22q12-q13	(Figlewicz et al 1994)
PRPH	peripherin	12q12	(Gros-Louis et al 2004)
SPAST	spastin	2p24-p21	(Meyer et al 2005)
SQSTM1	sequestosome 1	5q35	(Rubino et al 2012)
TAF15	TAF15 RNA polymerase II, TATA box binding protein	17q11.1-q11.2	(Couthouis et al 2011)

Table 1.2 Additional Genetic Loci Implicated in the Pathogenesis of FALS

1.2.5.1.11 Genetic Susceptibility Factors and Other Rare Causes of SALS

It has been documented that the majority of patients diagnosed with ALS, between 90 and 95%, will have developed an idiopathic form of the condition for which the cause(s) are still largely unknown (Byrne et al 2011). Estimates of heritability from studies conducted using twin data are predicted to lie between 0.38 and 0.78 (Al-Chalabi et al 2010). A 17 and 9-fold increase, respectively in the relative lifetime risk of the siblings and progeny of sporadic index cases in a large Swedish population based study has also been reported (Fang et al 2009, Hanby et al 2011). This is indicative of SALS being multifactorial in origin with a combination of complex genetic effects and environmental risk factors such as heavy metal exposure (e.g. lead, manganese and mercury) (Wang et al 2014), cigarette smoking (Armon 2009), de Jong et al 2012, Gallo et al 2009), lifetime physical activity (Huisman et al 2013) and traumatic head injury (Pupillo et al 2012, Schmidt et al 2010) contributing to its aetiology (Wingo et al 2011).

Both clinically and pathologically, SALS patients are virtually indistinguishable from their FALS counterparts suggesting that they share common mechanisms which underlie MN degeneration (Section 1.2.4) (Wijesekera & Leigh 2009). Indeed in a small proportion of cases, fewer than 10%, mutations have been identified within the coding regions of causal candidate genes of FALS including *C9ORF72* (Section 1.2.5.4), *SOD1* (Section 1.2.5.1.1), *TARDBP* (Section 1.2.5.2.1) and *FUS* (Section 1.2.5.2.2) (Andersen & Al-Chalabi 2011, Rademakers & van Blitterswijk 2013, van Blitterswijk et al 2012a). In most instances, however, the genetic component has yet to be determined. Genome-wide association studies (GWAS) appeared, at least initially, to have highlighted a number of promising susceptibility loci, including 9p21 (Section 1.2.5.4) which led to the discovery of a large, intronic hexanucleotide repeat expansion in *C9ORF72* (Renton et al 2011, DeJesus-Hernandez et al 2011) that is now thought to account for up to 43% of FALS and ~7% of apparently SALS cases (Cooper-Knock et al 2012b). Disappointingly, however, many GWAS findings are associated with risk alleles that have small odds ratios (OR's) and have yet to be convincingly replicated (Chio et al 2009b, Cronin et al 2009, Daoud et al 2010, Fernandez-Santiago et al 2011, Fogh et al 2011, Iida et al 2011, Kwee et al 2012, Nicholl et al 1999, Schymick et al 2007, van Es et al 2009b). In a recent report, published by Koppers et al (2013), sequencing of exons of potential candidate genes from several of these studies, including *UNC13A* and *C9ORF72* (Table 1.3), failed to establish a significant enrichment of coding variants in a large (n=2,122) SALS case-control population (Leblond et al 2014, Renton et al 2014) of Dutch descent. This provides evidence in support of the proposition of a rare variant hypothesis: Rather than the associated SNP or microsatellite marker representing a signpost that reflects the effects of a common proximal causal site it is now anticipated that there are multiple, rare and distant variants of substantially higher impact which are responsible for producing so called synthetic associations. In this scenario, a significant number of potential hits are expected to go undetected, not as a consequence of many individuals sharing identical weak effect variants, but because minority groups of SALS patients are likely to each harbour a different high impact variant (Dickson et al 2010, Robinson 2010).

The spontaneous occurrence of *de novo* mutations are also a possibility (Alexander et al 2002, Calvo et al 2014a, Chio et al 2011b, DeJesus-Hernandez et al 2010, Laffita-

Gene	Name	Locus	Reference
ALAD	aminolevulinate dehydratase	9q33.1	(Kamel et al 2003)
C9ORF72	chromosome 9 open reading frame 72	9p21.2	(Ahmeti et al 2013; Laaksovirta et al 2010; Le Ber et al 2009; Morita et al 2006; Shatunov et al 2010)
CABIN1	calcineurin binding protein 1	22p11	(Deng et al 2013b)
CAMK1G	calcium/calmodulin-dependent protein kinase IG	1q32	(Deng et al 2013b)
CENPV	centromere protein V	17p11.2	(Ahmeti et al 2013)
CRYM	crystallin, mu	16p12	(Daoud et al 2011)
CYP2D6	cytochrome P450, family 2, subfamily D, polypeptide 6	22q13.1	(Siddons et al 1996)
DPP6	dipeptidyl-peptidase 6	7q36.2	(Cronin et al 2008; van Es et al 2008)
ELP3	elongator acetyltransferase complex subunit 3	8p21.1	(Simpson et al 2009)
FGGY	FGGY carbohydrate kinase domain containing	1p32	(Chio et al 2009b; van Es et al 2009b)
ITPR2	inositol 1,4,5-triphosphate receptor type 2	12p12.1-p11.23	(van Es et al 2007)
KIFAP3	kinesin-associated protein 3	1q24.2	(Landers et al 2009)
LIF	leukemia inhibitory factor	22q12.2	(Giess et al 2000; Meyer & Potter 1995)
LUM	lumican	12q21.3	(Daoud et al 2011)
OGG1	8-oxoguanine DNA glycosylase 1	3p26	(Coppede et al 2007)
PLCD1	phospholipase C, delta 1	3p22.2	(Staats et al 2013)
SUSD2	sushi domain containing 2	22p11	(Deng et al 2013b)
UNC13A	unc-13 homolog A (*C. elegans*)	19p13.12	(Ahmeti et al 2013; van Es et al 2009c)

Table 1.3 Genetic Susceptibility Loci Implicated in the Pathogenesis of SALS

Mesa et al 2013, Zou et al 2013a). Whole exome sequencing of 47 SALS trio pedigrees [i.e. the proband and both unaffected parents] led to the identification of novel changes in *SS18L1* (alternatively named calcium-responsive transactivator (*CREST*)) (Chesi et al 2013); a subunit of the neuronal chromatin remodelling (nBAF) complex that has since been independently verified in a French cohort comprising a further 87 FALS patients (Teyssou et al 2014).

1.2.5.2 ALS-FTLD Loci

1.2.5.2.1 TARDBP

Transactive response (TAR) DNA binding protein 43kDa (*TARDBP*), situated at the chromosome 1p36.23 locus (Table 1.1), is a cause of AD inherited adult onset ALS (ALS10), bvFTLD and the combined ALS-FTLD syndrome (Borroni et al 2009, Chio et al 2010, Kabashi et al 2008, Kovacs et al 2009, Sreedharan et al 2008, Yokoseki et al 2008). More than 40 mutations primarily occurring in the C-terminus of the gene (Abel et al 2013, Renton et al 2014), a region considered important for normal protein-protein interactions and ribonucleoprotein (RNP) binding, are now thought to account for 4-5% of FALS cases with fewer than 2% of SALS and bvFTLD patients affected (Al-Chalabi et al 2012, Gitcho et al 2008, Lattante et al 2013, Van Deerlin et al 2008). A trend towards a “classical ALS” phenotype is observed with a slightly earlier than anticipated age of symptom onset, moderately prolonged survival and predominant upper limb involvement (Corcia et al 2012). Originally identified as a protein that bound the TAR element of human immunodeficiency virus (HIV), TDP-43 comprises nuclear export and import signals in addition to two RNA recognition motifs (RRMs) and a glycine rich, low sequence complexity PrLD (King et al 2012). Under normal physiological conditions it is ubiquitously expressed and is regarded to be essential for the regulation of gene transcription as well as multiple aspects of RNA metabolism including but not limited to microRNA (miRNA) biogenesis, stress granule (SG) formation, precursor messenger RNA (pre-mRNA) splicing, transport & stability, long non-coding RNA (lncRNA) processing and chromatin remodelling (Buratti & Baralle 2012, Lagier-Tourenne et al 2010, Polymenidou et al 2012). It is also known to bind a UG-rich sequence in intron 8 of the *CFTR* gene (cystic fibrosis transmembrane conductance regulator) in order to promote pathological skipping of exon 9 in patients with cystic fibrosis (CF) (Buratti et al 2004, Buratti et al 2001, Lukavsky et al 2013). Moreover, it has also been demonstrated to act as a scaffold for nuclear bodies (NB's) through its interaction with the SMN protein (Wang et al 2002).

The pathogenicity of mtTDP-43 towards MN's in ALS is not fully understood and it remains uncertain as to whether toxicity arises from a loss of function mechanism, gain of function mechanism or indeed a combination of the two (Iguchi et al 2013, Ling et al 2013, Su et al 2014, Vanden Broeck et al 2014). At steady state, TDP-43 is concentrated in the nucleus where it carries out the majority of its activities (Ayala et al 2008, Winton et al 2008). Aberrant shuttling of TDP-43, however, results in its depletion from the nucleus and redistribution into the cytoplasm (Che et al 2011, Highley et al 2014, Polymenidou et al 2011, Tollervey et al 2011, Van Deerlin et al 2008). Within the cytoplasm, the mislocalised protein forms aggregates which are a major constituent of neuronal and glial inclusion bodies which are immunoreactive for ubiquitin and p62 but negative for α-synuclein and the microtubule associated protein, tau (Arai et al 2006, Neumann et al 2006). These are present in more than ninety percent of non-SOD1 linked FALS and SALS cases as well as a subset of FTLD patients (~50%) who may or may not carry a mutation in the *TARDBP* gene (Ling et al 2013, Mackenzie et al 2007, Renton et al 2014, Tan et al 2007).

1.2.5.2.2 FUS

Missense mutations (n=78) in the fused in sarcoma or translocated in liposarcoma (*FUS*/*TLS*) gene, situated at the chromosome 16p11.2 locus (Table 1.1), account for a further 4-5% of AD inherited adult onset ALS (ALS6) as well as rarer instances of the combined ALS-FTLD syndrome (<1%) (Abel et al 2013, Kwiatkowski et al 2009, Van Langenhove et al 2010, Vance et al 2009). Approximately equal proportions of male and female patients are affected (Kinsley & Siddique 2001). Penetrance of the disease varies widely between pedigrees with 50 to 70% of individuals developing symptoms by the time they have reached their fifth decade and more than ninety percent becoming symptomatic before the age of 71 (Blair et al 2010). Phenotypes associated with some of the most common pathological changes resemble those of "classical ALS" (Section 1.2.1) that are characterised by predominant lower limb involvement, median onset of 45 years and an average disease duration of between 30 and 48 months (Groen et al 2010, Iguchi et al 2013, Millecamps et al 2010, Yan et al 2010). The gene encodes a ubiquitously expressed DNA/RNA binding protein that shares considerable structural and functional homology with TDP-43 (Renton et al 2014, Su et al 2014). It contains a nuclear export and import signal, RRMs, two arginine rich regions and a glycine rich, low complexity PrLD (King et al 2012) and is involved in many of the same activities which relate to genomic maintenance, SG formation and RNA metabolism/processing (Lagier-Tourenne et al 2010, Ling et al 2013). Both TDP-43 and FUS are found to associate with the survival motor neuron (SMN) complex that is important for the regulation of the spliceosome (Tsuiji et al 2013, Yamazaki et al 2012). Additionally, FUS has also been implicated in the DNA damage response & repair pathways (Wang et al 2013). The precise mechanism by which mutant forms of the protein exert their neurotoxicity towards MNs in ALS is not known. However, in a similar manner as was described previously for TDP-43 (Section 1.2.5.2.1), aberrant shuttling of mtFUS is expected to result in its depletion from the nucleus and the subsequent accumulation of misfolded aggregates within the cytoplasm which has led to both a loss of as well as gain of function mechanism having been proposed (Su et al 2014, Therrien & Parker 2014). It is of interest to note that mutation specific patterns of FUS pathology have been recorded which are found to correlate with disease severity. Round basophilic NCI's, for example, are associated with a rapidly progressive, young onset variant of ALS which begins in the late teens or early twenties (Baumer et al 2010) whereas tangle-like inclusions in residual MN's and glia of the CNS are a pathological feature of the more typical late onset ALS (Ling et al 2013, Mackenzie et al 2011).

1.2.5.2.3 ANG

Mutations of low penetrance in the gene encoding angiogenin (*ANG*), situated at the chromosome 14q11.2 locus, have been identified in rare instances of AD inherited adult onset ALS (ALS9) (Table 1.1), ALS-FTLD or PD of predominantly Scottish or Irish ancestry (Greenway et al 2006, Kirby et al 2013, Rayaprolu et al 2012, van Es et al 2009a, van Es et al 2011, Zou et al 2012). Patient carriers are characterised in approximately two-thirds of cases by a predominantly bulbar phenotype with a rapid decline in respiratory function that requires mechanical ventilation support, usually within the first 12 months of the initial manifestation of disease (Section 1. 1.4) (Greenway et al 2006, Seilhean et al 2004). ANG is a secreted protein found in serum. It is a member of the pancreatic ribonuclease (RNase) A superfamily and is a potent inducer of neovascularisation which shares functional homology with the vascular endothelial growth factor (VEGF); a potential modifier of ALS progression (Lambrechts et al 2003, Seilhean et al 2009) . Under hypoxic conditions, angiogenin binds actin at the outer surface of the endothelial cells where it is internalised and transported into the nucleus. Here it is responsible for stimulating stress induced ribosomal RNA (rRNA) transcription, a rate limiting step which has implications for ribosome biogenesis, protein maturation and ultimately cellular growth & survival (Greenway et al 2006, Yamasaki et al 2009). Treatment with exogenous ANG even after the initial onset of symptoms improved motor function in SOD1^{G93A} mice and increased life expectancy which has led to the postulation that the WT protein may play an important neuroprotective role within the mammalian system (Kieran et al 2008, Sebastia et al 2009).

1.2.5.2.4 ATXN2

Intermediate length polyglutamine (polyQ) tracts of 27 to 33 CAG repeats in exon 1 of Ataxin 2 (*ATXN2*), situated at the chromosome 12q24.12 locus (Table 1.1), have recently been confirmed in a minority of cases with a rare AD inherited adult onset form of ALS (ALS13) (~1%) and bvFTLD with non-fluent aphasia (<5%) (Elden et al 2010, Lee et al 2011, Ross et al 2011). Expansions of more than 34 CAG repeats have also been associated with PD (Section 1.2.1) and spinocerebellar ataxia type 2 (SCA2) (Gwinn-Hardy et al 2000, Imbert et al 1996, Nanetti et al 2009). Typically, patient carriers have a M:F ratio of 1.5:1 with signs of UMN and LMN dysfunction becoming apparent in the sixth or seventh decade and an average disease duration of approximately two to five years. Clinical manifestations include brisk deep tendon reflexes, pronounced fasciculations and weakness & spasticity of all four limbs (Van Langenhove et al 2012). Neuronal intranuclear inclusion bodies (NII's) positive for polyQ and p62 (sequestosome) are primarily concentrated within the pontine nuclei with more widespread TDP-43 proteinopathy apparent in the neocortex and SC. It has been shown to act *in vitro* and *in vivo* in an RNA dependent manner in order to influence TDP-43 toxicity, although the exact mechanism by which *ATXN2* mutations cause MN degeneration in ALS is not fully understood (Baumer et al 2014, Elden et al 2010).

1.2.5.2.5 VCP

Valosin-containing protein (*VCP*), situated at the chromosome 9p13.3 locus (Table 1.1), is a rare genetic cause of AD inherited adult onset forms of HSP (de Bot et al 2012), CMT (Gonzalez et al 2014), ALS (ALS14) (~1-2%) (Abramzon et al 2012), ALS-FTLD and IBMPFD/ALS (Bersano et al 2009, Gidaro et al 2008, Haubenberger et al 2005, Watts et al 2004, Weihl et al 2009); a multisystem disorder of variable penetrance which is characterised by FTLD with inclusion body myopathy (IBM) and PDB. Clinical manifestations of IBM and PDB which include atrophic, angulated muscle fibres and rimmed vacuoles with unremarked inflammation and an elevated rate of osteoclastic bone resorption may be apparent at the age of 40 (Daroszewska & Ralston 2006, Spina et al 2013) with evidence of impaired executive functioning and behavioural abnormalities or UMN and LMN signs not normally evident until the fifth or sixth decade (Gonzalez-Perez et al 2012, Jacquin et al 2013). Ubiquitin immunoreactive, TDP-43 positive NII's and dystrophic neurites (DN's) with some VCP staining and occasional NCI's are a prominent feature upon neurohistochemical evaluation (Forman et al 2006, Guyant-Marechal et al 2006). The VCP protein is a molecular chaperone of the AAA superfamily [**a**denosine triphosphatase (ATPase) **a**ssociated with diverse cellular **a**ctivities] that has been implicated in a diverse array of cellular processes from transcriptional activation of the NF-κB signalling cascade to mechanisms of double-stranded DNA break (DSB) repair, membrane fusion and protein degradation (Ju et al 2009, Vandermoere et al 2006, Vij 2008, Wolf & Stolz 2012, Zhang et al 2000). An *in vitro* loss of function mutation affecting the cell division control (CDC48) domain of exon 5 in neuroblastoma SH-SY5Y cell lines resulted in mislocalization of TDP-43 to the cytosol, ER stress and impaired proteasome activity with a concomitant increase in the extent of caspase mediated apoptosis (Gitcho et al 2009).

1.2.5.2.6 UBQLN2

Mutations of the ubiquilin 2 (*UBQLN2*) gene, situated at the chromosome Xp11.2.1 locus (Table 1.1), are responsible for 2% of FALS and FTLD cases (Deng et al 2011, Gellera et al 2013, Synofzik et al 2012, Williams et al 2012) and a further 0.4% of SALS cases (Daoud et al 2012a). Originally found to co-segregate with the disease in a five generation kindred of 19 ALS (ALS15)/ALS-FTLD affected family members both adult and juvenile onset forms have now been reported. The genetic trait has a dominant mode of transmission that exhibits incomplete penetrance (Deng et al 2011). Clinical manifestations include symptoms of dysarthria and dysphagia with spastic paralysis of the limbs and diminished fine motor dexterity which may occur in the presence or absence of behavioural and executive function deficits that are associated with FTLD (Fahed et al 2014). Age at diagnosis ranges between 16 and 71 years with a mean of 33.9±14 or 47.3±11 years for male and female patients, respectively and average survival of approximately 3 to 4 years. At autopsy, brain atrophy, AHC loss, CST degeneration and astrogliosis of the SC are apparent (Deng et al 2011, Gellera et al 2013). Ubiquitinated, p62 positive skein-like or compact ubiquilin 2 immunoreactive inclusion bodies that co-localise with TDP-43 (Section 1.2.5.3.1), FUS (Section 1.2.5.3.2) or OPTN (Section 1.2.5.1.7) but not SOD1 (Section 1.2.5.1.1) or tau protein (Section 1.2.5.2.1) have been described (Fahed et al 2014, Nolle et al 2013, Williams et al 2012). Single base substitutions in the N-terminal proteasome binding domain (PBD) (Daoud et al 2012a) or the PXX tandem repeat of the collagen-like region that is important for protein-protein interactions (Deng et al 2011, Fahed et al 2014) impair the normal function of ubiquilin 2 which leads to disturbances in autophagy, the UPS (Zhang et al 2014) and ER-associated protein degradation (ERAD) pathway (Xia et al 2014).

1.2.5.2.7 SIGMAR1

The ER chaperone *SIGMAR1* (**sigma** non-opioid intracellular **r**eceptor **1**), situated at the chromosome 9p13.3 locus (Table 1.1), has been identified as a genetic cause of AD inherited ALS-FTLD and pure FTLD in three Caucasian pedigrees of Australian or Polish ancestry (Luty et al 2010). A nonpolymorphic c.672*51G>T substitution which affects the three prime (3') untranslated region (UTR) was shown to disrupt mRNA splicing and transcript stability. This led to an increase in expression and a higher abundance of the SIGMAR1 protein in human post-mortem brain tissue and patient derived lymphocytes. *In vitro* experimentation also found overexpression of *SIGMAR1* to result in an aberrant 2.30 or 5.20-fold induction, respectively, in the nuclear-cytoplasmic shuttling of TDP-43 (Section 1.2.5.3.1) and FUS (Section 1.2.5. 3.2) (Luty et al 2010). Soon thereafter, a deleterious c.304G>C (p.E102Q) missense mutation in an evolutionary conserved residue of the transmembrane domain that is important for ligand binding was also identified as a cause of a rare AR inherited form of juvenile onset ALS (ALS16) (Table 1.1). Symptoms of lower limb weakness and spasticity in the absence of bulbar or respiratory signs were accompanied by exaggerated tendon reflexes and a typically slower than anticipated disease course (Al-Saif et al 2011). TDP-43 and FUS immunoreactive inclusions were prominent in the pyramidal cells of the cerebral cortex and hippocampal neurones of the dentate gyrus (Luty et al 2010). SIGMAR1 is a ubiquitously expressed protein considered to have neuroprotective effects under normal physiological conditions (Hayashi & Su 2004, Katnik et al 2006). It is important for maintaining aspects of learning and memory as well as having been implicated in the unfolded protein response (UPR), lipid raft formation and neurite outgrowth (Al-Saif et al 2011, Hayashi & Su 2003). Specifically, it has been shown to play a critical role in Ca^{2+} homeostasis, autophagy and mitochondrial cytochrome c mediated programmed cell death in response to ER stress and glutamate excitotoxicity (Section 1.2.4.2) (Prause et al 2013, Vollrath et al 2014).

1.2.5.2.8 CHMP2B

Heterozygous missense substitutions identified in the charged multivesicular body protein 2b (*CHMP2B*) gene (n=6), situated at the chromosome 3p12.1 locus (Table 1.1), are a rare cause of AD inherited adult onset ALS (ALS17) and bvFTLD (<1%) which also account for ~10% of instances involving PMA (Section 1.2.2.3) (Cox et al 2010, Ghanim et al 2010, Isaacs et al 2011, Momeni et al 2006, Parkinson et al 2006, Skibinski et al 2005). Towards the motor end of the spectrum the disease is characterised by a predominantly LMN phenotype. Clinical manifestations typically include a flaccid, atrophic tongue with severe fasciculations, dysarthria & dysphagia, dyspnoea (a shortness of breath), respiratory muscle weakness, bilateral wasting of the intrinsic hand muscles and an abnormal flexor plantar response with brisk deep tendon reflexes. Age and site of onset varies considerably and along with survival, which has a range spanning 15 months to 5½ years, appears to be mutation specific. Pathologically, *CHMP2B* cases are hallmarked by the presence of ubiquitinated p62 and TDP-43 immunoreactive inclusion bodies in surviving MN's of the cortex and ventral horn of the SC which stain negatively for the microtubule associated protein, tau and α-synuclein. There is also a lack of overt extramotor signs with substantial microglial activation occurring in subcortical regions (Cox et al 2010, Parkinson et al 2006).

The CHMP2B protein forms an essential component of the third endosomal sorting complex required for transport (ESCRT)-III; responsible for surrendering ubiquitin tagged cargo to multivesicular bodies (MVB's) which ultimately deliver them to the lysosomal machinery for degradation (Henne et al 2011, Skibinski et al 2005). An exon 6 mutation of the gene's acceptor splice site at the intron/exon boundary that produces a C-terminal truncated protein has been shown to disrupt this pathway (Han et al 2012, Urwin et al 2010, van der Zee et al 2008) leading to disturbances in intracellular Notch signalling and eye irregularities in the *Drosophila* invertebrate system (Cheruiyot et al 2014).

1.2.5.2.9 PFN1

Missense substitutions of incomplete penetrance (n=7) concentrated within or in close proximity to the actin binding domain of the profilin 1 (*PFN1*) gene, situated at the chromosome 17p13.2 locus (Table 1.1), are responsible for rare instances of AD inherited adult onset ALS (ALS18) (~1-2%) and bvFTLD (~0.5%) with a small number of SALS patients (~0.2%) also affected (Chen et al 2013, Ingre et al 2013, Tiloca et al 2013, van Blitterswijk et al 2013a, Wu et al 2012a, Yang et al 2013). In a meta-analysis of 5,118 cases and 13,089 neurologically healthy controls in the UK population an odds ratio (OR) of 2.44 ($p<0.05$) was produced for the dinucleotide variant c.350A>G (p.E117G) in exon 3 (Fratta et al 2014). The minor allele (T) of a synonymous c.334C>T (p.L112L) single nucleotide polymorphism (SNP) (rs13204) has also been reported to be a disease modifier of SALS in China with an OR of 0.73

(p<0.005) (Chen et al 2013). Phenotypic heterogeneity exists with bulbar or spinal onset occurring in the late twenties to early seventies and a median survival which spans a minimum of 36 months to almost three decades (Chen et al 2013, Ingre et al 2013, Wu et al 2012a). Upon neurohistochemical evaluation, TDP-43 pathology is observed with the presence of ubiquitinated, p62 positive inclusion bodies that are not immunoreactive for PFN1 (van Blitterswijk et al 2013a). Profilin 1 encodes a 140 amino acid peptide that is ubiquitously expressed and has been found to associate with SG's; cytoplasmic RNP granules composed of repressed translation complexes (Figley et al 2014). It is a major growth regulator that is required for the conversion of monomeric or globular (G)-actin into filamentous (F)-actin which is essential for actin polymerization (Mockrin & Korn 1980). In primary MN's which express mtPFN1, evidence of growth cone arrest and morphological deficits were apparent with a marked reduction in the ratio of (F) to (G)-actin (Wu et al 2012a). Homozygous knock-out (KO) mice were not viable, demonstrating embryonic lethality in an *in vivo* study conducted by Witke et al (2001) whilst heterozygous littermates exhibited a significantly shortened lifespan.

1.2.5.2.10 HNRNPA1

Exome sequencing and linkage analysis has recently highlighted the heterogeneous ribonucleoprotein A1 (*HNRNPA1*) gene, situated at the chromosome 12q13.1 locus (Table 1.1), as a rare cause of AD inherited adult onset ALS (ALS20) and IBMPFD/ ALS with FTLD (Section 1.2.5.2.5), otherwise known as multisystem proteinopathy (MSP), in a four generation kindred of American ancestry. Subsequent screening of a large FALS (n=212) and SALS (n=305) cohort identified two additional missense substitutions in the C-terminal, glycine-rich PrLD of isoform a and b at a frequency of 0.47 or 0.32%, respectively (Kim et al 2013). *HNRNPA1* encodes an RNA binding protein that has been found to interact with TDP-43 (Section 1.2.5.2.1) (Buratti et al 2005). It has the propensity to form spontaneously into self-seeding fibrils which is exacerbated by the presence of a disease causing mutation. In a *Drosophila* model that recapitulates many of the human pathological hallmarks of ALS-FTLD including TDP-43 proteinopathy defective isoforms of hnRNPA1 accelerated the accumulation of the protein into SG's and drove the formation of ubiquitinated, p62 and TDP-43 positive NCI's (King et al 2013).

1.2.5.3 FTLD Loci

1.2.5.3.1 MAPT

The microtubule associated protein tau (*MAPT*) gene, situated at the chromosome 17q21.32 locus, is associated with as many as 50% of familial FTLD cases (Hutton et al 1998, Onyike & Diehl-Schmid 2013, Rademakers et al 2004, Riedl et al 2014, Sieben et al 2012). Since its discovery almost two decades ago more than 40 genetic alterations/splicing defects and a further two extended haplotypes, namely H1 and H2 have been described (Park & Chung 2013). Patient carriers typically have a M:F ratio of 1.25:1 (n=8) with a median age at symptom onset of less than 50 years and an average disease duration of 9.40±5.0 years (Karageorgiou & Miller 2014, Le Ber 2013, Van Langenhove et al 2013). Symmetric frontal lobe atrophy, a characteristic feature upon neuroimaging of *MAPT* mutations in FLTD (Boeve & Hutton 2008), is linked to behavioural abnormalities, personality changes and dementia with rigid akinetic Parkinsonism & oculomotor dysfunction (Espay & Litvan 2011, Haugarvoll et al 2007, Park & Chung 2013, Slowinski et al 2007). At protein level, pathogenicity is conferred through a loss of function or haploinsufficiency mechanism whereby microtubule assembly and axonal transport is impaired, leading to an accumulation of hyperphosphorylated tau filaments which form aggregates within the cytoplasm of residual MNs and microglia of the CNS (Brandt et al 2005, Gasparini et al 2007, Goedert et al 2012, Iovino et al 2014, Robinson et al 2014).

1.2.5.3.2 PGRN

Mutations in the progranulin (*PGRN*) gene, situated at the chromosome 17q21.31 locus that is in close proximity to *MAPT* (Section 1.2.5.3.1) (Karageorgiou & Miller 2014), are thought to account for a further 5 to 25% of familial FTLD cases (Baker et al 2006, Pan & Chen 2013, Sieben et al 2012). So far at least sixty-seven different genetic alterations of pathological significance have been reported in the literature (Park & Chung 2013); giving rise to a heterogeneous clinical phenotype that varies greatly from bvFTLD or PNFA without apraxia of speech to semantic dementia and corticobasal syndrome (CBS) (Beck et al 2008, Le Ber et al 2008, Puoti et al 2014, Snowden et al 2006). Patient carriers typically have a M:F ratio of 0.69:1 (n=27) with median age at symptom onset of 60 years and an average survival of 5.80±1.9 years (Van Langenhove et al 2013). Initial manifestations may include behavioural abnormalities & personality changes as well as rigid akinetic Parkinsonism and language impairment (Boeve & Hutton 2008, Haugarvoll et al 2007). Evidence of asymmetric frontal lobe atrophy which extends to the temporal/inferior parietal lobes is present upon MRI (Rohrer et al 2010, Whitwell et al 2009). Reactive gliosis and white matter disease pathology have also been found to be prominent features of *PGRN* mutations (Kelley et al 2009, McMillan et al 2014). Moreover, tau negative and TDP-43 positive ubiquitinated neuronal cytoplasmic inclusion bodies (NCI's) have been detected in the superficial layers of the cerebral neocortex as well as the hippocampal granule cells of the dentate gyrus (Josephs et al 2011, Mackenzie et al 2010, Riedl et al 2014, Robinson et al 2014). Null mutations are thought to confer pathogenicity through a loss of function mechanism although the precise function of this particular growth factor in neuronal differentiation and survival has yet to be fully elucidated (Puoti et al 2014, Riedl et al 2014).

1.2.5.3.3 PSEN1

A dominant negative heterozygous 3bp TCG insertion of an arginine residue at the position of the 352nd codon (insR352) in exon 10 of the presenilin 1 (*PSEN1*) gene, situated at the chromosome 14q24.3 locus, has been reported in a single kindred in which there are at least three instances of dementia (Amtul et al 2002). Although not associated with altered CSF or plasma β-amyloid (Aβ) levels as seen in cases of ALZ, the mutation is thought to affect cleavage of amyloid precursor protein (APP) through its inhibition of gamma (γ)-secretase activity (Golde & Younkin 2001). The proband presented at 56 years of age with features of Parkinsonism, asymmetric paraparesis, forgetfulness, visual hallucinations, increased appetite (hyperphagia), personality and behavioural disturbances, delusions, hypersexuality, incontinence, cognitive decline and social disinhibition (Section 1.2.1) (Tang-Wai et al 2002). At autopsy cortical atrophy, thinning of the corpus callosum and enlarged lateral ventricles were apparent with marked striatal degeneration, neurophil vacuolation and gliosis. The presence of ubiquitinated NCI's, NII's and DN's immunoreactive for TDP-43 which stained negative for FUS and the microtubule associated protein, tau were consistent with a diagnosis of FTLD-U (FTLD with ubiquitin and TDP-43 +ve inclusions). The pathogenicity of the insR352 mutation, however, was called into question upon discovery of an IVS1+1G>A substitution in exon 1 of the *PGRN* gene (Section 1.2.5.3.2) in the same pedigree which abolishes a 5' splice site upstream of the ATG start codon encoded by a methionine residue and blocks protein synthesis (Boeve et al 2006).

1.2.5.4 *C9ORF72*

A long established association between the 9p21.2 locus of the human genome and a risk for developing ALS, bvFTLD or the combined ALS-FTLD syndrome can now be explained, at least partially, by the discovery in October 2011 of a pathogenic non-coding hexanucleotide G_4C_2 repeat expansion that is situated in the first intron of exon 1a containing transcripts or proximal promoter region of exon 1b containing transcripts of the previously uncharacterised chromosome 9 open reading frame 72 (*C9ORF72*) gene (DeJesus-Hernandez et al 2011, Renton et al 2011). Repeat-primed PCR and Southern blotting hybridization techniques have sort to size the expansion in post-mortem material isolated from human frontal cortex, cerebellum and brain-stem in addition to patient derived skin fibroblasts, peripheral whole blood and EBV-transformed, immortalised B-lymphocytes (LCL's) (Beck et al 2013, Buchman et al 2013, Dols-Icardo et al 2014, Harms et al 2013, Hubers et al 2013, van Blitterswijk et al 2013c). Somatic instability of the expanded G_4C_2 sequence may explain a large degree of the variability which arises between affected members of the same family and across different tissue types with average repeat lengths ranging in size between a few hundred and several thousand copies. Uncertainty, however, remains as to the precise number of repeats that are required in order to exert neurotoxicity towards MN's in ALS. Although a threshold of more than 30 copies is widely accepted, some studies have suggested as few as 20 or 22 copies could be pathological (Byrne et al 2013, Gomez-Tortosa et al 2013).

The gene itself is comprised of 11 exons which span a 27.3Mb region of the short arm of chromosome 9p. Multiple alternatively spliced transcripts are described (n=

5) (ensembl.org) including three that are protein coding: two full length transcripts with alternated first exons [Variant I (NM_001256054) exons 1a, 2-11 and Variant III (NM_018325) exons 1b, 2-11] and a stable truncation [Variant II (NM_145005) exons 1a, 2-5]. Since the methionine residue encoding the translation initiation ATG start site is situated in exon 2, transcript variants I to III produce only two protein isoforms: isoform a of 481a.a (54.3kDa) and isoform b of 222a.a (24.8kDa) (Flicek et al 2014). *C9ORF72* is predicted to be a putative member of the DENN superfamily of differentially expressed in normal and neoplastic domain containing proteins which are thought to function as GEF's for small Rab GTPases (Levine et al 2013, Zhang et al 2012); thus, implicating them in a possible role in membrane trafficking and the autophagosome-lysosome clearance pathway (Farg et al 2014).

By the autumn of 2013 several thousand incidences (n>3,300) (Woollacott & Mead 2014) of the *C9ORF72* G_4C_2 repeat expansion had been reported worldwide, making it the most common genetic cause of both conditions identified to date with as many as 43% of FALS (0.4-21% SALS) and approximately 25 to 30% of hereditary bvFTLD (2.0-23% sporadic bvFTLD) patients affected (Cooper-Knock et al 2012b, Cruts et al 2013, Devenney et al 2014, Gijselinck et al 2012, Majounie et al 2012, Smith et al 2013). It has yet to be determined, however, whether pathogenicity arises from a loss of function (haploinsufficiency) or gain of function mechanism mediated by repeat associated non-ATG (RAN) translation of DPR (dipeptide repeat) proteins (Gendron et al 2013b) or the formation of toxic RNA foci (Donnelly et al 2013).

1.3 Microarray Based Gene Expression Profiling

1.3.1 Affymetrix® Platform

The application of microarray based technology offers the end user a rapid, high-throughput approach to global gene expression profiling that is both reproducible and unbiased (Tang et al 2005). Since the advent of the Human Genome Project, launched almost twenty-five years ago (Watson 1990), it has become increasingly possible to simultaneously measure the activity of transcripts pertaining to many thousands of genes or EST's on a single GeneChip® or array (Sharp et al 2006b).

Briefly, total RNA isolated from the cellular model or tissue of interest is reverse transcribed into complementary DNA (cDNA) that is subsequently transformed *in vitro* to yield copy RNA (cRNA) which is fluorescently labelled with an covalently attached biotin molecule. The "target" sample is then fragmented and hybridized to oligonucleotide probes that are synthesised directly onto the glass slide by means of combinatorial chemistry and photolithography. On traditional 3' IVT expression arrays each transcript is represented by 11 probe pairs. These comprise a probeset which contains equal numbers of perfect match (PM) and mismatch (MM), in order to control for hybridization specificity, 25-mer oligonucleotide sequences that are scattered at random across the chip (affymetrix.com). Signal intensity readouts from the GeneChip® scanner once the array has been washed, stained and processed can be considered proportional to the amount of cRNA for any given transcript which has bound to its complementary sequence(s) on the GeneChip® and, hence, provides an accurate, robust and quantifiable measure of gene expression (Figure 1.2).

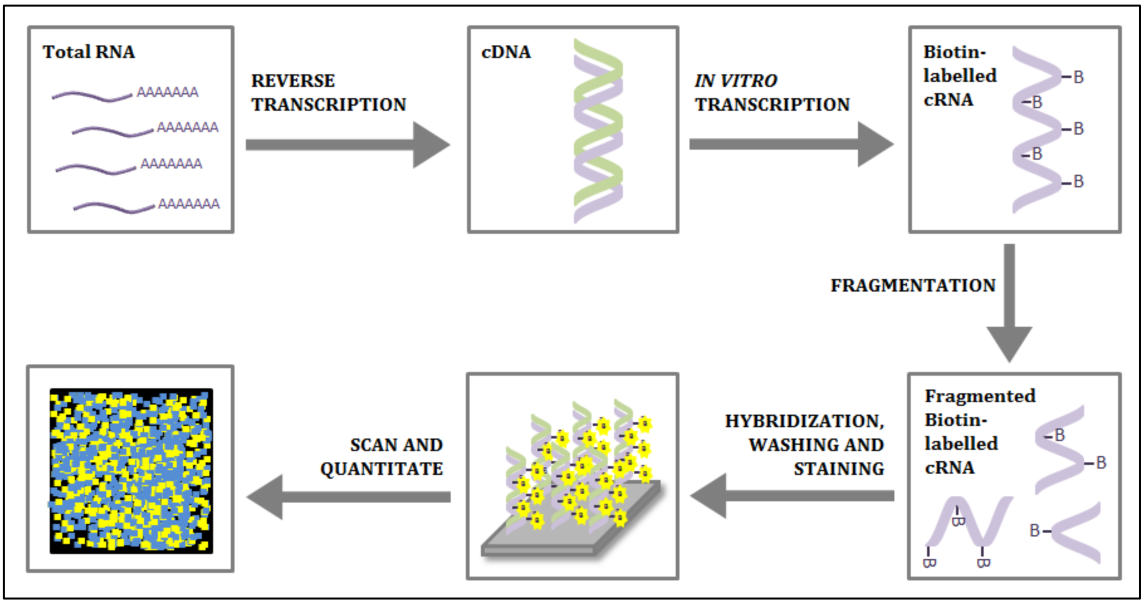


Figure 1.2 Schematic Overview of the Affymetrix® Oligonucleotide Microarray Platform for Global GEP of Peripheral Tissues in ALS

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, cDNA - complementary DNA, cRNA - copy RNA and GEP - gene expression profiling.

The microarray platform introduced by Affymetrix® has quickly become one of the most extensively used systems for generating gene expression profiling (GEP) data around the globe with a full range of different GeneChips® now supported including the Human Genome (HG) U133 Plus 2.0 GeneChip® [Chapter 3: 'Whole Blood Study'] and Human Exon 1.0ST GeneChip® [Chapter 5: '*C9ORF72* GEP Study' and Chapter 6: '*C9ORF72* Survival Study'] Arrays which are discussed in detail in Sections 2.3.1.8.1 and 2.3.2.4.1, respectively of Chapter 2: Materials and Methods (Auer et al 2009, Dalma-Weiszhausz et al 2006, Okoniewski et al 2007).

1.3.2 Limitations of Using Human Post-Mortem Tissue

Whilst invaluable insights have been gained, specifically with regards to elucidating further the neuropathophysiological mechanisms which underlie MN degeneration in ALS and indeed other neurodegenerative, as well as neuropsychiatric conditions, there are several limitations associated with the use of human post-mortem derived tissue for generating GEP's (Altar et al 2009, Bowser et al 2006, Cooper-Knock et al 2012c, Heath et al 2013, Malaspina & de Belleroche 2004, Papapetropoulos et al 2007, Tanaka et al 2006), and the subsequent identification of biologically meaningful markers of potential diagnostic and/or prognostic relevance that could in the future be applied in a clinical setting. Although representative of the most vulnerable neuronal cell populations, brain and spinal cord tissue can be difficult to obtain and is often in short supply; thus, restricting the sample sizes that can be used. This limits the statistical power of such studies which may ultimately compromise their reliability (Cooper-Knock et al 2012a). There have also been reports of significant levels of RNA degradation and protein modification that can occur *ex vivo.* Additional considerations include inter- and intra-individual variability, the extent of neuroinflammation at autopsy, PM delay and brain pH (Maes et al 2007). Decisions concerning whether to sample grey versus white matter, for example, or choosing to enrich for cortical MN's over AHC's will also have a profound impact. Moreover, transcriptional profiling of PM material inevitability reflects only the very terminal stages of disease progression (i.e. the point at which the majority of MN's will have degenerated and already been lost from the system) (Sharp et al 2006a). Hence, the difficulty in establishing whether the GE changes detected on the microarray have occurred in response to a pathogenic trigger, are a consequence of dying MN's initiating apoptosis (Section 1.2.4.8) or due to survival signals emanating from the remaining non-neuronal cell populations. The latter may be particularly problematic when preparing whole tissue homogenates rather than deploying laser capture microdissection (LCM) techniques to isolate specific cell subtypes (Lederer et al 2007). In an attempt to overcome some of the aforementioned issues discussed above, a number of more readily accessible tissues have been investigated (Table 1.4); which include peripheral whole venous blood specimens and immortalised, EBV-transformed B-lympho cytes (LCL's) that are reviewed briefly in Sections 1.4.1 and 1.4.2, respectively.

Peripheral Tissue	Advantages	Limitations
Whole Blood	- readily accessible - longitudinal collection - large sample volumes - good standardisation of technical procedures	- no direct involvement in ALS - unrelated to MN's - mixed cell population - high abundance of erythrocyte alpha/beta haemoglobin
PBMC	- readily accessible - longitudinal collection - homogeneous cell population	- no direct involvement in ALS - unrelated to MN's - *ex vivo* handling
LCL's	- non-invasive collection - good standardisation of technical procedures - almost limitless resource - large Biobank available - homogeneous cell population	- no direct involvement in ALS - unrelated to MN's
Muscle biopsy material	- direct involvement in ALS	- accessibility - invasive collection
CSF	- obtained from CNS	- invasive collection
Skin fibroblasts	- readily accessible - model system with the genetic background of the patient - can be reprogrammed into MN-like cells - source for generation of iPSC's	- no direct involvement in ALS

Table 1.4 Advantages and Limitations Associated with the Use of Peripheral Tissues for GEP Analysis in ALS

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, CNS - central nervous system, CSF - cerebrospinal fluid, GEP - gene expression profiling, iPSC - induced pluripotent stem cell, LCL - lymphoblastoid cell line, MN - motor neuron and PBMC - peripheral blood mononuclear cell.

1.3.3 The Use of Peripheral Tissues

Since the MN's which degenerate in ALS cannot be harvested during life, there are great benefits to be had in sampling peripheral tissues that lend themselves to better standardization of technical procedures, are readily accessible and can be collected in large volumes without the need for re-sampling or longitudinally over the course of the disease duration e.g. whole blood (Borovecki et al 2005, Grunblatt et al 2010, Maes et al 2007, Runne et al 2007, Saris et al 2009, Scherzer et al 2007, Tsuang et al 2005) (Section 1.4.1) and, immortalised B-lymphocytes (Section 1.4.2) (Antonell et al 2010, Bittel et al 2007, Kakiuchi et al 2008, Nishimura et al 2007, Talebizadeh et al 2014). The advantages and limitations of each of these in addition to peripheral blood mononuclear cells (PBMC's) (Bayatti et al 2014), skin fibroblasts (Raman et al 2014), muscle biopsy material (Calvo et al 2012) and CSF (Jones 2011) are summarised in Table 1.4.

1.4 GEP Studies in Neurodegenerative Disease

1.4.1 Examples Using Peripheral Whole Venous Blood

1.4.1.1 ALS

Currently in the literature there has only been a single published report by Saris et al (2009) which documents the use of peripheral whole blood for the generation of ALS related transcriptomics data. In this study, 79 spinal onset and 44 bulbar onset cases of an idiopathic nature that met the EEC of either 'definite' or 'probable' ALS (Section 1.1.3) were recruited from The Netherlands along with 123 unrelated, age as well as gender matched, neurologically normal healthy control subjects. These were further subdivided into a discovery cohort which comprised 30 SALS patients and controls (Dataset 1) plus two additional replication cohorts including one that contained a further 30 SALS patients and controls (Dataset 2) and a third containing the remaining 63 SALS patients and controls (Dataset 3).

Application of the Illumina based microarray platform using Sentrix® HumanRef-8 Expression BeadChip Arrays which represent >22,000 RefSeq curated gene targets identified 2,300 probes (9.4%) as being differentially expressed (DE) between the SALS and control groupings in the discovery cohort (student's t-test p<0.05) (Saris et al 2009); although no validation by qRT-PCR (quantitative real-time polymerase chain reaction) was performed. Dysregulation of *CHMP2B* (Section 1.2.5.2.8) (⇩1.06 -fold, p<0.001) and *RAB5A* (⇩1.12-fold, p<0.001) were of particular interest given their prior association with the disease. RAB5A is a member of the Ras superfamily of monomeric G-proteins that are responsible for regulating intracellular trafficking and endosome formation, transportation, membrane docking & fusion (Gohre et al 2012, Li et al 2013c, Lu et al 2014, Nayak et al 2013). They play a critical role in the autophagosome lysosome clearance pathway which is an important mechanism for cellular homeostasis and survival that has also been linked to the pathogenesis of ALS (Section 1.2.4.7) (Barmada et al 2014, Ferguson et al 2009, Hetz et al 2009, Li et al 2013b, Tarabal et al 2005). Moreover, the *RAB5A* guanine nucleotide exchange factor encoded by *ALSIN* (Section 1.2.5.1.2) is recognised as a causative gene of a rare AR inherited form of juvenile onset ALS (ALS2) (Table 1.1) (Yang et al 2001).

Saris et al (2009) proceeded in performing Weighted Gene Co-expression Network Analysis (WGCNA) on ~8,000 probes (36.4%) which had a statistically significant Benjamini-Hochberg false discovery rate (FDR) corrected mean detection signal of $p<0.05$. Hierarchical clustering produced five colour coded modules ranging in size between 199 and 842 genes which demonstrated an association with ALS disease status but were found not to correlate with specific clinical phenotypes such as age of onset, presentation or survival. Bonferroni multiple comparison tests identified Blue [$r_1=0.48$(⇧), $p=3.60E-05$] and Yellow [$r_1=0.61$(⇩), $p=6.20E-09$] modules which were highly preserved across all three datasets and comprised predominantly up-regulated or down-regulated clusters, respectively. Ingenuity Pathway Analysis of each of the top 500 ranking gene lists highlighted transcripts that are involved in the post-transcriptional or post-translational modification of mRNA's and proteins as being significantly over-represented in the Blue module with neurodegeneration of the CNS, OS response (Section 1.2.4.1) & inflammation (Section 1.2.4.6) enriched in the Yellow module. Of particular interest is the dysregulation of *ATXN2* (Section 1.2.5.2.4) (⇧1.10-fold, $p<0.001$) since polyQ expansions in this gene are associated with a rare AD inherited form of adult onset ALS (ALS13), bvFTLD with non-fluent aphasia, PD and SCA2 (Table 1.2) (Elden et al 2010, Imbert et al 1996). In a further analysis of the top 100 most highly interconnected hub genes, Saris et al (2009) also identified transcripts relating to cellular stress, apoptosis and the UPR which were shared in common between modules with those involved in vesicular trafficking or mitochondrial function found to be specific for either the Blue or Yellow modules, respectively. Similar findings to the latter have been recapitulated in the spinal cord, peripheral whole blood and muscle biopsy tissue of the transgenic $SOD1^{G93A}$ mouse model (Saris et al 2013).

Altered mRNA transcript levels of several genes (n=16) have also been reported in the motor and sensory cortices of five additional SALS patients (Wang et al 2006). These included ATP/GTP binding protein 1 (*AGTPBP1*) (⇩1.09-fold, $p<0.01$) which is thought to contribute to Purkinje cell degeneration and loss in hereditary forms of cerebellar ataxia (Fernandez-Gonzalez et al 2002, Lim et al 2006) and has since been validated in a third independent study comparing GEP's from 11 SALS patients and 9 neurologically healthy, control subjects (Lederer et al 2007). Other DE genes commonly dysregulated in peripheral whole blood and human post-mortem derived SC tissue include a number of those involved in DNA replication & repair as well as RNA processing, protein degradation, cellular response to stress, inflammation, Ca^{2+} homeostasis, cell cycle control, CNS vasculogenesis and glucose metabolism [*ABL1, CAMLG, CD74, CYBA, ENG, GYS1, POLD2, RELA, S100A9, SF1, SPN, SRPK1, TXN, UBL5, USP11* and *VIL2*] (Dangond et al 2004, Ishigaki et al 2002, Jiang et al 2005, Kudo et al 2010, Malaspina et al 2001, Offen et al 2009).

1.4.1.2 Other Neurodegenerative Disorders

1.4.1.2.1 Huntington's Disease

Huntington's disease (HD), which has a prevalence of 12.3 per 100,000 of the UK Caucasian population (Pringsheim et al 2012), is an adult onset movement disorder of monogenic inheritance that is caused by a polyQ expansion of 40 repeat lengths or greater in exon 1 of the *HTT* gene encoding the huntingtin protein (MacDonald et al 1993). The condition is characterised by the loss of gamma-Aminobutyric acid or GABAergic neurons and widespread reactive gliosis in the striatum and cerebral cortex (Runne et al 2007). Extrapyramidal signs include rigidity and bradykinesia, dystonia, reduced coordination, weight loss and chorea with cognitive decline and psychiatric disturbances (e.g. irritability, anxiety & depression) normally apparent before the onset of overt motor impairment (Ross & Tabrizi 2011).

Transcriptional profiling comparing pre-symptomatic (n=5) or symptomatic (n=12) HD patients to fourteen unrelated, age and gender matched, neurologically normal healthy control subjects identified 322 of ~11,000 probes (2.9%) common to both

Affymetrix Human Genome U133A GeneChip® Arrays and Amersham BioSciences CodeLink Uniset Human I and II bioarrays with an average expression ratio of >1.8 or <0.6 (student's t-test $p<0.0005$) for up and down-regulated changes, respectively. The majority of transcripts were increased in peripheral blood of patients relative to controls and reflected diverse biological processes including transcription/RNA processing, ubiquitin-mediated proteasomal degradation, vesicular trafficking and signal transduction. The top 30 highest ranking genes, as determined by probability value and fold-change, were assessed by qRT-PCR and a subset of 12 demonstrating the most significant DE selected to form a biomarker panel which could be applied, using principal component analysis (PCA) mapping software, to distinguish not only between HD and controls, but also between different stages of disease progression with pre-symptomatic patients clustering distinctly between individuals which are symptomatic and those that are neurologically healthy in two independent cohorts comprising a) 16 late pre-symptomatic, 14 symptomatic and 25 controls or b) nine early pre-symptomatic and a further nine controls. The panel also proved effective in a Phase I clinical trial in monitoring individual patient responses to the histone deacetylase (HDAC) inhibitor sodium phenylbutyrate (Borovecki et al 2005) which has been shown to exhibit neuroprotective properties in a transgenic mouse model of the disease (Gardian et al 2005). Moreover, an up-regulation in the expression of 7 of the 12 candidate genes (58.3%) was confirmed by qRT-PCR in human derived post-mortem tissue from the caudate nucleus of five additional HD brains and four controls (Borovecki et al 2005). In another study comparing HD (n=61), PD (n=20) and ischemic stroke (n=10) patients, the same approach was conducted by Lovrecic et al (2009) using a standard logistic regression based model which was successful in generating a positive predictive score of 78% with sensitivity 82% and specificity 53%. This finding, however, could not be replicated in lymphocytes suggesting that this particular panel of biomarkers may be specific to blood (Runne et al 2007).

1.4.1.2.2 Parkinson's Disease

PD affects approximately 1% of the population over the age of 65 (Wirdefeldt et al 2011) and is characterised as a slowly progressive neurodegenerative disorder that is characterised by a resting tremor, rigidity, gait abnormalities, asymmetric bradykinesia and postural instability. Pathologically the condition is hallmarked by the presence of α-synuclein containing LB's as well as a substantial loss of dopaminergic neurons from within the substantia nigra pars compacta region of the brain (Ali & Morris 2014).

Transcriptional profiling of 50 early stage PD patients with a mean Hoehn and Yahr score of 2.3 (range 1-4) and 55 unrelated controls including 33 disease mimics [ALZ, progressive supranuclear palsy (PSP), CBS or multiple systems atrophy (MSA)] and 22 neurologically healthy control subjects which were age, gender and blood count matched identified 22 unique genes represented on the Affymetrix Human Genome U133A GeneChip® Arrays as being DE between PD patients and controls with SAM (significance analysis of microarrays) FDR $p<0.03$ and a fold-change (FC) threshold of ±1.25. Functional categories that were highlighted included the cell cycle, DNA/RNA turnover, protein phosphorylation & transport, carbohydrate metabolism and apoptosis. Of particular interest is the down-regulation of the heat shock protein 70 (HSP70) co-chaperone suppression of tumorigenicity 13, *ST13* (⇩1.63-fold, $p<0.01$) which has been implicated in the aberrant folding of α-synuclein and its subsequent toxicity towards dopaminergic neurones in PD (Flower et al 2005, Klucken et al 2004). This was later confirmed in two independent qRT-PCR assays using different housekeeping genes (Scherzer et al 2007). The authors also divided the cohort into a training set (62.9%) [31 PD, 18 mimics and 17 controls] and a test set (37.1%) [19 PD, 15 mimics and 5 controls] in order to determine an optimum biomarker panel of 8 candidate genes that correlated significantly with the risk of developing PD [OR of third tertile leave one out cross-validation 5.7 with 95% confidence interval (CI) between 1.6 and 21, $p<0.01$] (Scherzer et al 2007). In a re-analysis of the aforementioned dataset, Soreq et al (2008) were able to further improve the discriminative power of the study by deploying distribution plots and PCA mapping to allow for the effective removal of outliers that may have arisen from technical inconsistencies. In doing so they have highlighted previously unreported changes in the mRNA transcript levels of genes relating to neuro-immune signalling (Soreq et al 2008). It is also worth noting that an intron 8 SNP encoded within one of these markers, *VDR* (vitamin D receptor), is found to be disproportionately over-represented in Korean PD sufferers relative to the general population (Butler et al 2001, Kim et al 2005, Li et al 2014).

In a more recently published report by Grunblatt et al (2010), 4 of 12 (33.3%) pre-selected candidates based upon prior GEP analyses of human post-mortem derived brain tissue [*ALDH1A1, HIST1H3, LAMB2* and *PSMA2*] (Grunblatt et al 2004, Hauser et al 2006, Lu et al 2005, Simunovic et al 2009, Zhang et al 2005) could successfully differentiate between sporadic PD cases [11 drug naïve and 116 mediated], disease mimics diagnosed with ALZ and neurologically healthy, elderly control subjects with a sensitivity and specificity of greater than 80% in qRT-PCR assays of RNA isolated from peripheral whole blood (Grunblatt et al 2010).

1.4.1.2.3 Alzheimer's Disease

ALZ represents the most common form of age-related dementia that afflicts between 3 and 7% of the global population older than 75 years (Abdulrahman & Jnr 2014, Takizawa et al 2014). Progressive memory loss and a decline in cognitive function is accompanied by reactive gliosis, atrophy of the basal forebrain and hippocampus, extracellular depositions of Aβ (senile plaques) and intracellular accumulations of hyperphosphorylated tau (neurofibrillary tangles) (Duyckaerts et al 2009, Sabuncu et al 2011).

Transcriptional profiling of peripheral blood mononuclear cells (PBMC's) from 14 mildly symptomatic sporadic ALZ patients [Mini Mental State Examination (MMSE) scores of 23.4±3 out of a possible 30] and an equal number of neurologically healthy age and education matched elderly control subjects using the National Institute on Aging (NIA) Human Mammalian Gene Collection (MGC) cDNA Arrays identified 942 of 6,424 probes as being DE including 849 (90.1%) down-regulated and 93 (9.9%) up-regulated transcripts with an average expression ratio of >1.2 or <0.9 and SAM 2-way analysis of variance (ANOVA) FDR threshold of $p<0.05$. Gene Set Enrichment Analysis (GSEA) using the online open source database that is freely available from the Gene Expression Omnibus (GEO) repository highlighted genes associated with apoptosis, protein translation & inflammation that were significantly increased and genes associated with cytoskeletal maintenance, cellular trafficking, mitochondrial function, lipid metabolism, redox homeostasis, neurotransmission, transcription &

DNA repair or cellular response to stress which were significantly decreased in the PBMC's of ALZ patients in relation to the controls (Maes et al 2007). Whilst a large proportion of these have been found to be gender specific, changes in 78% of those selected in males and 56% in females were confirmed in a qRT-PCR assay (albeit in the same cohort of samples used in the microarray experiments) and >160 probes exhibited similar expression changes in human derived post-mortem brain tissue (Blalock et al 2004, Colangelo et al 2002, Yao et al 2003) and/or transgenic animal models of the disease (Dickey et al 2003, Ho et al 2001, Reddy et al 2004).

1.4.1.2.4 Schizophrenia and Bipolar Disorder

Schizophrenia (SCHIZ) and Bipolar disorder (BPD) are severely debilitating chronic remitting and relapsing neuropsychiatric illnesses that each occur in approximately 1% of the population. The former is characterised by psychosis with symptoms of hallucinations & delusions, disorganised speech, catatonia and variable degrees of motor, cognitive and/or social dysfunction (Tandon et al 2013, Tandon et al 2009); whereas the latter, conversely, is a mood affective disorder that is characterised by episodes of mania and depression and is often associated with paranoia as well as sleep-wake disturbances (Fagiolini et al 2013, Oswald et al 2007).

Transcriptional profiling of individuals of Han Chinese descent including SCHIZ (n= 30) and BPD (n=16) patients diagnosed according to the IV criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM) and 28 unrelated, neurologically healthy control subjects identified 89 of 12,674 probes (~0.7%) on the Affymetrix U133A/plus2.0 GeneChip® Arrays as being DE between the two patient groupings and controls, applying a non-parametric ANOVA (Kruskal-Wallis) $p<0.005$ without performing a multiple comparisons correction. Two-dimensional (2D) hierarchical clustering using the Spearman's correlation statistic demonstrated three genetically defined subgroups on the HeatMap which corresponded to SCHIZ, BPD and control cases in the original microarray experiment. Logistic regression and ROC (Receiver Operating Characteristic) curve analysis from pair-wise comparisons of SCHIZvctrl, BPDvctrl and SCHIZvBPD determined linear and non-linear combinations of eight of the highest ranking genes, which were confirmed by qRT-PCR, to be successful in discriminating not only between a healthy versus disease status but also between

SCHIZ and BPD with an overall efficiency of 95% (Tsuang et al 2005). Many of these putative markers were found to reside at chromosomal loci which have previously been linked to SCHIZ [1cen.q12 (*ADSS*), 1q21 (*S100A9*), 20q13 (*DATF1*) and 22q13 (*APOBEC3B*)], BPD [4p16 (*CTBP1*) and 4q21 (*CXCL1*)] or alternatively both of these neuropsychiatric conditions [11q22 (*ATM*) and 19q13 (*CLC*)] (Badner & Gershon 2002, Cassidy et al 2007, Cheng et al 2006, Francks et al 2010, Fullerton et al 2010, Lewis et al 2003). Furthermore, an increase in the expression levels of chemokine (C-X-C motif) ligand 1 melanoma growth stimulating activity, alpha (*CXCL1*) (⇧1.58 -fold, p<0.001) has been independently verified in a second qRT-PCR cohort which was comprised of an additional 30 SCHIZ patients and 26 unrelated, neurologically healthy control subjects (Yao et al 2008).

1.4.2 Examples Using Immortalised Lymphoblastoid Cell Lines

1.4.2.1 ALS

To date, no reports have been published on the use of peripheral EBV-transformed B-lymphocytes (LCL's) to measure gene expression in ALS.

1.4.2.2 Other Neurodegenerative Disorders

1.4.2.2.1 Schizophrenia

Transcriptional profiles of EBV-transformed B-lymphocytes from two pairs of MZ (monozygotic) twins that have a homogeneous background and are discordant for SCHIZ [(A) 54 year old males one of whom had diabetes mellitus with both positive and negative symptoms and (B) 24 year old females with one individual exhibiting purely negative symptoms and signs of auditory hallucinations] were generated on the Affymetrix® platform using Human Genome U133A Plus 2.0 GeneChip® Arrays containing >22,000 probes for the interrogation of upwards of 14,500 genes. From the analysis of five independent replicates, performed for each pair, several (n=5) transcripts were identified as being DE (p<0.05) between affected and unaffected twin members according to GeneSpring conducted parametric and non-parametric testing. These included adrenomedullin (*ADM*) and selenoprotein X1 (*SEPX1*) that were significantly up-regulated and the B-lymphocyte and neuron specific CD200 antigen (*CD200*) which was significantly down-regulated (Kakiuchi et al 2008). The former two alterations have been verified in LCLs (Huang et al 2004) and plasma (Yilmaz et al 2007, Zoroglu et al 2002) or peripheral whole blood (Glatt et al 2005) in least one other independent SCHIZ cohort as reported elsewhere in the literature. *ADM* encodes a potent vasodilator peptide which is abundantly synthesised in the thalamus, hypothalamus and pituitary gland where it is responsible for controlling the body's neuroendocrine responses to stress (Taylor & Samson 2004). Although the precise molecular function of this member of the selenoprotein family has yet to be elucidated, Benton (2002) has suggested that in the presence of deficiency, preferential retention of selenium ions (Se^{2-}) within the brain could be contributing to mood abnormalities. The remaining immunoglobulin related genes (n=2) were considered potential artefacts of the EBV transformation process and subsequently had been excluded from all further analysis (Kakiuchi et al 2008).

1.4.2.2.2 Bipolar Disorder

Transcriptome profiling of immortalised, EBV-transformed B-lymphocytes (LCL's) generated from two pairs of male MZ twins, aged 42 and 49 years, respectively that were discordant for BPD using Affymetrix Hu95A GeneChip® Arrays which contain probes for the interrogation of ∼12,600 well characterised genes revealed overall down-regulation in the expression of 17 transcripts (∼0.1%) (⇩1.60-fold or greater, $p<0.05$) which are associated with the ER stress response pathway (Kakiuchi et al 2003). These included an ER chaperone, heat shock 70kDa protein 5 (*HPSA5*) which is known for its assistance in the refolding of aberrantly formed peptides (Ellgaard & Helenius 2003, Kleizen & Braakman 2004) as well as the HPSA5 regulator, X-box binding protein 1 (*XBP1*) (Dunys et al 2014, Zhang & Kaufman 2006). The former resides at the chromosome 22q12.3 locus which has previously been implicated in BPD (Marcheco-Teruel et al 2006, Mujaheed et al 2000, Potash et al 2008, Potash et al 2003). Moreover, a -116 C⇢G polymorphism identified within the upstream promoter region of the *XBP1* gene, which disrupts its putative binding site by altering the consensus motif from an ACGT to AGGT, is reported to be a significant risk factor for BPD in a Japanese cohort comprising 140 bipolar I and 57 bipolar II disorder cases and 451 unrelated neurologically healthy control subjects [OR 4.60 with 95% CI between 2.1 and 10.2] (Kakiuchi et al 2003). Upon induction of the ER stress response pathway by thapsigargin mediated Ca^{2+} ATPase inhibition the authors demonstrated substantially smaller elevations in the qRT-PCR mRNA levels of *XBP1* and *HPSA5A* transcripts in cultured LCL's from BPD patients versus controls in a direct comparison between the treated and untreated groups. Further *in vitro* experimentation introduced a 7 day pre-incubation period exposing the cells to therapeutic concentrations of the mood stabilizing compound, semisodium valproate, which led to enhanced activation of the transcription factor *ATF6* (activating transcription factor 6) and an amelioration of this potentially toxic outcome (Shen & Prywes 2005, Yoshida et al 2001).

The findings of Kakiuchi et al (2003), however, could not be replicated in a more recent case-control study of three additional pairs of Australian MZ twins including one male aged 23 years and two females aged 38 and 58 years, respectively which were profiled using the Affymetrix Human Genome U133 plus 2.0 GeneChip® Arrays (Section 1.3.2.2.2). In contrast, Matigian et al (2007) reported the DE of a number of transcripts involved in the WNT signalling cascade that influences cell migration & proliferation during embryonic development. It is also important for axon guidance in the CNS as well as being a key determinant of cell fate via its mediation of pro-apoptotic pathways.

1.5 Summary of Project Aims and Objectives

The principle aim of the PhD was to perform GEP of peripheral tissues in ALS. In the first instance whole blood was trialled since it lends itself to good standardisation of technical procedures, it is readily accessible and it can be collected in large volumes, longitudinally. However, in evaluating NuGEN Technologies Inc., UK patented linear single primer isothermal amplification (SPIA™) method this proved no more reliable than the previously unsuccessful Ambion® GLOBINClear™ protocol developed in house by Dr Rohini Raman (2011). Evidence is suggestive of the sheer abundance of erythrocyte derived alpha and beta haemoglobin transcripts (constituting up to 70% of the total RNA species isolated from peripheral whole blood) producing interference on the microarray which could mask the detection of other, less abundant transcripts of equal biological importance that are also contained within the sample. For this reason, we proceeded instead to investigate the use of immortalised EBV-transformed B-lymphocytes or lymphoblastoid cell lines (LCL's) (representing a genetically homogenous cell population which can be cultured *in vitro* to support downstream functional assays) in order to address the following: 1) Upon discovery, in 2011, of a large, intronic hexanucleotide G_4C_2 repeat expansion (DeJesus-Hernandez et al; Renton et al) of >30 copies in the previously uncharacterised *C9ORF72* gene, which is now recognised as the most frequent cause of ALS and bvFTLD, elucidate further the mechanism(s) of *C9ORF72* neurotoxicity in ALS and 2) Within this specific genetic subtype, establish whether there are modifiers of survival [i.e. a fast (<2yrs) versus slow (≥4yrs) disease progression] that can led us to identify potential new areas of future therapeutic research.

CHAPTER 2: MATERIALS AND METHODS

2.1 Clinical Characteristics

2.1.1 NuGEN Ovation® Whole Blood Study

Participants recruited into the NuGEN Ovation® Whole Blood Study were Caucasian and of North European descent. These were comprised of six Riluzole treated SALS [3-M, 3-F] patients and an equal number of age, as well as gender, matched neurologically normal, healthy control [3-M, 3-F] subjects. Age at symptoms onset ranged between 38 and 71 years with a mean of 60.3±15yrs (Table 2.1). Survival from the time of diagnosis to the point at which the tissue samples were donated ranged from 12 months to a minimum of 6 years with average disease duration of approximately 3 years and 4 months.

Sample ID	Diagnosis	Gender	Age at Onset	Survival
BLDCON01	control	M	48	n/a
BLDCON02	control	F	47	n/a
BLDCON04	control	M	54	n/a
BLDCON07	control	F	56	n/a
BLDCON08	control	M	40	n/a
BLDCON10	control	F	43	n/a
BLDPAT21	SALS	M	66	1yr
BLDPAT23	SALS	F	70	2yrs
BLDPAT26	SALS	F	38	≥4yrs
BLDPAT27	SALS	M	71	≥5yrs
BLDPAT35	SALS	M	71	2yrs
BLDPAT38	SALS	F	46	≥6yrs

Table 2.1 Clinical Characteristics of SALS Patient and Control Samples Recruited to the NuGEN Ovation® Whole Blood Study Symptom onset could be defined as the age at which the patient first presented with significant weakness. Survival was approximated to the nearest year and in instances where an individual was still reported to be alive, a minimum disease duration was calculated using the time of diagnosis to the point at which the tissue samples were donated [indicated by the greater than or equal to (≥) symbol].

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, BLDCON - blood control, BLD PAT - blood patient, F - female, M - male, n/a - not applicable and S - sporadic.

2.1.2 ECACC LCL Study

ECACC established lymphoblastoid cell lines (LCL's) (n=820) [120-FALS, 500-SALS and 200-CTRL] were obtained from patients and their spouses or unrelated carers attending clinics in the Birmingham (28.8%), London (29.6%) or Sheffield (41.6%) districts between November 2003 and June 2011 (Figure 2.1). The Birmingham hub included satellite centres from Belfast City Hospital (BBe) (n=11/236), Oxford (BOx) (n=3/236), Bristol's Frenchay Hospital (BBr) (n=2/236) and Liverpool (BLi) (n=27/236); The London hub included satellite centres from Plymouth Derriford Hospital (LPy) (n=2/243), Cambridge (LCa) (n=6/243), Southampton General Hospital (LSh) (n=9/243), Poole General Hospital (LPo) (n=17/243), London Royal Free Hospital (LRf) (n=2/243), Royal London Hospital (LRo) (n=3/243) and the London National Hospital (LNh) (n=14/243); The Sheffield hub included satellite centres from Preston (SPr) (n=10/341), Manchester (SMa) (n=19/341), Newcastle (SNc) (n=48/341), Nottingham (SNt) (n=22/341) and Durham (SDu) (n=5/341) (Figure 2.1).

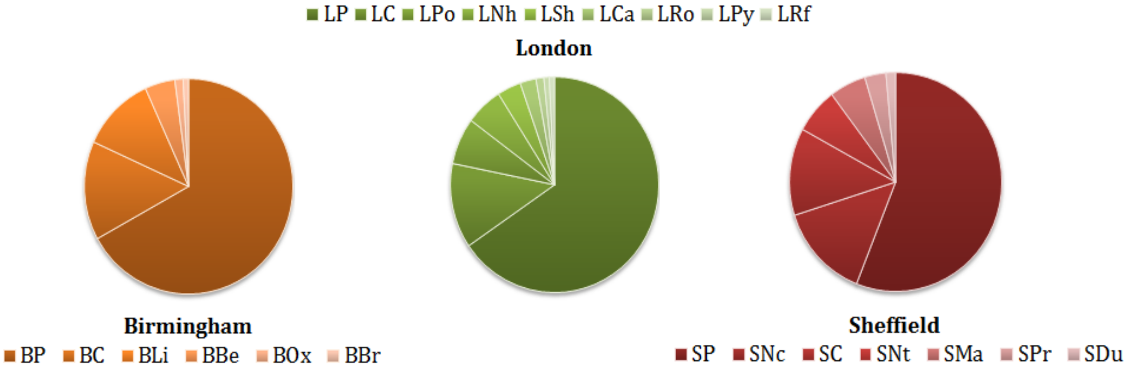
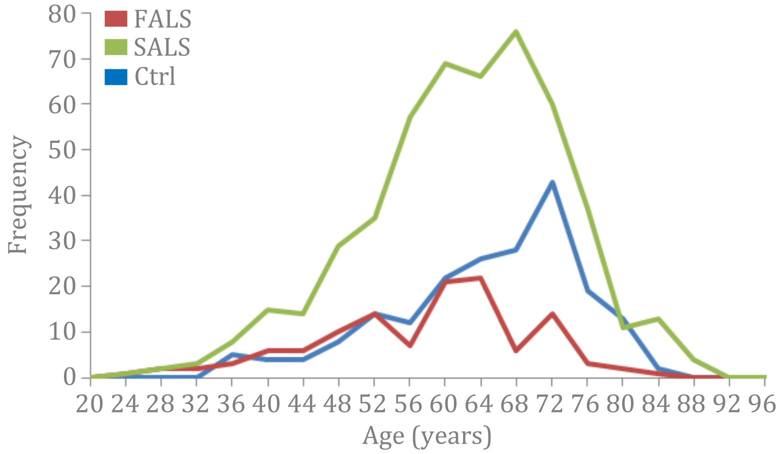


Figure 2.1 ECACC LCL Breakdown of UK Biosample Collection Centres Three National Research Hubs are represented in Orange [B] (Birmingham), Green [L] (London) and Red [S] (Sheffield) with the surrounding satellite centres encoded by the prefixes: Li - Liverpool, Be - Belfast City Hospital, Ox - Oxford, Br - Bristol Frenchay Hospital, Po - Poole General Hospital, LNh - London National Hospital, Sh - Southampton General Hospital, Ca - Cambridge, LRo - Royal London Hospital, LPy - Plymouth's Derriford Hospital, LRf - London Royal Free Hospital, Nc - Newcastle, Nt - Nottingham, Pr - Preston, Ma - Manchester and Du - Durham.

Abbreviations: BC - Birmingham control, BP - Birmingham patient, ECACC - European Collection of Cell Cultures, LC - London control, LCL - lymphoblastoid cell line, LP - London patient, SC - Sheffield control and SP - Sheffield patient.

All of the participants recruited to the study were Caucasian and of North European descent. Patients were diagnosed according to the World Federation of Neurology's amended EEC of 1998 (Section 1.1.3) (Figure 1.1) with either definite (n=248/620) or probable (n=345/620) ALS in 95.7% of cases, which included four incidences of concomitant FTLD (Section 1.2.1) and two incidences of concomitant PD (Section 1.2.1). In the remaining 4.3% of the cohort there were also several reported cases of rare variants of MND including PBP (n=23/620) (Section 1.2.2.1), PLS (n=3/620) (Section 1.2.2.2) and PMA (n=1/620) (Section 1.2.2.3). Two hundred neurologically normal, healthy control subjects selected from the National MNDA (Motor Neurone Disease Association) DNA Bank were age and gender matched to the SALS (n=500) population with the average FALS patient developing symptoms approximately five years earlier. M:F ratios were comparable across SALS cases and controls but were found to be slightly lower in cases of FALS (n=120) (Figure 2.2).



	FALS	**SALS**	**Control**
M:F	1.45:1	1.75:1	1.74:1
Age	55.4±12yrs	60.2±11yrs	63.2±11yrs
Total	**120**	**500**	**200**

Figure 2.2 Age Frequency Distribution of Patient and Control LCL's in the ECACC Microarray Study (n=820) [120-FALS, 500-SALS and 200-CTRL]

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, Ctrl - control, ECACC - European Collection of Cell Cultures, F - female, F - familial, LCL - lymphoblastoid cell line, M - male and S - sporadic.

All of the FALS cases were assigned to the discovery cohort. Controls and SALS, on the other hand, were ranked, in ascending order according to age, and allocated the number one (discovery cohort) (Section 4.1.1) or two (replication cohort) (Section 4.1.2) alternately down the list. A further detailed analysis of the two cohorts can be found at the beginning of Chapter 4: 'Characterisation of LCL's'.

2.2 Materials

This project was funded by EuroMOTOR (European Multidisciplinary ALS Network Identification to Cure Motor Neurone Degeneration) under the Seventh Framework Health Cooperation Programme (FP7/2007-2013) (euromotorproject.eu). The work was approved by the South Sheffield Research Ethics Committee [REC12/YH/0330; STH16573]. Prior to biosample collection informed written consent was obtained for all patient and control donors agreeing to participate in either of the two studies.

2.2.1 Biological Specimens

2.2.1.1 Peripheral Whole Blood

PAXgene® Blood RNA Collection Tubes (2.5mL) (PreAnalytiX, GmbH) and BD Vacutainer® Venous Collection Tubes (6.0mL) (BD Diagnostics) were purchased from BD Biosciences, UK.

2.2.1.2 Lymphoblastoid Cell Pellets

Frozen EBV-transformed, immortalised lymphoblastoid cell (LCL) pellets, preserved in RNA*later*™ (Sigma-Aldrich®, UK), were obtained from the National MNDA DNA Bank held at the Health Protection Agency's (HPA) European Collection of Cell Cultures (ECACC) (Public Health England, UK) (Section 2.3.2.1).

2.2.2 Solutions, General Chemicals and Laboratory Consumables

Nuclease free (NF) double-distilled water (ddH_20) was purchased from QIAGEN Ltd., UK. TE buffer [10mM tris-(hydroxymethyl)-aminomethane hydrogen chloride (Tris-HCl) and 1mM ethylenediaminetetraacetic acid (EDTA), pH 7.5 at 25^0C] was supplied by EPICENTRE® Biotechnologies (Illumina Inc., UK). TAE buffer [0.4mM Tris-acetate EDTA and 0.01mM Sodium EDTA, pH 8.2 at 25^0C] was prepared using reagents supplied by Sigma-Aldrich®, UK. Molecular grade agarose was purchased from Bioline, UK. The intercalating nucleic acid stain, GelRed™ was purchased from Biotium, UK. All other general chemicals were purchased from Thermo Fisher Scientific® Inc., UK including analytical grade isopropanol and absolute ethanol.

Stratagene qPCR Human Reference Total RNA [1µg/µL in 0.1mM EDTA/RNase-*free* H_20] was purchased from Agilent Technologies Ltd., UK. Actin, beta (*ACTB*) primers, designed by Dr Marta Milo (Department of Biomedical Science (BMS), University of Sheffield), were supplied by Invitrogen™ (Life Technologies Ltd., UK). Haemoglobin alpha 2 (*HBA2*) primers, designed by Dr Paul Heath (SITraN), were purchased from Sigma-Aldrich®, UK and optimised, previously by Dr Rohini Raman (Department of Neuroscience, University of Sheffield). 18S ribosomal RNA (*18SrRNA*) forward and reverse sequences were designed and optimised by Dr J Robin Highley (SITraN). All other standard qRT-PCR primers were synthesised and shipped from Eurofins MWG Operon, Germany. Stratagene Brilliant II and FastStart Universal SYBR® Green PCR Master Mixes were purchased from Agilent Technologies Ltd., UK and Roche Diagnostics (GmbH, Germany), respectively. The IDT PrimeTime® Mini qPCR Assays were supplied by Integrated DNA Technologies® Inc., USA. Brilliant III Ultra-Fast qRT-PCR Master Mix was purchased from Agilent Technologies Ltd., UK. Thin-walled 96-well plates and optical caps were manufactured by Geneflow Ltd., UK.

For performing gel shift assays precast 15-well (15µL) 4-20% polyacrylamide mini-PROTEAN® TBE™ gels were purchased from Bio-Rad Laboratories Ltd., UK. Neutr Avidin™ biotin-binding protein and a 1X phosphate buffered saline (PBS) solution, supplied at pH of 7.2±0.05 (Invitrogen Gibco®), were purchased from Thermo Fisher Scientific® Inc., UK. A 1X Tris Borate EDTA (TBE) buffer solution [89mM Tris-borate and 2M EDTA, pH 8.3±0.1 at 25^0C] was prepared using reagent supplied by Sigma-Aldrich®, UK. Ethidium bromide was also purchased from Sigma-Aldrich®, UK. DNA Loading Buffer Blue (5X) and the molecular weight markers HyperLadder™ IV (100 -1000bp) and HyperLadder™ V (25-500bp) were purchased from Bioline Reagents Ltd., UK.

Human Genome U133 (HG_U133) Plus 2.0 GeneChip® Arrays used in the analysis of Chapter 3: 'Whole Blood Study' and the Human Exon 1.0ST GeneChip® Arrays used in the analysis of Chapter 5: '*C9ORF72* GEP Study' and Chapter 6: '*C9ORF72* Survival Study', were purchased from Affymetrix® Ltd., UK. More traditional 3'IVT Expression Arrays were selected for the whole blood study to maintain consistency between the JB and RR (Raman 2011) generated datasets and in order to draw direct comparisons between the NuGEN Ovation® Whole Blood Solution (Section 3.5.1.2.1) and the

Ambion® GLOBINClear™ (Section 3.5.1.2.2) protocols. For the subsequent profiling of EBV-transformed, immortalised B-lymphocytes (LCL's) (Section 2.1.2), for which a large bank of cases and controls was available, the more comprehensive Human Exon 1.0ST GeneChip® Arrays were chosen since they provide better coverage [>1. 4M probesets with sequences designed to span the entire length of the gene, rather than being targeted at the far 3' end of the transcript, which may be prone to small amounts of degradation during storage/handling (Section 2.3.2.4.1)] and in addition to differential expression, are also beneficial in detecting novel alternative splicing events.

2.2.3 Reagents and Kits

The PAXgene® Blood RNA Isolation Kits (PreAnalytiX, GmbH) and RNeasy® Mini Kits were purchased from QIAGEN Ltd., UK. DNase I (RNase-*free*™) (2,000 units/mL) and 10X deoxyribonuclease (DNase) reaction buffer [25mM $MgCl_2$ (magnesium chloride), 5mM $CaCl_2$ (calcium chloride) and 100mM Tris-HCl (Tris hydrochloride), pH 7.6 at 25^0C] were purchased from New England BioLabs® Ltd., UK. Eukaryotic Total RNA 6000 Nano LabChip® Kits were purchased from Agilent Technologies Ltd., UK. ABI High Capacity RNA to cDNA Synthesis Kits (Applied Biosystems®) were purchased from Life Technologies Ltd., UK.

The NuGEN Ovation® Amplification System V2, Whole Blood Solution and Encore™ Biotin Module were purchased from NuGEN Technologies Inc., The Netherlands. The MinElute® Reaction Clean-Up Kits were purchased from QIAGEN Ltd., UK. The Ambion® TURBO DNA-*free*™ DNase Treatment and Removal Kit (Applied Biosystems®) was purchased from Life Technologies Ltd., UK.

Ambion® Kits required for the Whole Transcriptome (WT) Expression Assay were purchased from Life Technologies Ltd., UK. The GeneChip® Eukaryotic Poly-A RNA Control, Fragmentation & Terminal Labelling Kits were purchased from Affymetrix® Ltd., UK. The SAPE (Streptavidin Phycoerythrin) staining solution, stringency wash buffers and hybridization reagents were also purchased from Affymetrix® Ltd., UK.

2.3 Methods

2.3.1 GEP from Peripheral Whole Blood

2.3.1.1 Tissue Collection and Storage

Patient donors and their spouses or unrelated carers were fasted overnight prior to phlebotomy which was performed between the hours of 8.00 and 11.00am. Whole venous blood was collected directly into sterile (2.5mL) evacuated PAXgene® Blood RNA Collection Tubes containing a proprietary reagent for the immediate stabilization of intracellular RNA. Blood specimens were transported at RT (room temperature) and stored at -20^{0}C upon arrival, for no more than 3 years.

2.3.1.2 PAXgene® Extraction of Total RNA from Whole Blood

Blood specimens were defrosted overnight in the refrigerator, set at 4^{0}C, and equilibrated to RT for a minimum of 2 hours, to ensure the complete lysis of blood cells, immediately prior to extraction using the PAXgene® Blood RNA Isolation Kit. Briefly, PAXgene® Blood RNA Collection Tubes (2.5mL) were centrifuged for 10 minutes at 5,000g, the supernatant was discarded and the pellet re-dissolved in RNase-*free*™ water. This step was repeated using 350μL re-suspension buffer and the samples incubated in a 55^{0}C shaking water bath, set a 190rpm for 10 minutes, in the presence of 40μL proteinase K and 300μL binding buffer in order to bring about protein digestion. An additional centrifugation step through the PAXgene® shredder column was required for 3 minutes at 13,000g to homogenise the cell lysate and to remove any residual debris. The supernatant was then transferred into a fresh microcentrifuge tube and the binding conditions adjusted with absolute ethanol. After a brief 1 to 2 second centrifugation at 1,000g the lysate was pipetted directly onto the PAXgene® RNA spin column and centrifuged for a further minute at 13,000g, to permit selective binding of the RNA onto the silica membrane. The membrane was then treated for 15 minutes at RT with 10μL DNase I and 70μL DNA digestion buffer to eradicate unwanted traces of bound DNA. A series of subsequent wash steps were performed in pre-optimised buffers in order to remove any remaining contaminants. The liquid flow-through was discarded and the spin columns transferred to fresh microcentrifuge tubes. Two applications of elution buffer, each followed by a centrifugation step for 1 minute at 13,000g eluted the RNA. Samples (40µL) were heat-denatured for 5 minutes at 65^0C and snap-cooled on ice.

2.3.1.3 RNA Yield and Quality Assessment

Nucleic acid concentrations were determined using the NanoDrop™ 1000 Spectrophotometer (Thermo Fisher Scientific® Inc., UK). The ratio of sample absorbance (A) at 260/280 or 260/230nm wavelengths was used in order to measure the purity of the isolated material. RNA that is pure should have a value of approximately 2.0±0.2. Anything below 1.8 ($A_{260/280}$) is indicative of DNA/protein contamination or may be due to some residual carryover ($A_{260/230}$) of phenolic compounds and/or chaotropic salts from the extraction process. A small quantity of sample (1µL) was also removed to perform a Eukaryotic Total RNA 6000 Nano Assay on the Agilent 2100 Bioanalyzer (Agilent Technologies Ltd., UK). An algorithm applied by the software assesses the degree of separation between 18S and 28S ribosomal peaks on the electropherogram trace in order to compute an RNA integrity number (RIN) between 0 (undetectable, completely degraded) and 10 (high quality, intact RNA) (Schroeder et al 2006). In a study conducted by Copois et al (2007) the authors suggest that a threshold of 7.8 is sufficient for the generation of robust microarray gene expression data.

2.3.1.4 cDNA Synthesis

2.3.1.4.1 cDNA Synthesis for qRT-PCR

Total RNA isolated from peripheral whole blood was reverse transcribed into single-stranded complementary DNA (ss-cDNA). cDNA synthesis was performed using the ABI High Capacity RNA to cDNA Synthesis Kit in accordance with the manufacturers guidelines. To 1µg of starting material, a 1X enzyme and reverse transcriptase (RT) buffer mix was added and the total reaction volume (20µL) made up in NF ddH_20. A no-RT control to check for the presence of potentially contaminating genomic DNA was prepared as described without the addition of RNA-dependent DNA polymerase that is required for reverse transcription. Sample preparations were incubated in a G-storm GS2 Thermal Cycler (GRI Gene Technologies Ltd., UK) at 37^0C for 1 hour and heat-denatured at 95^{0}C for 5 minutes. In each reaction it is assumed that there is an approximate 1:1 conversion of RNA to cDNA. The cDNA products were diluted in NF ddH$_2$0 and stored at 4^{0}C overnight or at -20^{0}C prior to use in either traditional SYBR® Green qRT-PCR or IDT PrimeTime® Mini qPCR Assays at an optimised concentration of 12.5ng/μL.

2.3.1.4.2 cDNA Synthesis for Linear SPIA™ Amplification

The Ovation® RNA Amplification System V2 was used in order to generate reverse transcribed cDNA for the NuGEN Technologies Inc. patented SPIA™ method of single primer isothermal amplification. Approximately 50ng total RNA dissolved in NF dd H$_2$0 was combined with the first-strand primer mix and incubated in a pre-warmed MJ Research PTC-100® Peltier Thermal Cycler (Bio-Rad Laboratories Inc., UK) at an annealing temperature of 65^{0}C for 5 minutes. The tubes were snap-cooled on ice for a minimum of 2 minutes prior to the addition a first-strand buffer and enzyme master mix. Incubation occurred at 48^{0}C for 60 minutes and the samples heat-denatured at 70^{0}C for 15 minutes. Second-strand cDNA synthesis was performed at 37^{0}C for 30 minutes followed by an additional incubation step at 75^{0}C for 15 minutes. The tubes were cooled to 4^{0}C and placed on ice before proceeding immediately with the SPIA™ amplification protocol outlined in Section 2.3.1.5.1.

2.3.1.5 NuGEN Ovation® Whole Blood Solution

2.3.1.5.1 NuGEN Linear SPIA™ Amplification

Linear SPIA™ amplification was performed using the NuGEN Ovation® Whole Blood Solution in conjunction with the NuGEN Ovation® RNA Amplification System V2. The procedure was carried out under sterilised conditions in the Clean View UV Cabinet (Cleaver Scientific Ltd., UK). Briefly, products of the cDNA synthesis reaction (Section 2.3.1.4.2) were combined with an SPIA™ Master Mix containing a unique DNA/RNA chimeric primer, DNA polymerase and RNase H. The reaction was incubated in a pre-warmed MJ Research PTC-100® Peltier Thermal Cycler for 1 hour at 37^{0}C. After the first 30 minutes the programme was paused to permit the separate addition of the Ovation® Whole Blood Reagent and, following a second 30 minute incubation the tubes were heat-denatured to 95^{0}C, for 5 minutes and snap-cooled on ice for at least 2 minutes before being stored at -20^{0}C, prior to purification (Section 2.3.1.5.2).

2.3.1.5.2 QIAGEN MinElute® Purification of NuGEN Amplified Material

Amplified SPIA™ cDNA was purified using the QIAGEN MinElute® Reaction Clean-Up Kit, according to the recommendations of NuGEN Technologies Inc., UK. Briefly, the samples were combined with binding buffer ERC and passed through a QIAGEN MinElute® Spin Column at a centrifugation speed of 13,000g for 1 minute. Under a high chaotropic salt concentration the cDNA is adsorbed onto the silica membrane whilst unwanted traces of enzymes/detergents and unincorporated nucleotides are effectively removed from the system. The membrane is washed with buffer PE and 80% freshly prepared ethanol solution. Following each addition the columns were centrifuged at 13,000g, for 1 minute and the flow-through, containing contaminants was discarded. The purified products were eluted in 30µL NF ddH$_2$0 at RT and quantified using the NanoDrop™ 1000 Spectrophotometer (Section 2.3.1.3), prior to being stored at -20^{0}C.

In addition, pre-amplified material from BLDPAT23 was treated with the Ambion® TURBO DNA-*free*™ DNase Treatment and Removal Kit. Briefly, 10µg of sample was combined with a 1X TURBO DNase buffer and 2 units of TURBO DNase enzyme in a 50µL reaction volume. Following 30 minutes incubation at 37^{0}C, 0.1 volumes of re-suspended DNase inactivation reagent was added and the sample maintained at RT for 5 minutes. A short centrifugation step was performed at 10,000g for 90 seconds and the supernatant containing purified cDNA carefully transferred to a fresh 0.5mL Eppendorf tube.

2.3.1.5.3 Encore™ Biotin-Labelling of Fragmented cDNA Targets

The NuGEN Encore™ Biotin Module was used to generate fragmented, biotinylated ss-cDNA targets suitable for hybridization onto Affymetrix® Human Genome U133 Plus 2.0 GeneChip® Arrays. A fragmentation buffer/enzyme master mix was applied to 4.4µg purified SPIA™ cDNA dissolved in NF H$_2$0 to create a final reaction volume of 32µL. The samples were incubated in a pre-warmed MJ Research PTC-100® Peltier

Thermal Cycler at 37^{0}C for 30 minutes before reaching a denaturation temperature of 95^{0}C for 2 minutes and snap-cooled on ice. A second incubation in the presence of a proprietary labelling buffer, reagent and enzyme mater mix was then performed at 37^{0}C for 60 minutes, followed by 70^{0}C for 10 minutes. This resulted in attachment of a single biotin molecule to the 3-hydroxyl terminal nucleotide of each SPIA™ cDNA fragment; with typical fragments ranging in length between 50 and 100bp. Products were analysed on the Agilent Bioanalyser (Section 2.3.1.3) and stored at -20^{0}C.

A detailed description of the Ambion® GLOBINClear™ procedure, carried out by Dr Rohini Raman (Raman 2011), can be found on page 67 of her doctoral dissertation titled: "Gene Expression Profiling to Identify Biomarkers of Motor Neuron Disease".

2.3.1.6 Quantitative Real-Time PCR

Quantitative RT-PCR (qRT-PCR) was performed in duplicate 10μL reaction volumes (Table 2.2) containing 12.5ng of cDNA template, optimum concentrations of forward (F') and reverse (R') primer sequences, a 1X Stratagene Brilliant II SYBR® Green/2X FastStart Universal SYBR® Green PCR Master Mix and RNase-*free*™ water. Each run also included a negative no-RT and no template control (NTC). Haemoglobin, alpha 2 (*HBA2*) transcript levels were measured pre- and post-SPIA™ amplification using the standard housekeeping gene actin, beta (*ACTB*) which served as a positive endogenous control. *ACTB* was selected over other commonly chosen normalisers, such as 18S ribosomal RNA (*18SrRNA*) and glyceraldehyde-3-phosphate dehydrogenase (*GAPDH*) since it was found to exhibit the most stable level of expression, across all of the samples in the experiment, using MAS 5.0 pivot data displayed by GeneChip® Operating Software (GCOS), Affymetrix® Ltd., UK.

A "Normal 2 Step" profile for qRT-PCR products of less than 150bp was set up with FAM as the reporter dye and ROX the internal reference control, using a Stratagene Mx3000P™ Real Time PCR Thermal Cycler from Agilent Technologies Ltd., UK. An initial temperature step at 95^{0}C for 10 minutes was required in order to activate the SureStart *Taq* DNA polymerase. This was followed by 40 cycles of heat denaturation at 95^{0}C for 30 seconds and primer annealing/extension at 60^{0}C for 60 seconds. The programme ended with three final temperature steps; one at 95^{0}C for 60 seconds, a

Gene	Transcript	Region	Primer Sequence (5’ ---> 3’)	Tm	GC%	Amplicon	Optimum conc.
HBA2	ENST00000251595	Exon 1-2	F’ GCCCTGGAGAGGATGTTCCT R’ CGTGGCTCAGGTCGAAGTG	61.0 60.7	60.0 63.2	70bp	300/300nmol
Housekeeping Gene							
ACTB	ENST00000331789	Exon 4	F’ TCACCGAGCGCGGCT R’ TAATGTCACGCACGATTTCCC	61.2 59.0	73.3 47.6	60bp	300/300nmol

Table 2.2 qRT-PCR Primers and Optimum Concentrations for Validation of the NuGEN Ovation® Whole Blood Study

Abbreviations: 3’ - three prime, 5’ - five prime, *ACTB* - actin, beta, F’ - forward primer sequence, *HBA2* - haemoglobin, alpha 2, qRT-PCR - quantitative real-time PCR, R’ - reverse primer sequence and Tm - melting temperature.

second at 60^0C for 30 seconds and a third at 95^0C for 30 seconds.

This technology utilises fluorescence based detection chemistry, which enables the investigator to accurately detect and quantify the abundance of a particular nucleic acid transcript during each amplification cycle of the PCR reaction. It is reliant upon an intercalating dye, in this case SYBR® Green I, that binds indiscriminately and with high affinity to the minor groove of newly synthesised double-stranded DNA/cDNA. SYBR® Green I absorbs light at a maximum wavelength of 497nm and, in its excited state, it has an emission peak of around 520nm. During the exponential phase, the quantity of fluorescently labelled product accumulates, in a linear manner, as more and more amplicons are created. This leads to a quantifiable increase in the signal intensity readout; which is a measure directly relating to the length of the amplified target, as well as, the number of copies produced. Version 4.10, build 389 of Stratagene MxPro™ QPCR Software (Agilent Technologies Ltd., UK) records the Ct or cycle threshold value which is defined as the minimum number of cycles required before the signal can be detected above background levels of the NTC. Relative mean concentrations were determined by calculating the differences in Ct values between the gene of interest and the endogenous housekeeping control.

2.3.1.7 Agarose Gel Electrophoresis

In order to ascertain whether pre- and post-SPIA™ amplified PCR products were of an anticipated size for measurements of *ACTB* and *HBA2* transcript levels in peripheral whole blood three SALS patient and control samples were selected at random to perform agarose gel electrophoresis. PCR products (7µL) and a 25-500bp molecular weight marker (5µL) (HyperLadder™ V) were run at 120V for approximately 30 to 40 minutes on a 3.0% agarose gel made up in a 1X TAE buffer solution [0.4Mm Tris-acetate and 0.01mM Sodium EDTA, pH 8.2 at 25^0C] and 3X concentration of the intercalating nucleic acid stain GelRed™ (a non-toxic alternative to Ethidium Bromide) [APPENDIX FIGURE A3]. The bands which formed were visualised under a UV light source using the Syngene GENi Gel Documentation System.

2.3.1.8 Affymetrix® HG_U133 Plus 2.0 GeneChip® Arrays

2.3.1.8.1 HG_U133 Plus 2.0 GeneChip® Arrays

Affymetrix® HG_U133 Plus 2.0 GeneChip® Arrays are high-density oligonucleotide arrays with 1.3M distinct features, comprising ~54,000 probesets [11 pairs of PM and MM probes of 25-mer synthesised *in situ* directly onto the glass slide by photo-lithography. The latter deviates from its complementary target by a single base at the 13th position where an adenine (A) is substituted for thymine (T) and guanine (G) is substituted for cytosine (C), or vice versa] for the detection of >47,000 unique transcripts and variants including more than 38,500 well characterised genes which are represented in the National Centre for Biotechnology Information (NCBI) (ncbi.nlm .nih.gov) GenBank®, dbEST or RefSeq database (Benson et al 2014, Boguski et al 19 93, Pruitt et al 2014). Compared to previous generations, Plus 2.0 GeneChip® Arrays provide coverage of an additional 6,500 genes (Boguski & Schuler 1995, Schuler 19 97, Schuler et al 1996) with sequence clusters generated from the UniGene build 133 (April 2001) and 159 (January 2003) of the human genome.

2.3.1.8.2 Hybridization

SPIA™ ss-cDNA targets, post-fragmentation and labelling, were hybridized onto the Affymetrix® HG_U133 Plus 2.0 GeneChip® Arrays following recommendations made by NuGEN Technologies Inc., UK and in accordance with the instructions contained in the GeneChip® Expression Analysis Technical Manual (Affymetrix® Ltd., UK) for use with the Affymetrix® GeneChip® 3' IVT Expression Kit.

GeneChips® were equilibrated to RT immediately prior to their use. Reagents were thawed on ice and the 20X Eukaryotic hybridization control stock heated to 65^{0}C for 5 minutes or until the cRNA was completely re-suspended. A hybridization cocktail was prepared in 1.5mL Eppendorf tubes by combining 50µL of sample with the 20X Eukaryotic hybridization control stock (11µL) [bacterial genes *bioB, bioC* and *bioD* of the *E. coli* biotin synthesis pathway and the recombinase protein *cre* from the P1 bacteriophage at respective concentrations of 1.5 (represents the limit of detection), 5, 25 and 100pM (American Type Culture Collection)], 2X hybridization buffer (100 µL) [100mM 2-(*N*-morpholino)ethanesulfonic acid (MES), 0.01% Tween-20 (pH 6.6 at 25^{0}C), 1M [Na$^+$] and 20mM EDTA], 10% dimethyl sulfoxide (DMSO) (22µL), 2nM concentrations of control oligonucleotide B2 (3.7µL) and sufficient amounts of RNase-*free*™ water to bring the total reaction volume up to 220µL.

Control oligonucleotide B2 hybridizes to the checkerboard pattern in each corner of the array as well as predefined features along its outer edge. These distinct patterns are important in aiding Microarray Suite version 5.0 (MAS5.0) (Affymetrix® Ltd., UK) in correctly aligning each array to a grid during the initial stages of image handling. Signal intensities generated from the serial concentrations of *bioB, bioC, bioD* and *cre* are used to provide the software with additional information on the efficiency of the hybridization, washing and staining procedures.

After the preparation of the hybridization cocktail, the tubes were flicked to mix and their contents collected by centrifugation. The reaction mixture was heated to 99⁰C for 2 minutes, then cooled to 45⁰C for 5 minutes and centrifuged at maximum speed for 1 minute. The microarrays were primed with 200µL of pre-hybridization mix before being loaded into the GeneChip® Hybridization Oven 640 (Affymetrix® Ltd., UK) with rotation set at 60rpm. Following an incubation step at 45⁰C for 10 minutes, the pre-hybridization mix was discarded and replaced with an identical volume, 200µL of the hybridization cocktail before being returned to the oven for 18±2 hours overnight.

2.3.1.8.3 Washing, Staining and Scanning

Post-hybridization washing and staining was performed on the GeneChip® Fluidics Station 450 applying fluidics protocol FS450_0004 and the standard 49 format Euk-GEWS2v4_450 script, which are outlined in the GeneChip® Expression Wash, Stain and Scan User Manual for Cartridge Arrays (Affymetrix® Ltd., UK). Briefly, the hybridization cocktail was removed and stored at 4⁰C. Cartridges were loaded with 200 µL non-stringent Wash Buffer A [6X SSPE containing 0.02M EDTA, 3M NaCl (sodium chloride), 0.2M NaH_2PO_4 (monosodium phosphate) and 0.01% Tween-20] and equilibrated to RT. Fresh solutions of staining reagents were then prepared. The SAPE mix for the first and third stain contained 2X stain buffer (300µL) [100nM MES, 1M [Na^+] and 0.05% Tween-20], 1mg/mL (6µL) SAPE, 50mg/mL (24µL) Bovine Serum Albumin (BSA) and 270µL molecular biology grade water for a final reaction volume of 600μL per sample. The antibody (Ab) mix for the second stain contained the same 2X stain buffer (300μL), 10mg/mL (6μL) Goat IgG (immunoglobulin G) stock, 0.5mg /mL (3.6μL) biotinylated Ab, 50mg/mL (24μL) BSA and 266.4μL molecular biology grade water, again to achieve a final volume of 600μL per sample.

Two post-hybridization washes, one with non-stringent Wash Buffer A at 25^{0}C, for 10 cycles with 2 mixes per cycle and another, with stringent Wash Buffer B [100mM MES, 0.1M [Na^+] and 0.01% Tween-20] at 50^{0}C, for 4 cycles with 15 mixes per cycle was followed by the first stain in SAPE solution at 25^{0}C for 10 minutes. A post-stain wash with non-stringent Wash Buffer A at 25^{0}C for 10 cycles with 4 mixes per cycle is then followed by a second and third stain at 25^{0}C for 10 minutes in the Ab solution and 10 minutes in the SAPE solution. A final wash step is then performed with non-stringent Wash Buffer A at 30^{0}C for 15 cycles with 4 mixes per cycle. The cartridges are filled with 250μL of Array Holding Buffer prior to scanning.

2.3.1.9 Bioinformatics Analysis

2.3.1.9.1 Affymetrix® GeneChip® Operating Software

Images processed by the Affymetrix® GeneChip® Scanner 3000 were extracted using the GeneChip® Operating Software (GCOS) version 1.2 (Affymetrix® Ltd., UK).

2.3.1.9.2 GeneSpring GX v11.5.1

CEL files containing information regarding probeset signal intensities as well as the percentages of present (P) or absent (A) calls for patients and controls recruited to the NuGEN Ovation® Whole Blood Study were imported into GeneSpring GX software version 11.5.1 (Agilent Technologies Genomics Ltd., UK) (Chu et al 2001, Dresen et al 2003, Xu et al 2004). Raw expression values were log2 transformed and a PLIER (Probe Logarithmic Intensity Error) 16 normalisation procedure applied without the need for performing a baseline conversion to the median of all the samples (Gyorffy et al 2009). DE transcripts were detected at the 5% significance level by means of an unpaired student's t-test with an FDR corrected $p<0.05$ and FC threshold of greater than or equal to (≥) to plus or minus (±) 1.50.

2.3.1.9.3 Gene Ontology Enrichment Analysis

Affymetrix® ID's were uploaded into the Database for Annotation, Visualisation and Integrated Discovery (DAVID) bioinformatics resource version 6.7 from the National Institute for Allergy and Infectious Diseases (NIAID) which is freely available online at david.abcc.ncifcrf.gov (Huang da et al 2009a, Huang da et al 2009b). Applying an *Homo sapiens* background, functional annotation clustering analysis was performed on GOTERM_BP_FAT and GOTERM_MF_FAT gene ontology (GO) terms with 'Medium' classification stringency [Kappa: similarity term overlap 3, similarity threshold 0.50; Classification: Initial group membership 3, final group membership 3 and multiple linkage threshold 0.50]. Those categories identified as being significantly enriched within the patient populations were defined as having a minimum EASE score above 1.30 and Benjamini-Hochberg FDR corrected $p<0.05$. Kyoto Encyclopaedia of Genes and Genomes (KEGG) pathways were also interrogated using a Fishers Exact t-test conducted at the 5% significance threshold.

An overview of the workflow and analysis pipeline for the 3' IVT Expression Arrays used in the assessment of the JB NuGEN Ovation® WB Solution versus RR Ambion® GLOBINClear™ protocol, for performing GEP from peripheral whole blood in ALS, is provided in Figure 2.3. CEL files generated by Dr Rohini Raman (Raman 2011) were re-analysed in GeneSpring GX v11.5.1 using the same methods as described above in Section 2.3.1.8.2.

2.3.2 GEP from Lymphoblastoid Cell Lines

2.3.2.1 Tissue Collection and Storage

Peripheral whole blood (6.0mL) was collected directly into sterile BD Vacutainer® Venous Collection Tubes containing anticoagulants, in order to prevent clotting, and 1.0mL acid citrate dextrose solution B (ACD-B) [14.7g/L dextrose, 13.2g/L trisodium citrate and 4.8g/L citric acid]. The samples were transported at RT to the HPA ECACC where isolated peripheral blood lymphocytes were transformed *in vitro*, by Epstein-Barr viral (EBV) infection, into stabilised immortal polyclonal B-cell lines. Suspension cultures were grown for up to 8 weeks in T25 tissue culture flasks containing 30 to

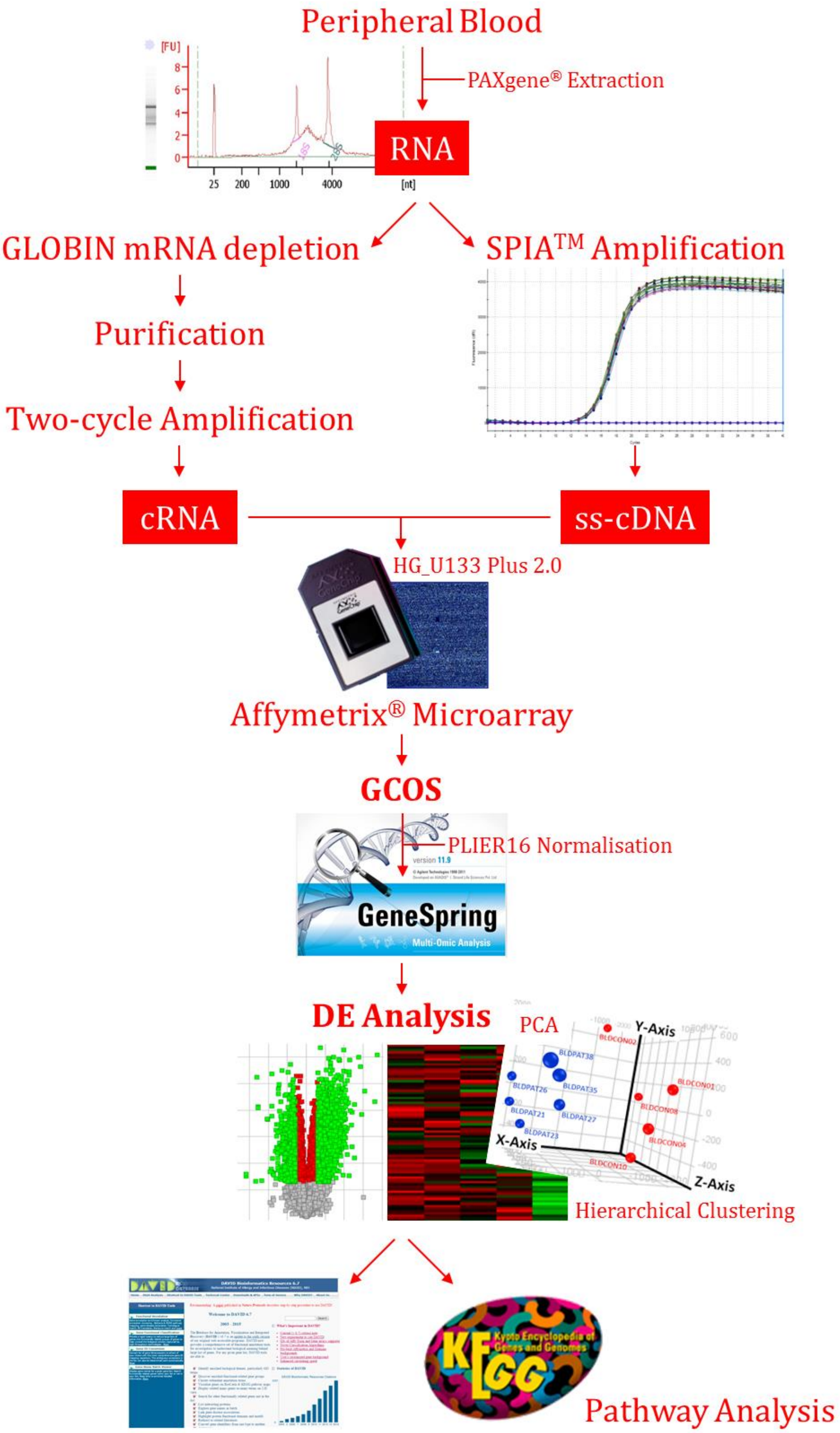


Figure 2.3 Flowchart Schematic of 3' IVT Expression Array Analysis Pipeline Established for Peripheral Whole Blood in ALS.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, cRNA - copy RNA, DE - differential expression, GCOS - GeneChip® Operating Software, HG - Human Genome, IVT - *in vitro* transcription, KEGG - Kyoto Encyclopaedia of Genes and Genomes, mRNA - messenger RNA, PCA - principal component analysis, SPIA™ - single primer isothermal amplification and ss-cDNA - single-stranded complementary DNA.

40mL Roswell Park Memorial Institute (RPMI) 1640 medium [37^{0}C incubator with 5% carbon dioxide ($C0_2$) levels]; supplemented with 20% Foetal Bovine Serum (FBS) and 2mM concentrations of the essential amino acid, glutamate. Frozen cell pellets (LCL's), containing approximately $2x10^{7}$ cells per sample, were preserved in 300µL RNA*later*™. These were shipped on dry ice and stored at -80^{0}C upon arrival.

2.3.2.2 QIAGEN Extraction of Total RNA from Frozen LCL's

Frozen lymphoblastoid cell pellets, preserved in RNA*later*™, were thawed on ice for a minimum of 1 hour prior to extraction using the RNeasy® Mini Kit. The tubes were flicked gently until the pellet was dislodged and vortexed at a low speed in order to re-suspend the cells. A 75µL suspension, containing approximately $5x10^{6}$ cells, was transferred to a sterile 1.5mL microcentrifuge tube. The samples were centrifuged at 13,000g for 1 minute and the supernatant containing the RNA*later*™ stabilization reagent discarded. Cell lysis was immediately brought about by the addition of 600µL buffer RLT. The denaturant within this buffer, guanidine thiocyanate, also functions to preserve RNA integrity through its inhibition of RNase activity. The samples were then vortexed at maximum speed for 1 minute to ensure complete homogenisation of the cell lysate. Appropriate binding conditions were achieved with the addition of 1 volume of freshly prepared 70% ethanol solution. The lysate was pipetted up and down three times to mix and 700µL transferred to an RNeasy® spin column, placed inside a 2mL collection tube, which was centrifuged at 10,000g for 15 seconds. The liquid flow-through was discarded and the procedure repeated with the remaining 500µL of sample in order to permit selective binding of up to 100µg total RNA, of > 200bp in length, to the silica membrane. A series of subsequent wash steps flushes the membrane of any remaining contaminants. Following each separate addition of 700µL buffer RW1 and 500µL buffer RPE the spin columns were centrifuged for 15 seconds at 10,000g and the liquid flow-through discarded. A second application of 500µL buffer RPE with a centrifugation step at 10,000g for 2 minutes removed any residual ethanol which would otherwise have had the potential to interfere with a number of downstream reactions. A dry spin at 13,000g for 1 minute was performed using a fresh 2mL collection tube in order to reduce the carryover of buffer RPE. The spin columns were transferred to sterile 1.5mL microcentrifuge tubes and the total RNA eluted in 40µL RNase-*free*™ water, requiring a further centrifugation step at 13,000g for 1 minute. Nucleic acid concentrations could then be determined using the NanoDrop™ 1000 Spectrophotometer. RNA products were subsequently stored at -80^{0}C. The quality of the extracted material was later assessed on the Agilent 21 00 Bioanalyser (Section 2.3.1.3).

RNA products of particularly poor quality (RIN score below 5.0) underwent DNase treatment to purify the isolated material and to remove potentially contaminating genomic DNA. Briefly, 10µg total RNA was incubated in a pre-warmed MJ Research PTC-100® Peltier Thermal Cycler at 37^{0}C for 10 minutes in the presence of 2 units of DNase I (1µL) and a 1X DNase reaction buffer [10mM Tris-HCl, 2.5mM $MgCl_2$ and 0.5mM $CaCl_2$, pH 7.6 at 25^{0}C]. The program was paused and, following the separate addition of 5mM EDTA, the samples were heated to an inactivation temperature of 70^{0}C for 10 minutes. Tubes were snap-cooled on ice for a minimum of 2 minutes and their contents collected by centrifugation. In instances where there was no visible improvement in the electropherogram trace of the Agilent 2100 Bioanalyser repeat RNA extractions were performed.

2.3.2.3 Affymetrix® WT Sense-Target Labelling Assay

2.3.2.3.1 Linear Amplification

Total RNA isolated from peripheral LCL's was prepared for exon level microarray analysis using the Ambion® Whole Transcriptome (WT) Expression Kit. The protocol utilises a proprietary reverse transcription priming method, designed to specifically prime non-ribosomal RNA including both polyadenylated and non-polyadenylated mRNA. Briefly, on Day 1, total RNA is reverse transcribed into cDNA, which is then converted into anti-sense copy RNA (as-cRNA) by *in vitro* transcription (IVT) using a T7 RNA polymerase. Purification of the amplified as-cRNA was carried out on Day 2, the product of which then became the template for the synthesis of ss-cDNA.

Day 1 On ice, an initial 3µL reaction volume was prepared containing ~300ng total

RNA made up in NF ddH$_2$0. Serial dilutions of positive premixed exogenous controls for the *Bacillus subtilis* genes lys (1:100,000), phe (1:50,000), thr (1:25,000) and dap (1:6,667) was performed according to instructions contained within the Affymetrix GeneChip® Eukaryotic Pol-A RNA Control Kit. In the first dilution, 2μL Poly-A control stock is added to 38μL of the supplied dilution buffer (1:20). After thorough mixing and a short spin in the microcentrifuge, 2μL of the first dilution is added to a further 98μL of dilution buffer (1:50) to prepare the second dilution. The same volume of the second dilution (2μL) is again added to 98μL of dilution buffer (1:50) to prepare the third dilution. The fourth and final dilution was prepared by mixing 7μL of the third dilution with 21μL of dilution buffer (1:4).

Pre-prepared total RNA was then combined with 2μL of the fourth dilution of Pol-A spike in controls prior to the introduction of the first-strand cDNA buffer (4μL) and enzyme (1μL) master mix. Gentle vortexing and a brief 5 second centrifugation step ensured thorough mixing and that the contents of the reaction were collected at the bottom of the tube before proceeding immediately with a 2 hour incubation in a pre-warmed MJ Research PTC-100® Peltier Thermal Cycler. The samples were heated to 25^{0}C for 60 minutes, followed by 42^{0}C for a further 60 minutes and then cooled to 4^{0}C for a minimum of 2 minutes. The temperature of the lid was maintained at 50^{0}C throughout the cycle. At the end of the programme the tubes were centrifuged for 5 seconds and placed on ice. A second-strand cDNA buffer (12.5μL) and enzyme (5μL) master mix was then added and the reaction volume made up to 60μL with NF ddH$_2$0. The tubes were vortexed, spun-down in a microcentrifuge and incubated, this time with the heated lid disabled, at 16^{0}C for 60 minutes followed by 65^{0}C for 10 minutes and then 4^{0}C for at least of 2 minutes. At the end of the programme the tubes were again centrifuged for 5 seconds and placed on ice. An IVT buffer (24μL) and enzyme (6μL) master mix was prepared at RT and 30μL transferred to each 60μL second-strand cDNA sample. The tubes were vortexed, spun-down in a microcentrifuge and incubated at 40^{0}C for 16 hours with the heat lid set at 50^{0}C, and then maintained at 4^{0}C overnight.

Day 2 Purification of the newly synthesised as-cRNA was reliant on a magnetic bead-based assay developed by Ambion® which removes unincorporated nucleotides and traces of unwanted salts, enzymes as well as inorganic phosphates. At RT the nucleic acid binding beads (10μL) are combined with a concentrated buffer (50μL) and 60μL applied to the sample. After pipetting up and down three times to mix, the reaction was transferred to the well of a U-bottom plate, 60μL analytical grade isopropanol was added and the mixture pipetted up and down a further three times. The samples were gently shaken (setting G) on a Grant Bio PMS-1000 microplate shaker (Grant Instruments Ltd., UK) for 5 minutes in order to facilitate the binding of as-cRNA to the nucleic acid binding beads. The U-bottom plate was removed and placed on the Magnetic Stand-96 (Life Technologies Ltd., UK) for 10 minutes until the solution was completely transparent and the beads had formed a tight pellet against the magnets. The supernatant was then carefully aspirated and discarded ensuring not to disturb the pellet. Working quickly to prevent the beads from drying out, 100μL nucleic acid wash solution was added, the samples were shaken at a moderate speed (setting M) for 2½ minutes, the beads captured on the magnetic stand for 10 minutes and the supernatant discarded. This step was repeated and the samples shaken vigorously (setting V) for 1 minute to evaporate any residual ethanol. To each of the wells, 40μL of pre-heated (55^{0}C) elution solution was applied and the magnetic beads pipetted up and down several times until fully dispersed. Following a 2 minute incubation at RT, the samples were shaken vigorously for 3 minutes, the beads then captured on the magnetic stand for 60 seconds and purified as-cRNA transferred to sterile 0.2mL Eppendorf tubes on ice. As-cRNA concentrations were measured on the NanoDrop™ 1000 Spectrophotometer as previously described (Section 2.3.1.3).

To perform the sense-strand cDNA synthesis, 2μL of random primers were initially combined with 10μg as-cRNA in a total reaction volume of 24μL which is equivalent to an as-cRNA concentration of 455ng/μL made up in NF ddH$_2$0. The samples were incubated, with the heated lid set at 75^{0}C, to a denaturation temperature of 70^{0}C for 5 minutes, followed by 25^{0}C for another 5 minutes and then cooled to 4^{0}C for at least 2 minutes. At the end of the programme tubes were centrifuged for 5 seconds and placed on ice. A second cycle sense-strand cDNA synthesis buffer (8μL) and enzyme (8μL) master mix was prepared and 16μL transferred to the reaction mixture. The tubes were vortexed, spun-down in a microcentrifuge and incubated, with the heated lid set at 75^{0}C, to an annealing temperature of 25^{0}C for 10 minutes, then 42^{0}C for 1 hour 30 minutes followed by a heat denaturation step at 70^{0}C for 10 minutes before being cooled to 4^{0}C for a minimum of 2 minutes. At the end of the programme, the tubes were centrifuged for 5 seconds and placed on ice. The as-cRNA template was then degraded by the addition of 2µL RNase H. Pipetting up and down three times ensured the complete transfer of the enzyme from the pipette tip to the sample. The tubes were vortexed, spun-down in a microcentrifuge and incubated at 37^{0}C for 45 minutes, with the heated lid set at 75^{0}C, followed by 95^{0}C for 5 minutes before being cooled to 4^{0}C for at least 2 minutes. At the end of the programme, tubes containing the newly synthesised ss-cDNA were centrifuged for 5 seconds and placed on ice.

Purification of the ss-cDNA was achieved applying the same basic principles of the magnetic bead-based assay described above, with a few minor adjustments made to the protocol. Briefly, introducing 18µL of NF ddH$_2$0 water brought the final reaction volume up to 60µL. At RT nucleic acid binding beads (10µL) were combined with a concentrated buffer (50µL) and 60µL applied to the sample. After pipetting up and down 3 times to mix the reaction was transferred to the well of a U-bottom plate, 120µL of absolute ethanol added and the mixture pipetted up and down a further 3 times. Samples were gently shaken (setting G) for 5 minutes, the beads captured on a magnetic stand for 10 minutes and the supernatant discarded. Two applications of nucleic acid wash solution (100µL) were each followed by a moderate shake (setting M) for 2½ minutes and a capture time of 10 minutes before carefully aspirating and discarding the supernatant. Residual ethanol was evaporated by vigorously shaking the plate (setting V) for 1 minute. Purified ss-cDNA was then eluted by adding 30µL elution solution preheated to 55^{0}C and pipetting up and down until the beads were fully dispersed. Following a 2 minute incubation step at RT the samples were shaken vigorously for a further 3 minutes, the beads captured on the magnetic stand for 60 seconds and the ss-cDNA transferred on ice to sterile 0.2mL Eppendorf tubes. Again concentrations were measured using the NanoDrop™ 1000 Spectrophotometer as previously described (Section 2.3.1.3). The products were stored at -20^{0}C.

2.3.2.3.2 Fragmentation

The ss-cDNA targets were fragmented into lengths of approximately forty to seventy nucleotides (~40-70nt) applying the Affymetrix® GeneChip® WT Fragmentation and Terminal Labelling Kit. To 5.5µg of starting material, NF ddH$_2$0 water was added to bring the total reaction volume up to 31.2µL. A fragmentation master mix containing a 10X cDNA fragmentation buffer, 1,000 units Apurinic/Apyrimidinic Endonuclease 1 (APE 1), 10 units Uracil-DNA Glycosylase (UDG) and RNase-*free*™ water (10µL) was prepared on ice and 16.8µL transferred to each cDNA sample. The tubes were flicked to mix and the contents collected by centrifugation immediately prior to an incubation step at 37^{0}C for 60 minutes in a pre-warmed MJ Research PTC-100® Peltier Thermal Cycler with the heated lid set at 100^{0}C. The enzymes were heated to an inactivation temperature of 95^{0}C for 2 minutes and the tubes snap-cooled on ice. A 1µL aliquot was retained for size distribution analysis on the Agilent 2100 Bioanalyser (Section 2.3.1.3).

2.3.2.3.3 Labelling

To a 45µL fragmentation reaction, 15µL labelling master mix was applied containing terminal deoxynucleotidyl transferase (TdT) (2µL), 5X TdT buffer (12µL) and 5mM concentrations of DNA labelling reagent (1µL). The tubes were flicked to mix and the samples centrifuged for 5 seconds immediately prior to an incubation step at 37^{0}C for 60 minutes in a pre-warmed MJ Research PTC-100® Peltier Thermal Cycler with the heated lid maintained at 100^{0}C. At the end of the programme the samples were heated to a denaturation temperature of 70^{0}C for 10 minutes, before being cooled to 4^{0}C for a minimum of 2 minutes and placed on ice. The products were stored at -20^{0}C.

2.3.2.3.4 Electrophoretic Mobility Gel-Shift Assay

The biotinylation efficiency of a proportion of the samples selected at random from each fragmentation and labelling batch was assessed in an Electrophoretic Mobility Shift Assay (EMSA) using the NeutrAvidin™ biotin-binding protein (Holden & Tacon 2011, Ludwig et al 1995) in accordance with the recommendations of Affymetrix® Ltd., UK. Precast 15-well (15µL) 4 to 20% polyacrylamide gels were loaded into the Mini-PROTEAN® Tetra Cell (Bio-Rad Laboratories Inc., UK) and the system filled with a 1X TBE buffer solution containing 89mM Tris-borate and 2mM EDTA, pH 8.3±0.1 at 25^{0}C. Two 1µL aliquots for each sample were transferred to separate Eppendorf tubes and heated to 70^{0}C for 2 minutes. A 2mg/mL concentration of NeutrAvidin™

biotin-binding protein was prepared in a 1X PBS solution, pH 7.2±0.05 at 25^{0}C and 5μL added to the first aliquot with the volume of the second aliquot being made up with PBS. The tubes were vortexed, spun-down in a microcentrifuge and incubated at RT for 5 minutes. Molecular weight markers HyperLadder™ IV (100-1000bp) and V (25-500bp) were loaded into the first and final lane of each gel. The samples were then combined with 5X DNA loading buffer (5μL), the mixture pipetted up and down 3 times to mix and 10μL loaded onto the gel which was run at 150 volts for 1 hour. After electrophoresis the gel was stained in a 0.001% ethidium bromide solution in 1X TBE buffer for 20 to 30 minutes and visualised under a UV light source using the Syngene GENi Gel Documentation System.

2.3.2.4 Affymetrix® Human Exon 1.0ST Arrays

2.3.2.4.1 GeneChip® HuEx-1_0-st-v2

The Affymetrix® high-density Human Exon 1.0ST GeneChip® Arrays (HuEx-1_0-st-v 2) contain more than 5.5M distinct features spotted directly onto a 5μm square glass slide by means of photolithography. In total there are in excess of 1.4M probesets [4 PM probes assigned to each individual exon] for the interrogation of upwards of one million exon clusters, within probe selection regions of empirically supported transcribed sequences, including putative full length mRNA transcripts: from the RefSeq (ncbi.nlm.nih.gov/refseq) (Pruitt et al 2014), GenBank® (ncbi.nlm.nih.gov/genbank) (Benson et al 2014) (n=289,961), Ensembl (ensembl.org) (n=306,583) (Fernandez-Suarez & Schuster 2010, Flicek et al 2014) or dbEST (ncbi.nlm.nih.gov/genbank/d best) (n=665,175) (Boguski et al 1993) databases; synteny mapped mouse/rat genomes (genome.ucsc.edu) (n=220,262) (Kuhn et al 2013), in addition to, those which have been predicted computationally in Ensembl, TWINSCAN (mblab.wustl.edu/ns can) (Brent 2008, Gross & Brent 2006), Exoniphy (cgwb.nci.nih.gov) (Blanchette et al 2004, Kent et al 2003), MITOMAP (mitomap.org) (Brandon et al 2005, Kogelnik et al 1996, Ruiz-Pesini et al 2007), VEGA (Vertebrate Genome Annotation) (sanger.ac. uk/resources/databases/vega) (Wilming et al 2008), GENSCAN (genes.mit.edu/gen scan) (Burge & Karlin 1997, Burge & Karlin 1998), or using structural RNA prediction software (genome.ucsc.edu) (Karolchik et al 2014), GeneID (genome.crg.es/soft ware.geneid) (Guigo 1998, Parra et al 2000) and the microRNA (miRNA) registry (s anger.ac.uk/software/Rfam/mirna) (Griffith-Jones 2004) for the discovery of novel expression changes and/or alternative splicing events that have not previously been reported (n=883,105).

Each 25-mer oligonucleotide probe is designed to target the sense-strand of the July 2003 NCBI build 34 of the human genome. On average, a typical gene composed of 10 exons will be represented by approximately 30 to 40 probes distributed across the entire length of the protein coding transcript and not just the far 3' end which is associated with the more traditional IVT expression arrays. Another distinguishing feature of the Human Exon 1.0ST GeneChip® Arrays is the strategy that Affymetrix® has adopted for subtracting background noise. Rather than possessing a paired MM probe for each PM probe, they have utilised a surrogate approach that incorporates measurements of background signal intensities from a smaller number of around a thousand, pooled probes with identical GC contents; referred to as an 'antigenomic' background probeset.

2.3.2.4.2 Hybridization

Sense-strand cDNA targets, post-fragmentation and labelling, were hybridized onto Human Exon 1.0ST GeneChip® Arrays according to the manufacturer's instructions provided in the GeneChip® Hybridization, Wash and Stain Module (Affymetrix® Ltd., UK). GeneChips® were equilibrated to RT immediately prior to use. Reagents were thawed on ice and the 20X Eukaryotic hybridization control stock heated to 65^{0}C for 5 minutes or until the cRNA had been completely re-suspended. The hybridization cocktail was prepared in 1.5mL Eppendorf tubes by combining the remainder of the sample [58 to 60μL depending on whether a 2μL aliquot had been removed in order to perform an EMSA (Section 2.3.2.3.4)] with 3nM control oligonucleotide B2 (3.7μL), 20X Eukaryotic hybridization controls (11μL) [*bioB, bioC, bioD* and *cre* at respective concentrations of 1.5 (represents the limit of detection), 5, 25 and 100pM (American Type Culture Collection)], 2X hybridization mix (110μL), 7% DMSO (15.4μL) and a sufficient quantity of RNase-*free*™ water in order to bring the total reaction volume up to 220μL. The tubes were flicked to mix and their contents collected by centrifugation. The hybridization cocktail was heated to 99^{0}C for 5 minutes, cooled to 45^{0}C for 5 minutes and centrifuged at maximum speed for 1 minute. Arrays were loaded with 200µL of sample and incubated at 45^{0}C in the GeneChip® Hybridization Oven 640 (Affymetrix® Ltd., UK) for 16±0.5 hours overnight with rotation set at 60rpm.

2.3.2.4.3 Washing, Staining and Scanning

Post-hybridization, washing and staining was performed on the GeneChip® Fluidics Station 450 (Affymetrix® Ltd., UK) according to instructions contained in the Whole Transcript Sense Target Labelling Assay Manual for fluidics protocol FS450_0001 that has been specifically developed for the Human Exon 1.0ST GeneChip® Arrays. Briefly, the hybridization cocktail was removed and stored at 4^{0}C. Cartridges were loaded with 200µL non-stringent Wash Buffer A [6X SSPE (3M NaCl, 0.2M NaH_2PO_4, 0.02M EDTA) and 0.01% Tween-20] and equilibrated to RT. Fresh solutions of the staining reagents were prepared. SAPE mix for the first and third stain contained 2X stain buffer (300µL) [100mM MES, 1M [Na^+] and 0.05% Tween-20], 50mg/mL BSA (24µL), 1mg/mL SAPE (6µL) and 270µL of molecular biology grade water for a final volume of 600µL per sample. The Ab mix for the second stain contained the same 2X stain buffer (300µL), 10mg/mL Goat IgG stock (6µL), 0.5mg/mL biotinylated Ab (3.6 µL), 50mg/mL BSA (24µL) and 266.4µL of molecular grade water, again to achieve a final volume of 600µL per sample.

Two post-hybridization washes, one with non-stringent Wash Buffer A at 30^{0}C for 10 cycles with 2 mixes per cycle and another with stringent Wash Buffer B [100mM MES, 0.1M [Na^+] and 0.01% Tween-20] at 50^{0}C for 6 cycles with 15 mixes per cycle, was followed by the first stain in SAPE solution at 35^{0}C for 5 minutes. A post-stain wash with non-stringent Wash Buffer A at 30^{0}C for 10 cycles with 4 mixes per cycle was followed by a second and third stain at 35^{0}C for 5 minutes in the Ab solution and 5 minutes in the SAPE solution. A final wash step was performed with non-stringent Wash Buffer A at 35^{0}C for 15 cycles with 4 mixes per cycle and the cartridges filled with 800µL Array Holding Buffer prior to being scanned on the GeneChip® Scanner 3000 (Affymetrix® Ltd., UK).

It is important to note that in the design of this study several steps were taken so as to avoid any potential confounding effects of merging datasets from different batches of microarrays: 1) Kits and reagents were ordered in bulk from the same supplier so consistent LOT numbers could be maintained; 2) The time that had elapsed between processing each of the batches was kept to a minimum; 3) The same stopping points, storage conditions & number of freeze thaw cycles were strictly adhered to for each run; 4) Groupings were assigned randomly and re-assigned at each level from RNA extractions right the way through to the point at which the cartridges were scanned and 5) Each of the groups contained roughly equal proportions of female and male samples with a mixture of controls, FALS and SALS cases of variable age, onset and disease duration.

2.3.2.5 Bioinformatics Analysis

2.3.2.5.1 Affymetrix® GeneChip® Operating Software

Images processed by the Affymetrix® GeneChip® Scanner 3000 were extracted using GCOS version 1.2 (Affymetrix® Ltd., UK). Reports were generated at gene (transcript clusters) and exon (probesets) level which plotted signal distributions and other QC metrics used to evaluate the efficiency of individual hybridizations.

2.3.2.5.2 Partek® Genomics Suite™

CEL files which had passed the QC metrics assessed by Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK) (Section 2.3.2.5.2) were imported into Partek® Genomics Suite™ software version 6.60 copyright © 2013 (Partek® Inc. St Louis, MO, USA) (Downey 2006, Fan et al 2011). Raw expression values were log2 transformed, a pre-background adjustment for GC content was applied and a quantile normalisation procedure performed using the Robust Multi-array Average (RMA) median polish probeset summarization algorithm (Irizarry et al 2003, Qu et al 2010) which excludes outlying values falling below 1 or greater than 3 standard deviations away from the mean (Wu et al 2004). Only core meta-probesets were considered (n =287,329). At transcript level these include ~22,000 unique clusters which relate to full-length protein coding mRNA sequences in the RefSeq and GenBank® databases. DE transcripts were determined at the 5% significance threshold (Partek® unadjusted $p<0.05$) by means of a 2-way ANalysis of COVAriance (ANCOVA) statistical test which controls for the effects of age and gender. Lists were subsequently filtered to remove unannotated transcripts (n=4,377/22,011) and a FC threshold of ≥ ±1.20 applied.

Aberrant splicing events were predicted at the same level of statistical significance using the Partek® alternative splicing index (ALT-SPLICE ANOVA) in which exon to exon comparisons were drawn between disease and control groupings for each gene in relation to the transcript's overall DE [Partek® unadjusted p-value (fold-change) ≥0.05 and p-value (alt. splicing) <0.05]. To reduce the probability of predicting false outcomes attributed to a type I error: a) Probesets with a maximum value for log2 transformed signal intensities below 3 across all the GeneChips® in the experiment were removed except for instances where a significant difference in the expression of a single exon exists between the two groupings; b) Exons residing in genes whose expression at the level of the whole transcript was found to be significantly altered were excluded and c) Filtered transcript clusters with no observable differences in the expression levels of individual exons [Partek® unadjusted p<0.05, FC ≥ ±1.20] (Gillett et al 2009, Rabin et al 2010, Tian et al 2011). Additional transcripts (n=2,077 /17,273) with fewer than four or more than forty probesets were also removed since the presence of a such small/large number of markers makes it prohibitively more difficult to interpret the alternative splicing events predicted to occur within these genes (Whistler et al 2010). Graphical outputs were obtained using easyExon 1.0.4 Java-based platform copyright © 2008 which is freely available online at microarray. ym.edu.tw/easyExon (National Yang-Ming University, Taiwan) (Chang et al 2008).

2.3.2.5.3 Qlucore Omics Explorer

Partek® GC-RMA normalised pivot data could also be interpreted visually in Qlucore Omics Explorer software version 2.3 (Lund, Sweden). F-test statistical outputs for the ANOVA were filtered at the 5% significance level (p<0.05) in order to generate lists of variables or genes (transcripts) which are best able to separate patient and control groupings on a PCA plot or hierarchically clustered HeatMap. Any potentially confounding effects due to 'Age' (continuous) or 'Gender' (nominal) were eliminated as factors and the lists filtered to remove unannotated transcripts (n=3,356/22,011) using the NetAffx™ Analysis Centre, which is freely available online at affymetrix.co m/analysis/index/affx (Affymetrix® Ltd., UK) (Liu et al 2003), before applying a FC threshold of ≥ ±1.20.

2.3.2.5.4 Gene Ontology Enrichment Analysis

Affymetrix® transcript cluster ID's (gene level) or probeset identification numbers (exon level) were uploaded into DAVID bioinformatics resource version 6.7 (Section 2.3.1.8.3). With a *Homo sapiens* background applied, function annotation clustering analysis was performed on GOTERM_BP_FAT and GOTERM_MF_FAT gene ontology (GO) terms using 'Medium' classification stringency [Kappa: similarity term overlap 3, similarity threshold 0.50; Classification: Initial group membership 3, final group membership 3 and multiple linkage threshold 0.50]. Those categories identified as being significantly enriched within the patient populations were defined as having a minimum EASE score above 1.30 and Benjamini-Hochberg FDR corrected $p<0.05$.

An overview of the workflow and analysis pipeline for the Human Exon 1.0ST Gene Chip® Arrays used for the transcriptional profiling of peripheral EBV-transformed B-lymphocytes (LCL's) in *C9ORF72*-related ALS [Chapter 5: '*C9ORF72* GEP Study' and Chapter 6: '*C9ORF72* Survival Study'] is provided in Figure 2.4.

2.3.2.6 Quantitative Real-Time PCR

2.3.2.6.1 Primer Design

Gene level expression changes observed on the Human Exon 1.0ST GeneChip® Arrays were validated by qRT-PCR. Standard primers ordered from Eurofins MWG Operon, Germany were designed using the NCBI Primer-BLAST tool which is freely available online at ncbi.nlm.nih.gov/tools/primer-blast. The reference sequence (RefSeq) of the full protein-coding transcript was obtained in FASTA format from ensembl.org and primers were designed to the region exhibiting the largest and most significant FC between the patient and control groupings. This was determined by plotting the mean probeset signal intensities from Partek® GC-RMA normalised pivot data along the y-axis against the Affymetrix® probeset identification numbers along the x-axis using Microsoft Excel 2010 (Microsoft Corporation, UK). Standard error of the mean (SEM) was calculated by dividing the standard deviation (stdev) by the square root of n which represents the number of samples in each group. Oligonucleotide probes were mapped to the genome and their specificity for the gene of interest confirmed using the GATExplorer platform which is freely available online at bioinfow.dep.us

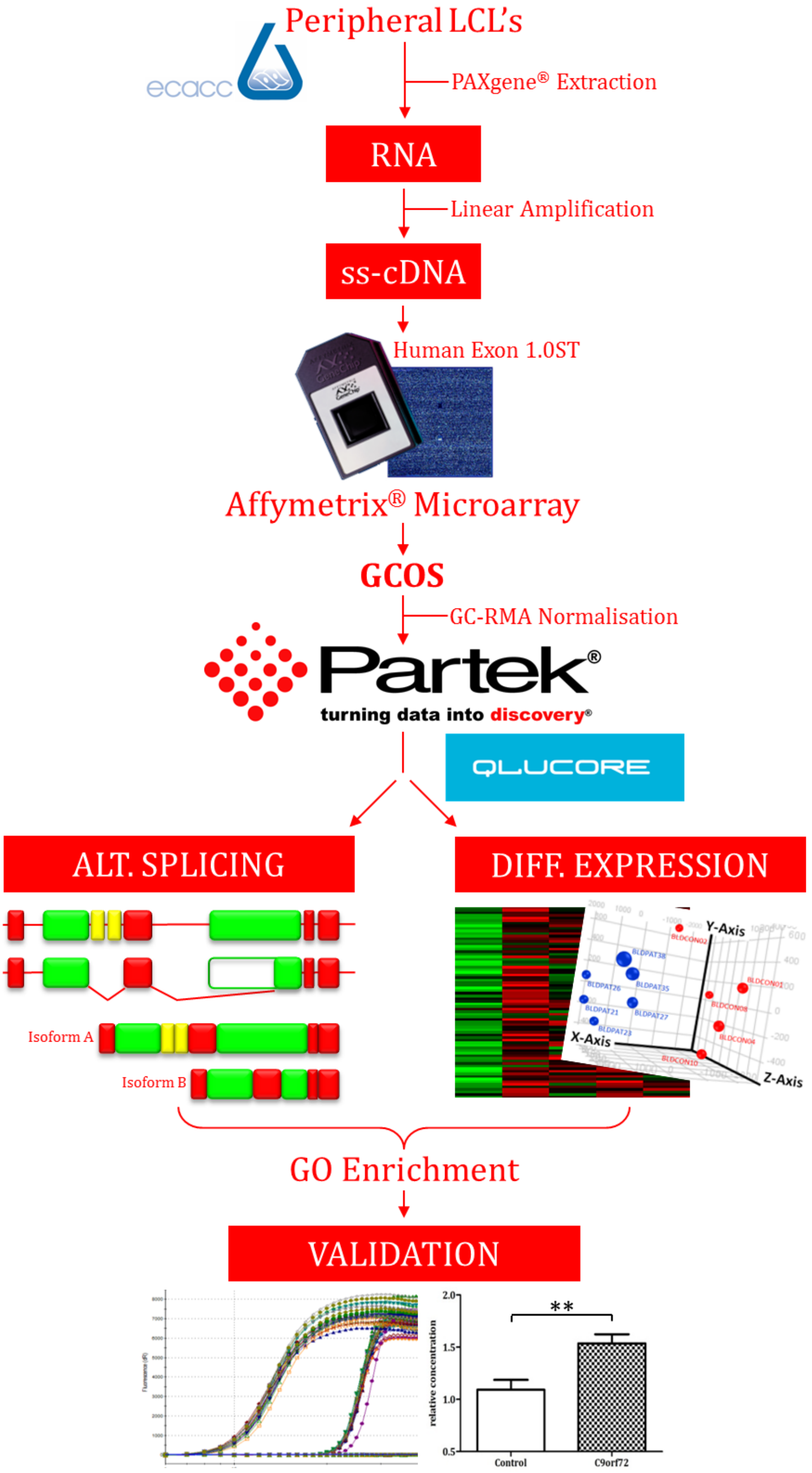


Figure 2.4 Flowchart Schematic of the Human Exon 1.0ST GeneChip® Array Analysis Pipeline Established for Peripheral EBV-Transformed B-Lymphocytes (LCL's) in ALS.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, C - cytosine, EBV - Epstein Barr virus, G - guanine, GCOS - GeneChip® Operating Software, GO - gene ontology, LCL - lymphoblastoid cell line, RMA - Robust Multi-array Average, ss-cDNA - single-stranded complementary DNA and ST - sense target.

al.es/xgate/principal.php (Bioinformatics and Functional Genomics Research Group at the Salamanca Cancer Research Centre, Spain). Predicted dissociation curves for RT-PCR products could be visualised using uMELT™ software version 2.0.2 which is freely available online at dna.utah.edu/umelt/um.php (Wittwer lab for DNA Analysis University of Utah, USA).

For optimal qRT-PCR efficiency, amplicon sizes were restricted to ~100±5bp. The oligonucleotides were around 15 to 25bp in length to ensure adequate specificity to their targeted sequence on the cDNA template but also that they remain sufficiently short to bind with ease under the appropriate annealing conditions. In order to limit the level of background genomic DNA amplification, primer pairs were designed to span an exon-exon junction wherever possible. GC content ranged between 35 and 60% with no more than three guanine (G) or cytosine (C) residues occurring within the last five at the 3' end of the sequence. This was important since the formation of a third hydrogen bond between these two residues means they have the propensity to bind to one another with a much higher affinity than the alternate pair of adenine (A) and thymine (T) residues. Although the presence of a small number of G's and C's at the 3' end can improve the degree of association between the primer and cDNA template, having more than three results in too strong an association which causes a rise in melting temperature (Tm) and prevents the GC clamp from denaturing at the correct temperature. Tm is defined as the temperature at which 50% of the DNA duplex will separate to become single-stranded molecules and is usually optimal in the region of 58 to 60^{0}C.

2.3.2.6.2 Primer Optimisation and Standard Curve Analysis

Primer optimisation was performed in triplicate 10µL reaction volumes using reverse transcribed Stratagene qPCR Human Reference Total RNA at an initial concentration of 12.5ng/µL. Oligonucleotide sequences were assayed at differing combinations of forward (F') and reverse (R') concentrations ranging between 150 and 600nmol. A NTC control was also included in each run [F' - 300nmol, R' - 300nmol] (Table 2.3). The standard deviation of the mean was calculated as a measure of the consistency between replicates of any given concentration and was used in order to determine the optimum combination of F' and R' primers for each gene which was selected as

		Reverse (R') primer		
		150nmol	300nmol	600nmol
Forward (F') primer	150nmol	150/150	150/300	BLANK
	300nmol	300/150	300/300	300/600
	600nmol	BLANK	600/300	600/600

Table 2.3 qRT-PCR Primer Optimization Oligonucleotides purchased from Eurofins MWG Operon, Germany were optimized for use in SYBR® Green qRT-PCR Assays using differing combinations of forward (F') and reverse (R') primer concentrations.

Abbreviations: qRT-PCR - quantitative real-time PCR.

a target for qRT-PCR validation. Specificity could be confirmed by the presence of a single peak on the dissociation melting curve.

A standard curve was also produced by performing a two-fold serial dilution of the starting material using NF ddH$_2$0. Cycle threshold (Ct) values (y-axis) were plotted against the log of each known concentration of universal cDNA (copy number) along the x-axis. Efficiency and the coefficient of correlation (R^2) were computed from the gradient of the incline. For reactions that were 100% efficient (slope - 3.32, $R^2 > 0.99$) the amount of PCR product should be seen to double with every amplification cycle.

2.3.2.6.3 RNA Pooling

RNA was pooled from 75 *C9ORF72+* cases (i.e. all 39 from the microarray experiment plus an additional 36 G_4C_2 repeat carriers from the ECACC discovery and replication cohorts combined) and 35 neurologically normal, healthy control subjects matched for age and gender to incorporate measurements from a greater number of samples in each run. This approach was used in order to maximise the statistical power of the qRT-PCR assay whilst avoiding potential complications associated with running the experiments on multiple 96-well plates at differing time points and with different batches of reagents. Each pool combined 200ng of good quality RNA (RIN score ≥ 7.0), from five randomly selected patient or control derived LCL samples to achieve a total input of 1µg of starting material per cDNA synthesis reaction (Table 2.4).

Controls											
C1	SNc0038	M	C2	BC6295	F	C3	SNc0041	F	C4	LC0311	M
	SC3489	F		SC3021	F		SC3406	M		BC6323	M
	BBe0006	F		SMa0156	M		SC3278	F		BLi0083	F
	LCa0076	M		BC6448	F		BC6507	M		BC6234	M
	SC3709	F		BLi0169	M		SC3150	M		SC3282	F
C5	SMa0033	M	C6	SDu0012	F	C7	SNc0023	M			
	BLi0245	M		LPo0027	M		LC0573	M			
	LPo0033	M		SNc0096	F		BC6231	M			
	LC0455	F		LCa0022	F		SC3052	M			
	SNc0045	F		SNt0035	M		LC0194	M			
C9ORF72+											
P1	LNh0101	M	P2	SPr0059	F	P3	LP0008	M	P4	SMa0006	M
	BP6072	F		LP0657	M		BBr0015	F		LP0665	F
	BLi0236	F		SNc0204	F		LP0305	M		BP6063	M
	LP0125	M		LPy0018	F		BP6165	F		SP3534	F
	SP3148	F		LP0440	F		LP0437	M		LP0480	M
P5	SP3127	F	P6	SMa0166	M	P7	SP3469	M	P8	SP3183	M
	LSh0038	M		SNc0189	M		SP3341	F		SP3222	F
	BP6029	F		SP3057	M		SP3298	F		SP3058	M
	SP3560	M		SP3122	M		SP3420	F		SP3431	F
	SP3118	F		SP3041	F		SP3413	M		SP3042	M
P9	LP0064	M	P10	SP3010	F	P11	BP6391	M	P12	BLi0254	M
	SNc0059	F		BP6107	M		LP0475	M		BP6334	M
	SP3433	M		LP0203	F		BP6208	F		BP6059	M
	LP0207	F		LP0454	M		LP0497	M		SP3090	M
	SP3288	M		LP0359	M		BP6098	M		LNh0040	M
P13	BP6363	F	P14	SP3462	F	P15	LP0091	M			
	BP6308	F		LP0717	M		SPr0026	F			
	LSh0002	M		LPo0036	M		SP3006	M			
	LPo0005	M		BLi0251	F		SP3471	M			
	SP3087	M		LP0073	F		LP0248	F			

Table 2.4 ECACC LCL Pooled RNA Samples for qRT-PCR Validation RNA of good quality [RIN score ≥7.0 on the Agilent 2100 Bioanalyser] was pooled from 75 *C9ORF72+* cases and 35 neurologically normal, healthy control subjects which had been matched for age and gender. Patient (P) and control (C) groupings were assigned at random with each pool incorporating material from five samples (200ng total RNA per sample).

Abbreviations: (+) - positive, BC - Birmingham control, Be - Belfast City Hospital, BP - Birmingham patient, Br - Bristol Frenchay Hospital, *C9ORF72* - chromosome 9 open reading frame 72, Ca - Cambridge, Du - Durham, ECACC - European Collection of Cell Cultures, F - female, LC - London control, LCL - lymphoblastoid cell line, Li - Liverpool, LNh - London National Hospital, LP - London patient, M - male, Ma - Manchester, Nc - Newcastle, Nt - Nottingham, Pr - Preston, Po - Poole General Hospital, Py - Plymouth Derriford Hospital, qRT-PCR - quantitative real-time PCR, RIN - RNA integrity number, SC - Sheffield control, Sh - Southampton Hospital and SP - Sheffield patient.

2.3.2.6.4 cDNA Synthesis

Stratagene qPCR Human Reference Total RNA and pooled mRNA samples derived from patient or control LCL's were reverse transcribed into ss-cDNA using the ABI High Capacity RNA to cDNA Synthesis Kit as previously described in Section 2.3.1.4. 1. Products were diluted in NF ddH_20 to a concentration of 12.5ng/µL and stored at -20^0C prior to use in either traditional SYBR® Green or IDT PrimeTime® Mini qPCR Assays.

2.3.2.6.5 SYBR® Green Assays

Traditional qRT-PCR was performed in duplicate 10µL reaction volumes containing 12.5ng of cDNA template, optimum concentrations of F' and R' primers (Table 2.5), a 1X Stratagene Brilliant II SYBR® Green PCR Master Mix and RNase-*free*™ water as previously described in Section 2.3.1.6. Negative no-RT and NTC's were included in each run. Relative concentrations were normalised against the housekeeping gene *18SrRNA* and visualised using GraphPad Prism® software version 5.04 copyright © 1992-2014 (GraphPad Software Inc., USA). Significance values were calculated in Microsoft Excel 2010 (Microsoft Corporation, UK) using a one-tailed student's t-test. Gene expression changes were confirmed if the direction of change was the same as the microarray with $p<0.05$.

2.3.2.6.6 PrimeTime® Mini qPCR Assays

PrimeTime® Mini qPCR Assays from Integrated DNA Technologies INC., USA were also performed in duplicate 10µL reaction volumes with a negative no-RT and NTC. Each well contained 12.5ng of cDNA template, 500nM F'/R' primer and 250nM probe re-suspended in TE buffer [10mM Tris-HCl and 1mM EDTA, pH 7.5 at 25^0C], RNase-*free*™ water and 2X Brilliant III Ultra-Fast qPCR Master Mix (Table 2.6). The samples were run applying a "Normal 2 Step" profile on the Stratagene Mx3000P™ Real Time PCR Thermal Cycler as outlined previously in Section 2.3.1.6. Relative concentrations were normalised against the standard housekeeping gene *18SrRNA* and visualised in GraphPad Prism® software version 5.04 copyright © 1992-2014 (GraphPad® Software Inc., CA USA). Significance values were calculated using Microsoft Excel 2010 (Microsoft Corporation, UK) using a one-tailed student's t-test. Expression changes were confirmed if the direction of change was identical to the microarray with a p<

Gene	**Transcript**	**Region**	**Primer Sequence (5’ ---> 3’)**	**Tm**	**GC%**	**Amplicon**	**Optimum conc.**	**Efficiency**
C9ORF72	ENST00000379997	3’UTR	F’ GTATCAGAGGCATGAGTGTGTTT R’ GATGTATGAAAGGCTGACACTGA	58.7 58.5	43.5 43.5	98bp	150/150nmol	99.8%
C9ORF72	ENST0000038003	3’UTR	F’ GGAAACGTTCCCCTGGATCAT R’ CACCTGACATCCCCTCACAG	60.1 59.8	52.4 60.0	104bp	150/150nmol	101.1%
DENR	ENST00000280557	3’UTR	F’ GTCCTTGGCATTTTCACTGTTC R’ CAGTCTCCCGTTTATTTGACTTTG	58.4 58.3	45.5 41.7	74bp	150/300nmol	102.4%
FGFR1	ENST00000341462	Exon 11-13	F’ AGTCGGACGCAACAGAGAAA R’ TGGAGGCATACTCCACGATG	57.3 59.4	50.0 55.0	147bp	300/150nmol	115.3%
HNRNPA0	ENST00000314940	3’UTR	F’ CCTGCTAGTTGCGTGTTGAATTA R’ AGTACAAGAGATGGATGCACAGA	59.6 59.2	43.5 43.5	104bp	300/600nmol	96.0%
HNRNPF	ENST00000443950	Exon 3	F’ CTCAGTGATGGCTACGGCTT R’ CTCACTGTCGCCGTATCTGT	59.4 59.4	55.0 55.0	96bp	150/300nmol	102.3%
ITGAE	ENST00000263087	Exon 15-16	F’ TGGGGGATCTCAGTCAGGATA R’ CGTCCCAGTGTCCATTGTAGA	59.1 59.5	52.4 52.4	120bp	150/150nmol	110.8%
ITGAE	ENST00000263087	Exon 20	F’ ATCTTCCAGCTGCCCTATGA R’ GTGGTGGCCAACTGTAATTCTG	58.2 59.8	50.0 50.0	74bp	150/150nmol	111.8%
KARS	ENST00000319410	5’UTR	F’ ACTGAGCAAGAAGTGGTGGTA R’ ACCCCCTAACAAGCCTTACAG	59.0 59.4	47.6 52.4	83bp	150/150nmol	97.4%
MRPL41	ENST00000371443	Exon 2	F’ CTGGAGGTTCGTGCAGATCA R’ CTCACGTAGGGCTTGAGCTT	59.8 59.8	55.0 55.0	84bp	150/150nmol	107.5%
NUDT21	ENST00000300291	3’UTR	F’ GATCCCTAAATTGCCACCTTTCT R’ TGAGCAGAACCGAAAGTAAATAAAC	58.7 58.1	43.5 36.0	109bp	300/150nmol	95.3%
PHAX	ENST00000297541	Exon 2	F’ TCGAGCTGTTGAAAGTGTGGA R’ ACTGCTCTGGCCAAACTGAA	59.9 59.8	47.6 50.0	139bp	150/300nmol	103.0%

PRPF19	ENST00000227524	Exon 11	F’ CTTCCCCCGATGCCACTATC R’ ATCATCGGAGGAGCTCAGGA	60.0 59.8	60.0 55.0	137bp	300/300nmol	99.4%
PURA	ENST00000331327	Exon 1	F’ GGCGTGTTTATGCGAGTGAG R’ CCGAGTACTTGCAGAAGGTGT	59.4 59.8	55.0 52.4	106bp	150/150nmol	108.7%
RBM3	ENST00000376759	Exon 2-3	F’ ATCTCTGAGGTGGTCGTTGT R’ GGTTGGTGAAGGTGATGAAAC	58.4 59.7	50.0 50.0	76bp	300/150nmol	100.4%
RPL22	ENST00000234875	3’UTR	F’ ATAGCTGCCTCATGCCACTT R’ TGGTAGCCCCTTTCAGTTGTC	59.5 59.9	50.0 52.4	90bp	600/300nmol	100.4%
TAF13	ENST00000338366	Exon 4	F’ TGGAAGACAAGGTCGAGTACA R’ AACCCTGGCAAACTTCCTTG	59.0 58.6	45.5 58.6	76bp	300/150nmol	98.3%
UTP15	ENST00000296792	Exon 2-4	F’ AGACCCCTGTTCAGATTAAGGA R’ TGAATTCTTGAGGAAGCTGTGAC	58.4 58.9	45.5 43.5	100bp	150/150nmol	102.9%
ZCRB1	ENST00000266529	3’UTR	F’ GGCTTTATTCATGCCTGATTTGTTT R’ TCGGTCTTCAGGAAGTTTGTTTT	59.1 58.7	36.0 39.1	75bp	300/150nmol	102.8%
Housekeeping Gene								
18SrRNA	ENST00000606783	5’ UTR	F’ CTGCGGCTTAATTTGACTCAAC R’ CAAATCGCTCCACCAACTAAGAA	58.5 59.3	45.5 43.5	131bp	300/600nmol	115.5%

Table 2.5 ECACC Eurofins MWG Operon qRT-PCR Primer Sequences and Optimum Concentrations

Abbreviations: bp - base pairs, *C9ORF72* - chromosome 9 open reading frame 72, *DENR* - density-regulated protein, F’ - forward primer sequence, *FGFR1* - fibroblast growth factor receptor 1, *HNRNPA0* - heterogeneous nuclear ribonucleoprotein A0, *HNRNPF* - heterogeneous nuclear ribonucleoprotein F, *ITGAE* - integrin, alpha E, *KARS* - lysyl-tRNA synthetase, *MRPL41* - mitochondrial ribosomal protein L41, *NUDT21* - nudix (nucleoside diphosphate linked moiety X)-type motif 21, *PHAX* - phosphorylated adaptor for RNA export, *PRPF19* - PRP19/PSO4 pre-mRNA processing factor 19 homolog (*S. cerevisiae*), *PURA* - purine-rich element binding protein A, R’ - reverse primer sequence, *RBM3* - RNA binding motif (RNP1, RRM) protein 3, *RPL22* - ribosomal protein L22, *TAF13* - TAF13 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 18kDa, Tm - melting temperature, *UTP15* - UTP15, U3 small nucleolar ribonucleoprotein, homolog (*S. cerevisiae*), UTR - untranslated region, *ZCRB1* - zinc finger CCHC-type and RNA binding motif 1 and *18SrRNA* - 18S ribosomal RNA.

Gene	PrimeTime®	RefSeq	Region	Primer Sequence (5’ ---> 3’)	Probe Sequence (5’ ---> 3’)	Amplicon
CLNS1A	Hs.PT.56a.24955799	NM_001293	Exon 1-2	F’ CCAGTGAGAATCCTAATCCAGAG R’ ACTGAGGCTGTGCTGAAC	56-FAM/TTACATCGC/ZEN/TGAGAGCCGCCTG/3IABkFQ	103bp
EIF4H	Hs.PT.56a.24792841	NM_022170	Exon 4-6	F’ AGTCATCCCTGAAGCCAGA R’ AGGCAGAAAACAAGATAAAGGTG	56-FAM/CAGAAAAGG/ZEN/TGGACCAGATGACAGAGG/3IABkFQ	134bp
FUS	Hs.PT.58.40679981	NM_001170634	Exon 6-9	F’ CCTTGCACAAAGATGGTGTTG R’ GGCGGCAGAGGTGGCAT	56-FAM/AAATTTGGT/ZENGGCCCTCGGGAC/3IABkFQ	128bp
GEMIN6	Hs.PT.56a.22216821	NM_024775	Exon 1-2	F’ CTGTCACTCGGACCTCTTTG R’ TGAGTACCCAGAGTTGCGA	56-FAM/AAGGCCCCT/ZEN/TAGAATGGCAAGATTACAT/3IABkFQ	123bp
HNRNPH2	Hs.PT.58.904078	NM_019597	Exon 1b-2	F’ GTGGCAAGTTTGGCTCAATG R’ TCGTCTACCGTCTCGCTAT	56-FAM/TGGTGTAGC/ZEN/TCTAACGATACCGGGT/3IABkFQ	99bp
KARS	Hs.PT.56a.39151267	NM_001130089	Exon 1-2	F’ CCCTAACAAGCCTTACAGCA R’ GGCCGAGGTGAAAGTGG	56-FAM/CGTCAACAT/ZEN/GGCAGAGCACCCT/3IABkFQ	113bp
NCBP2	Hs.PT.56a.39258425	NM_007362	Exon 3-4	F’ GCATCTGCGCGTGAGTA R’ GAACTCTTCAGCAAAAGTGGTG	56-FAM/TGGGTCTGG/ZEN/ATAAAATGAAGAAAACAGCATG/3IABkFQ	110bp
POLR2G	Hs.PT.56a.39433782	NM_002696	Exon 3-5	F’ GTGGGTTGGAGTTAGGATCA R’ GAGGTCGTGGATGCTGTT	56-FAM/AGGGATGGA/ZEN/ATGTCGAGAGATGAAGC/3IABkFQ	130bp
UNRIP	Hs.PT.56a.24263685	NM_007178	Exon 8-10	F’ AGGAGCTGAAGGAAAGATGC R’ GCCTTTGGAAATGTGTGCTTC	56-FAM/AGAAGATAG/ZEN/TGGTGAGCTGGCAAAGC/3IABkFQ	137bp
Housekeeping Gene						
18SrRNA	Hs.PT.39a.22214856.g	NR_003286	Exon 1	F’ GGACATCTAAGGGCATCACAG R’ GAGACTCTGGCATGCTAACTAG	56-FAM/TGCTCAATC/ZEN/TCGGGTGGCTGAA/3IABkFQ	n/a

Table 2.6 ECACC PrimeTime® Mini qPCR Primer and Probe Sequences

Abbreviations: bp - base pairs, *CLNS1A* - chloride channel, nucleotide-sensitive, 1A, *EIF4H* - eukaryotic translation initiation factor 4H, F’ - forward primer sequence, *FUS* - fused in sarcoma, *GEMIN6* - gem (nuclear organelle) associated protein 6, *HNRNPH2* - heterogeneous nuclear ribonucleoprotein H2 (H’), *KARS* - lysyl-tRNA synthetase, *NCBP2* - nuclear cap binding protein subunit 2, 20kDa, *POLR2G* - polymerase (RNA) II (DNA directed) polypeptide G, R’ - reverse primer sequence, *UNRIP* (*STRAP*) - UNR-interacting protein (serine/threonine kinase receptor associated protein) and *18SrRNA* - 18S ribosomal RNA.

0.05.

For improved specificity IDT utilises 5’ nuclease chemistry in which a non-extendable DNA hydrolysis probe is fluorescently labelled with a reporter dye and either one or two quenchers. When the probe is intact, the two molecules are maintained in close proximity to one another allowing energy emitted by the reporter to be absorbed by quencher(s). During the extension phase of the amplification reaction the hydrolysis probe is cleaved by the 5’ to 3’ exonuclease activity of SureStart *Taq* DNA polymerase causing the two molecules to dissociate from the target. A consequence of the spatial separation of the reporter dye and quencher(s) is a sharp increase in fluorescence which is then detected and recorded by the instrument.

CHAPTER 3: WHOLE BLOOD STUDY

3.1 Clinical Characteristics of the NuGEN Cohort

An overview of the clinical characteristics of participants recruited into the NuGEN Ovation® Whole Blood Study is provided in Table 2.1 (Section 2.1.1). Briefly, these comprised 6 Riluzole treated SALS patients of North European, Caucasian descent and an equal number of neurologically normal, healthy control subjects that were as far as possible age and gender matched. Age at symptom onset ranged between 38 and 71 years with a mean of 60.3±15yrs and an average disease duration of ~3 years and 4 months.

3.2 PAXgene® Blood RNA Extraction

PAXgene® isolated material extracted from whole venous peripheral blood derived from each of the 12 individuals in the final NuGEN microarray cohort (Section 3.1) yielded between 2.82 and 9.32µg total RNA for downstream applications including linear SPIA™ amplification (Section 3.3.1) and cDNA synthesis prior to performing qRT-PCR (Section 3.4). Measurements of concentration and purity (Section 2.3.1.3) obtained using the NanoDrop™ 1000 Spectrophotometer were found to be reasonably consistent across patient and control groupings with respective means of 65.00 ±25ng/µL and 69.37±28ng/µL and $A_{260/280}$ ratios close to 2.20. Distinct separation of the 18S and 28S ribosomal peaks could also be observed on the electropherogram traces displayed by the Agilent 2100 Bioanalyser with rRNA ratios of 1.70±0.2 and RNA integrity values of 7.5 or above (Table 3.1) [Mean RIN 8.1±0.5 for SALS patients and 8.2±0.5 for controls] (Figure 3.1).

3.3 Human Genome U133 Plus 2.0 GeneChip® Arrays

3.3.1 NuGEN Ovation® Whole Blood Solution

Control ID	RNA Concentration	RNA Yield	$A_{260/280}$	RIN
BLDCON01	48.66 ng/µL	3.89 µg	2.23	8.4
BLDCON02	77.91 ng/µL	6.23 µg	2.21	7.7
BLDCON04	35.29 ng/µL	2.82 µg	2.46	8.8
BLDCON07	46.36 ng/µL	3.71 µg	2.16	7.7
BLDCON08	101.26 ng/µL	8.10 µg	2.23	8.8
BLDCON10	80.53 ng/µL	6.44 µg	2.12	7.9
Mean Values	**69.37 ng/µL**	**5.55 µg**	**2.24**	**8.2**

Patient ID	RNA Concentration	RNA Yield	$A_{260/280}$	RIN
BLDPAT21	47.08 ng/µL	3.77 µg	2.28	8.4
BLDPAT23	116.48 ng/µL	9.32 µg	2.15	7.5
BLDPAT26	77.65 ng/µL	6.21 µg	2.12	8.0
BLDPAT27	80.54 ng/µL	6.44 µg	2.14	8.1
BLDPAT35	45.55 ng/µL	3.64 µg	2.25	8.8
BLDPAT38	48.91 ng/µL	3.91 µg	2.14	7.7
Mean Values	**65.00 ng/µL**	**5.20 µg**	**2.18**	**8.1**

Table 3.1 PAXgene® Blood RNA Isolation Kit Extractions: An Assessment of Quality and Yield from Samples in the NuGEN Ovation® Whole Blood Study Measurements of concentration (ng/µL) and purity ($A_{260/280}$), as determined by the ratio of absorbance (A) at 260/280nm, were assessed using NanoDrop™ 1000 Spectrophotometer (Section 2.3. 1.3) (Thermo Fisher Scientific® Inc., UK). Total RNA yields were calculated in micrograms (µg) and RNA integrity numbers (RIN's) computed on a scale of zero (undetectable, completely degraded) to ten (high quality, intact RNA) using Agilent 2100 Bioanalyzer (Agilent Technologies Ltd, UK). Mean values recorded across the blood control (top) [BLDCON] or blood patient (bottom) [BLDPAT] groupings are represented in bold.

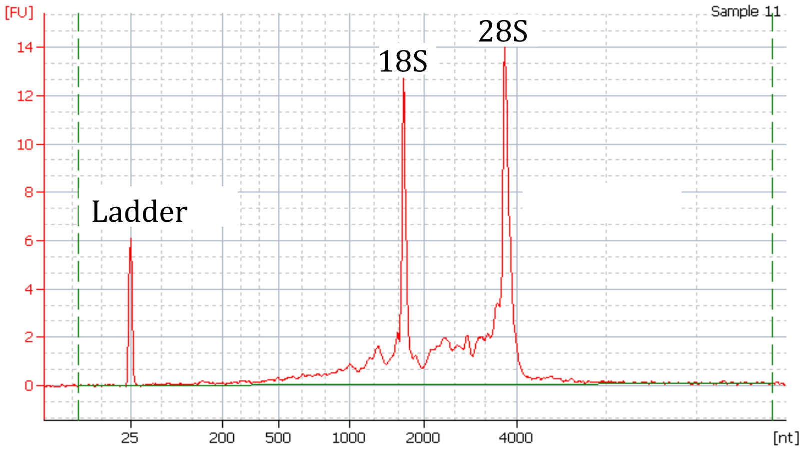


Figure 3.1 Agilent 2100 Bioanalyzer Assessment of PAXgene® Blood RNA Integrity Agilent RNA 6000 Nano Ladder with a 25 nucleotide [nt] molecular weight marker and peaks corresponding to the 18S and 28S ribosomal RNA's (rRNA's) have been labelled accordingly. Fragment lengths were plotted along the x-axis with RNA concentrations defined by arbitrary units of fluorescence [FU] plotted along the y-axis. In this example blood control [BLDCON] 01 was selected as a representative electropherogram trace for the purposes of illustration.

3.3.1.1 NuGEN Ovation® RNA Amplification System V2

Total RNA using a 50ng input of starting material was reverse transcribed into ss-c DNA following the NuGEN Technologies Inc., UK patented SPIA™ method outlined in the previous Materials & Methods Chapter (Section 2.3.1.4.2 and 2.3.1.5.1). Yields of between 4.83 and 6.51µg were achieved, as determined by the NanoDrop™ 1000 Spectrophotometer (Section 2.3.1.3). Mean concentrations were largely comparable across the blood patient [BLDPAT] (179.23±21ng/µL) and blood control [BLDCON] (199.39±10ng/µL) groupings with $A_{260/280}$ ratios consistently above the previously accepted threshold of 1.8. Pre-amplified material extracted from BLDPAT23, which produced the lowest RNA integrity value [RIN score 7.5 (Table 3.1)] also underwent DNase treatment (Section 2.3.1.5.2) in order to remove any potentially contaminating genomic DNA that may have been present in this sample. Nucleic acid products were purified using the QIAGEN MinElute® Reaction Clean-Up Kit before being run on the Agilent 2100 Bioanalyser (Section 2.3.1.3). An illustrated electropherogram trace (right) and corresponding gel image (left) typically generated by the instrument is depicted in Figure 3.2 (Table 3.2).

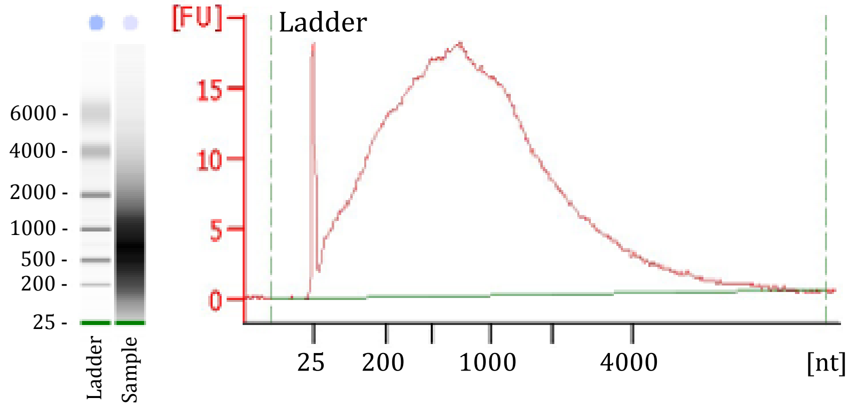


Figure 3.2 Agilent 2100 Bioanalyzer Assessment of Purified SPIA™ ss-cDNA Integrity Electropherogram trace (right) and corresponding gel image (left) for blood patient [BLDPAT] 21 and the external RNA 6000 Nano Ladder with a 25nt molecular weight marker and 0.2, 0.5, 1.0, 2.0, 4.0 and 6.0kb fragments which are loaded at a total concentration of 150ng/µL. Fragment lengths [nt] are indicated along the x-axis with RNA concentrations defined by arbitrary units of fluorescence [FU] along the y-axis.

Abbreviations: cDNA - complementary DNA, SPIA™ - single primer isothermal amplification and ss - single-stranded.

		Purified SPIA™ ss-cDNA				Biotin-Labelled ss-cDNA		
Control ID	**DNase**	**Concentration**	**Yield**	**$A_{260/280}$**	**RIN**	**Concentration**	**Yield**	**RIN**
BLDCON01	N	205.10 ng/µL	6.15 µg	2.38	2.2	96.00 ng/µL	4.80 µg	2.6
BLDCON02	N	206.25 ng/µL	6.19 µg	1.89	2.2	110.00 ng/µL	5.50 µg	2.6
BLDCON04	N	193.35 ng/µL	5.80 µg	2.38	2.0	93.00 ng/µL	4.65 µg	2.5
BLDCON07	N	205.17 ng/µL	6.16 µg	2.18	2.2	114.00 ng/µL	5.70 µg	2.5
BLDCON08	N	182.32 ng/µL	5.47 µg	1.88	2.3	105.00 ng/µL	5.25 µg	2.5
BLDCON10	N	204.16 ng/µL	6.12 µg	1.83	1.9	111.00 ng/µL	5.55 µg	2.5
Mean Values		**199.39 ng/µL**	**5.98 µg**	**2.09**	**2.1**	**104.83 ng/µL**	**5.24 µg**	**2.5**

		Purified SPIA™ ss-cDNA				Biotin-Labelled ss-cDNA		
Patient ID	**DNase**	**Concentration**	**Yield**	**$A_{260/280}$**	**RIN**	**Concentration**	**Yield**	**RIN**
BLDPAT21	N	217.05 ng/µL	6.51 µg	1.86	2.4	96.00 ng/µL	4.80 µg	2.6
BLDPAT23	Y	167.51 ng/µL	5.03 µg	1.92	2.0	92.00 ng/µL	4.60 µg	2.5
BLDPAT26	N	191.50 ng/µL	5.75 µg	1.89	2.1	108.00 ng/µL	5.40 µg	2.5
BLDPAT27	N	168.34 ng/µL	5.05 µg	1.87	2.0	110.00 ng/µL	5.50 µg	2.5
BLDPAT35	N	170.16 ng/µL	5.11 µg	2.41	2.2	102.00 ng/µL	5.10 µg	2.5
BLDPAT38	N	160.82 ng/µL	4.83 µg	2.40	2.0	96.00 ng/µL	4.80 µg	2.5
Mean Values		**179.23 ng/µL**	**5.38 µg**	**2.06**	**2.1**	**100.67 ng/µL**	**5.03 µg**	**2.5**

Table 3.2 Purified SPIA™ ss-cDNA: An Assessment of Quality and Yield Pre- (Left)/Post- (Right) Fragmentation & Labelling Measurements of concentration (ng/µL) and purity ($A_{260/280}$), as determined by the ratio of absorbance (A) at 260/280nm wavelengths, assessed using the NanoDrop™ 1000 Spectrophotometer (Thermo Fisher Scientific® Inc., UK) (Section 2.3.1.3). Yields were calculated in micrograms (µg) and RNA integrity numbers (RIN scores) computed on a scale of zero (undetectable, completely degraded) to ten (high quality, intact RNA) using the Agilent 2100 Bioanalyzer (Agilent Technologies Ltd., UK). Mean values recorded across the blood control [BLDCON] (top) or blood patient [BLDPAT] (bottom) groupings are represented in bold.

Abbreviations: cDNA - complementary DNA, DNase - deoxyribonuclease, N - untreated, ss - single-stranded, SPIA™ - single primer isothermal amplification and Y - treated.

3.3.1.2 NuGEN Encore™ Biotin Module

The NuGEN Encore™ Biotin Module (Section 2.3.1.5.3) generated between 4.60 and 5.70µg biotinylated ss-cDNA fragments [Mean concentration of 100.67±7ng/µL for the SALS patients and 104.83±9ng/µL for the controls] of ~50 to 2,000 nucleotides in length (Table 3.2). These included >80% of targets with fewer than two hundred bases which were suitable for hybridization onto Affymetrix® Human Genome U133 Plus 2.0 GeneChip® Arrays (Section 2.3.1.7) (Figure 3.3).

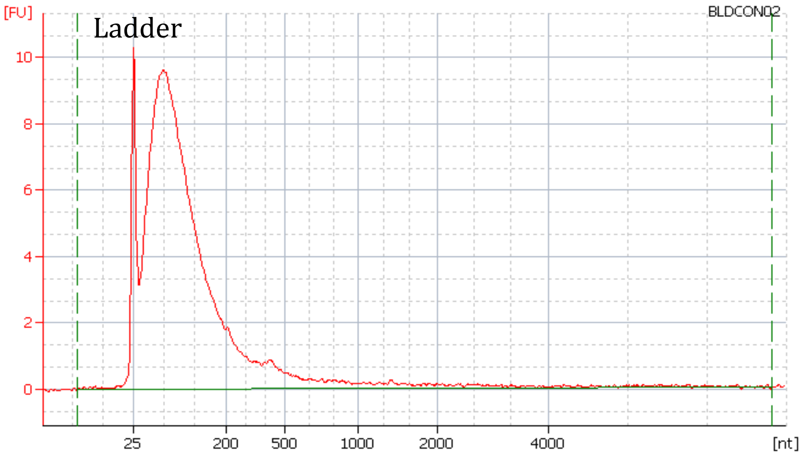


Figure 3.3 Agilent 2100 Bioanalyzer Assessment of Fragmented SPIA™ ss-cDNA Integrity Fragment lengths in nucleotides [nt] are indicated along the x-axis with RNA concentrations, defined by arbitrary units of fluorescence [FU], along the y-axis. In this instance the representative electropherogram trace was selected from blood control [BLDCON] 02.

Abbreviations: cDNA - complementary DNA, SPIA™ - single primer isothermal amplification and ss - single-stranded.

3.3.2 Affymetrix® Expression Console™ QC Metrics

3.3.2.1 Eukaryotic Hybridization Controls

Signals produced by the bacterial spike in controls BioB, BioC, BioD (three *E. coli* derived genes of the biotin synthesis pathway) and CreX (a recombinase gene from the P1 bacteriophage) (Section 2.3.1.7.2) were called absent for BLDCON02, 08 and 10 and BLDPAT21, 27 and 35. For this reason these 6 SALS cases and controls were not represented on the plots displayed in Figure 3.4. Given that all the samples had been processed together and in the same batch, it can be speculated, therefore, that these failings have most likely arisen due to a technical error in which the hybridization controls were not spiked in at correct concentrations sufficient for detection on Affymetrix® Human Genome Plus 2.0 GeneChip® Arrays. Subsequent assessment of the remaining 6 SALS cases and controls identified BLDCON07, highlighted in red, as a potential outlier (Figure 3.4) which requires careful consideration before determining whether or not this sample should be included in any further downstream comparative analyses.

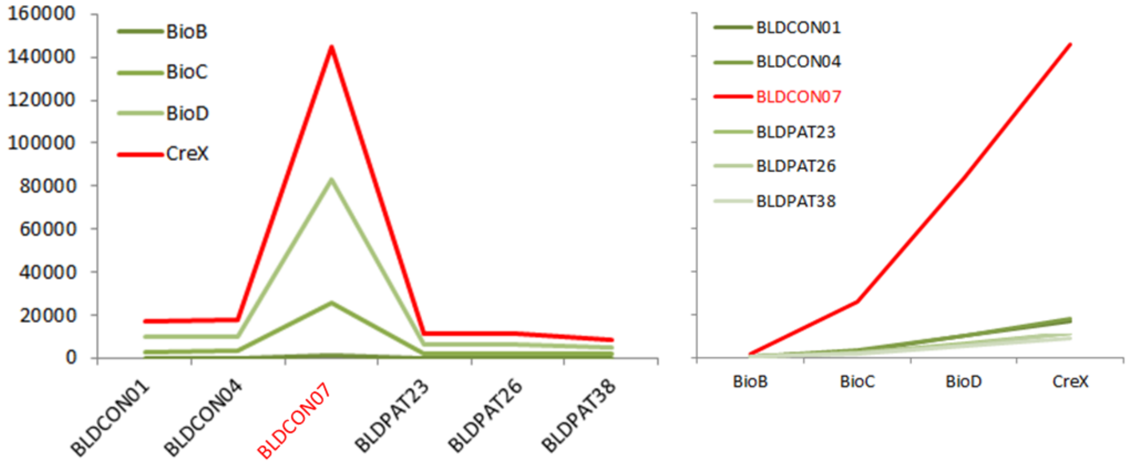


Figure 3.4 Eukaryotic Hybridization Controls for Samples in the NuGEN Ovation® Whole Blood Study Three bacterial derived genes of the *E. coli* biotin synthesis pathway [BioB, BioC and BioD] and the recombinase gene CreX from the P1 bacteriophage were spiked in at increasing concentrations (left-hand panel) [1.5pM (representing the limit of detection), 5pM, 25pM and 100pM, respectively] immediately prior to labelling, in order to monitor the efficiency of the hybridization reaction. In the right-hand panel mean signal intensities (y-axis) for probesets spotted onto the Affymetrix® Human Genome U133 Plus 2.0 GeneChip® Arrays, which correspond to each of the aforementioned genes (x-axis) are also provided. Assessment of Affymetrix® QC metrics was performed using the Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK) (Section 2.3.1.7.2). Intensity plots were generated in Microsoft Excel 2010 (Microsoft Corporation UK). Potential outliers are highlighted in red.

Abbreviations: BLDCON - blood control, BLDPAT - blood patient and QC - quality control.

3.3.2.2 GeneChip® Normalisation

3.3.2.2.1 Noise (Raw Q)

Noise (Raw Q) measures the extent of pixel to pixel variation between the individual spots, otherwise referred to as ‘features’, on the Affymetrix® Human Genome U133

Plus 2.0 GeneChip® Arrays. Its value can be computed from data that is contained within the .DAT files, using the Microarray Suite 5.0 (MAS 5.0) statistical algorithm, applied in Expression Console™ software version 1.3.0.187. Noise is calculated as a function of the amount of inherent electrical noise that is associated with the operation of each individual scanner as well as the quality of the samples being hybridized (Figure 3.5).

$$Raw\ Q\ = \left(1/_N\right) * \left(\sum stdev_n \Big/ \sqrt{pixel_n}\right) * SF * NF$$

N = number of background features on the array

stdev = standard deviation

pixel = total number of pixels

n = nth background feature

SF = scaling factor

NF = normalisation factor

Figure 3.5 Noise (Raw Q) Calculation Microarray Suite (MAS) 5.0 statistical algorithm for measuring the extent of pixel to pixel variation between individual spots or so called 'features' on the Affymetrix® Human Genome U133 Plus 2.0 GeneChip® Arrays in the NuGEN Ovation® Whole Blood Study. Noise (Raw Q) values computed in Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK). Equation adapted from the Report File Glossary pdf available at Affymetrix.com.

Values for noise (Raw Q) were found to be consistent across multiple batches [Batch 1 run on the 14th June 2011 0.657±0.02 and Batch 2 run on the 23rd June 2011 0.623 ±0.03; two-tailed student's t-test not significant] with a slight difference having been observed between alternate sample types [Blood control (BLDCON) 0.620±0.02 and Blood patient (BLDPAT) 0.659±0.03; two-tailed student's t-test producing a p-value below the 5% significance threshold ($p<0.05$*)] (Figure 3.6).

3.3.2.2.2 Scaling Factor

One key assumption, fundamental to most normalisation procedures that have been described for high throughput arrays to date, including Affymetrix® Human Genome U133 Plus 2.0 GeneChip® Arrays is that the majority of transcripts should remain un-

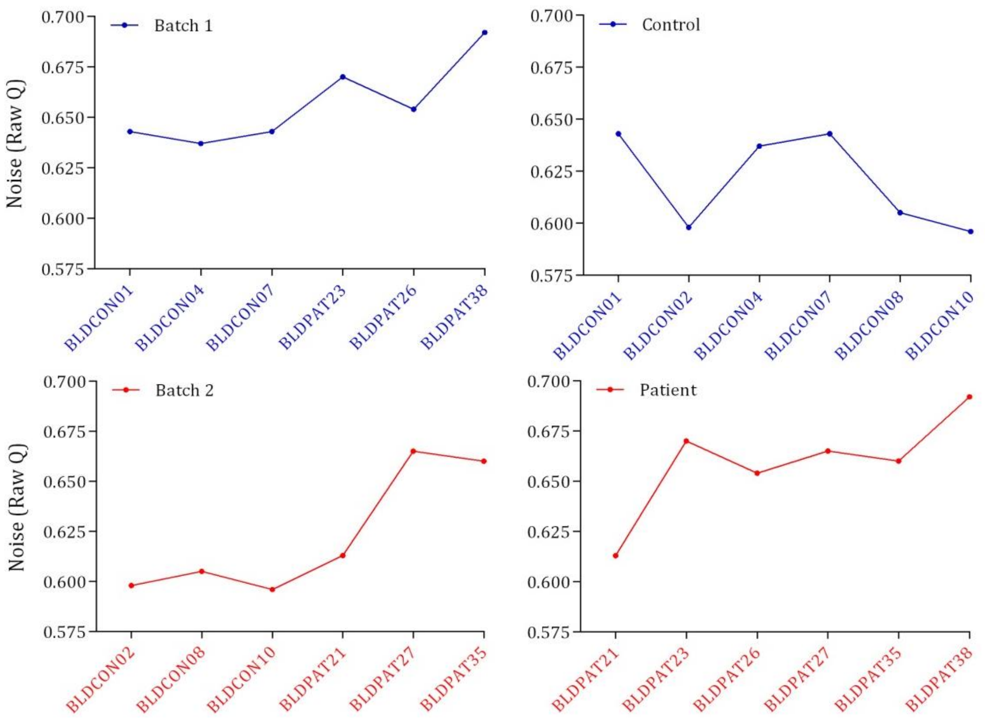


Figure 3.6 Noise (Raw Q) Measurements for Samples in the NuGEN Ovation® Whole Blood Study A Microarray Suite (MAS) 5.0 statistical algorithm was applied in Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK) in order to measure the extent of pixel to pixel variation between individual spots or so called 'features' on the Affymetrix® Human Genome U133 Plus 2.0 GeneChip® Arrays. GraphPad Prism® software version 5.04 © 1992-2014 (GraphPad Software Inc., CA USA) was used to plot the data and two-tailed student's t-tests performed to draw comparisons between the different experimental batches (left panel) [p-value was not significant] and sample types (right panel) [Average noise: 0.659 for SALS patients versus 0.620 in controls ($p<0.05$*)].

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, BLDCON - blood control, BLD PAT - blood patient and S - sporadic.

altered regardless of which experimental conditions are under manipulation; for example, healthy versus disease status in the NuGEN Ovation® Whole Blood Study. In other words, if this statement holds true then the proportion of transcripts that are classified as either up (⇧)- or down (⇩)-regulated, for a given threshold of statistical significance, should not influence the overall fluorescence intensity of each GeneChip® which should remain comparable across the study.

A MAS 5.0 statistical algorithm deployed by Expression Console™ software version 1.3.0.187 is used to apply a scaling factor (SF) which standardises the mean probeset signal intensities, in order to control for brightness. In this scenario, a measurement close to 1.000 indicates that the average array intensity is approximately equal to its target intensity. According to the manufacturer's website SF values are expected to vary considerably across species, and between different tissue/sample types, explaining why currently no set guidelines have been published. Nevertheless, Affy metrix. com does advocate that there should be no more than a 3-fold difference in the minimum and maximum SF values recorded for a particular experiment. Excluding BLDCON07 (19.673), this was found to be broadly the case for samples in the NuGEN Ovation® Whole Blood Study [Mean SF values: BLDCON's 4.581±2.7 versus BLDPAT's 2.725±2.9 and Batch 1 run on the 14th June 2011 1.662±0.6 versus Batch 2 run on the 23rd June 2011 5.158±3.1 with respective fold changes of 1.70 or 3.10].

3.3.2.3 RNA Quality

Affymetrix® have selected the standard housekeeping genes *ACTB* and *GAPDH* with which to assess the quality of input RNA; owing to their long transcript lengths and ubiquitous expression. The probesets for these genes are designed to span their five prime (5'), mid (M) and three prime (3') regions. Similar signal intensities across all three regions is indicative of the presence of good quality RNA that is intact and has been labelled reliably along the full length of its sequence. For samples in the NuGEN Ovation® Whole Blood Study, 3'/M ratios [*ACTB* 2.04±0.44-fold and *GAPDH* 1.80±0. 51-fold] were found to be reasonably consistent, with slightly higher and more variable changes recorded for the 3'/5' ratios [*ACTB* 5.68±1.6-fold and *GAPDH* 2.43±0. 71-fold]; suggesting that a small amount of RNA degradation may have occurred at the far 5' end of the transcript. However, given that these are 3' IVT expression arrays this is not expected to cause further downstream complications (Figure 3.7).

3.3.2.4 Overall Signal Quality

3.3.2.4.1 Average Background

The average background signal intensity values ranged from 25.575 (BLDCON07) to 27.534 (BLDPAT23) for the 12 SALS patient and control samples in the final NuGEN Ovation® Whole Blood Study. Consistency was observed between multiple batches [Batch 1 run on the 14th June 2011 27.100±0.75 versus Batch 2 run on the 23rd June 2011 26.602±0.62; two-tailed student's t-test not significant] as well as across alter-

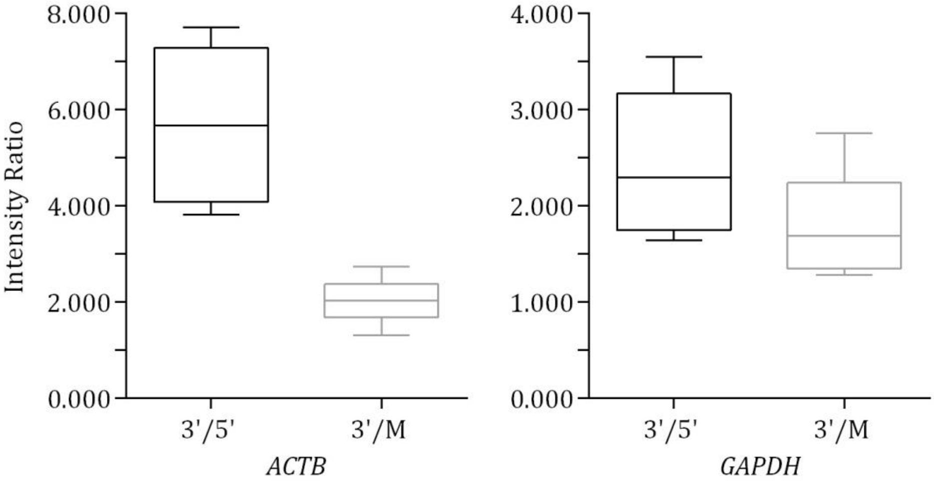


Figure 3.7 RNA Quality Control Check for Samples in the NuGEN Ovation® Whole Blood Study Microarray Suite (MAS) 5.0 signal intensity ratios between 3' and 5' ends (■) or 3' end and M (middle region) (■) of the standard house-keeping genes beta, actin (*ACTB*) [left-hand panel] and glyceraldehyde-3-phos phate dehydrogenase (*GAPDH*) [right-hand panel] plotted along the y-axis. Box and whisker plots were generated, applying a Tukey multiple comparisons test, using GraphPad Prism® software version 5.04 © 1992-2014 (GraphPad Software, Inc. CA USA). Assessment of Affymetrix® QC metrics was performed using Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK).

Abbreviations: 3' - three prime, 5' - five prime and QC - quality control.

nate sample types [BLDCON's 26.520±0.80 and BLDPAT's 27.182±0.44; two-tailed student's t-test not significant] (Table 3.8).

3.3.2.4.2 Average Percentage Presence Calls

In total, 54,675 probesets are represented on the Affymetrix® Human Genome U133 Plus 2.0 GeneChip® Arrays. Each one is comprised of 11 probe pairs which contain a mix of PM, as well as, MM 25-mer oligonucleotide sequences pertaining to a similar number of gene transcripts or EST's (Section 2.3.1.7.1). On average, 44.5% of genes were called as present (P) for controls (n=24,330), compared to 51.2% of genes for SALS patients (n=27,994) in the NuGEN Ovation® Whole Blood Study. A scatter dot plot displaying the mean and standard error of the mean (SEM) flagged BLDCON07, highlighted in red, as a potential outlier which had a significantly lower %P then the remainder of the cohort (p<0.01**) (Figure 3.8).

3.3.2.5 Relative Log Expression Signal

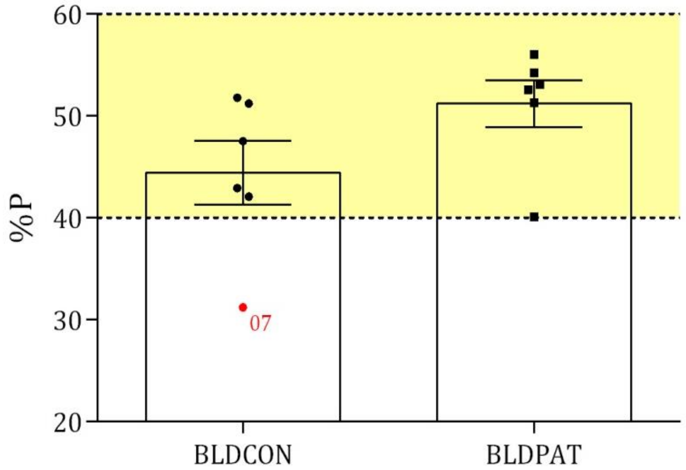


Figure 3.8 Average Percentage Presence Calls for Samples in the NuGEN Ovation® Whole Blood Study Scatter dot plot was generated using GraphPad Prism® software version 5.04 © 1992 to 2014 (Graph Pad Software, Inc. CA USA) displaying the mean and standard error of the mean (SEM) number of probesets as a percentage (%) of the 54,67 5 total which were called present (P) on Affymetrix® Human Genome U133 Plus 2.0 GeneChip® Arrays for SALS patient (■) and control (•) samples in the NuGEN Ovation® Whole Blood Study. The range of %P calls which was considered acceptable is represented by the YELLOW shaded region between the two dashed lines at the 40 and 60% threshold. Any potential outliers were highlighted in red. Assessment of QC metrics was performed using Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK).

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, BLDCON - blood control, BLDPAT - blood patient, QC - quality control and S - sporadic.

The mean absolute relative log expression (RLE) can be used as a measure of how the signal intensities on each individual GeneChip® compare with those across the rest of the experiment. A cohort which exhibits relative homogeneity should have a score close to zero with a small spread of values around the mean. This was found to be largely the case for samples in the NuGEN Ovation® Whole Blood Study with the exception of BLDCON07 which is highlighted in red (Figure 3.9).

3.3.2.6 Pearson's Correlation Coefficient

For each pair of GeneChips® in a microarray experiment the Expression Console™ software version 1.3.0.187 determines a Pearson's product-moment correlation coefficient (r), from the covariance divided by the product of the standard deviations. This is computed on a scale of -1 to 1 where zero equals no correlation (i.e. the data points are randomly distributed) and a value approaching plus (positive) or minus

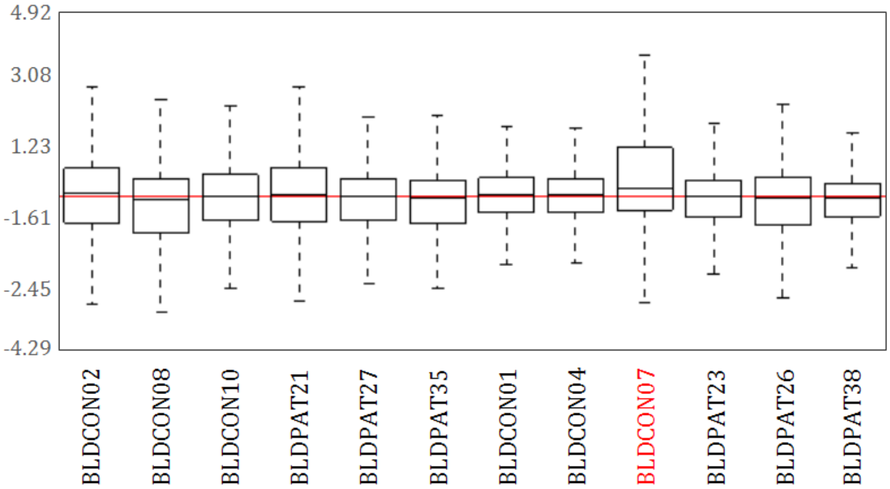


Figure 3.9 Mean Absolute Relative Log Expression (RLE) Boxplots for Samples in the NuGEN Ovation® Whole Blood Study RLE means and standard deviations for blood patient [BLDPAT] and control [BLDCON] samples in the NuGEN Ovation® Whole Blood Study. Whiskers represent minimum (lower) and maximum (upper) average probeset signal intensity values for each Affymetrix® Human Genome U133 Plus 2.0 GeneChip® Array in the experiment. Assessment of QC metrics was performed using Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK). Potential outliers are highlighted in red.

Abbreviations: QC - quality control.

(negative) one is indicative of their being a strong linear relationship between the X and Y variables (Figure 3.10). This data can be illustrated qualitatively on a coloured matrix as depicted in Figure 3.11. Of the samples in the NuGEN Ovation® Whole Blood Study BLDCON07, highlighted in red, produced by far the weakest correlation (r) with a score less than half the average of the remaining cohort.

$$r_{Pearsons} = \frac{\sum XY - \frac{\sum X \sum Y}{N}}{\sqrt{\left(\sum X^2 - \frac{(\sum X)^2}{N}\right)\left(\sum Y^2 - \frac{(\sum Y)^2}{N}\right)}}$$

X - Signal intensity values (Sample X)

Y - Signal intensity values (Sample Y)

N - Number of samples or GeneChips® in the experiment

Figure 3.10 Pearson's Product-Moment Correlation Coefficient (r) Calculation Equation adapted from Hartman et al 2015, which is freely available online at gcat.davidson.edu/DGPB/clust/background (Davidson College, NC USA © 2015).

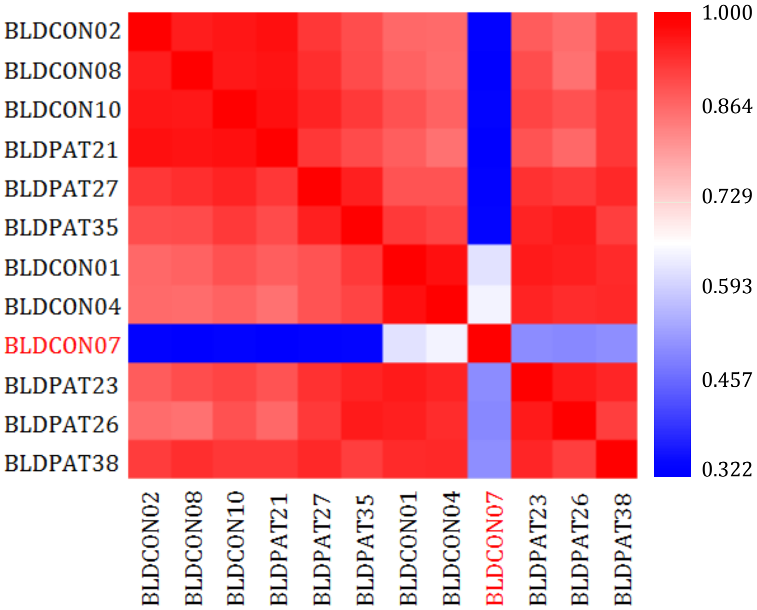
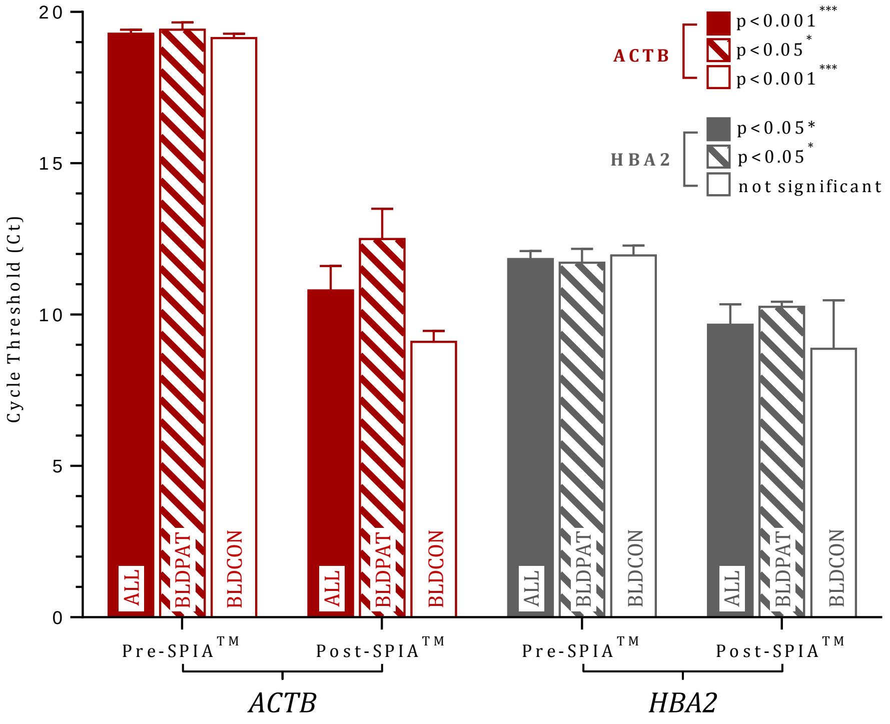


Figure 3.11 Pearson's Correlation Coefficient (r) for Samples in the NuGEN Ovation® Whole Blood Study For each pair-wise comparison in the coloured matrix a value for r is assigned on a scale of 0. 322 (Blue) to 1.000 (Red) where the higher the score is indicative of a stronger linear relationship between the X and Y variables. Potential outliers are highlighted in red. Assessment of the Affymetrix® QC metrics were performed in Expression Console™ software version 1. 3.0.187 (Affymetrix® Ltd., UK).

Abbreviations: BLDCON - blood control, BLDPAT - blood patient and QC - quality control.

3.4 Pre- and Post-SPIA™ qRT-PCR Measurements

In order to monitor the efficiency of the NuGEN Ovation® Whole Blood Solution (Section 2.3.1.4.2 and 2.3.1.5.1) a qRT-PCR experiment was performed using traditional SYBR® Green technology as outlined in Section 2.3.1.6. Relative Haemoglobin, alpha 2 (*HBA2*) mRNA transcript levels were measured against the standard housekeeping control, actin, beta (*ACTB*) (Figure 3.12) immediately prior to and following NuGEN Technologies Inc., UK patented SPIA™ method of linear single primer isothermal amplification. *ACTB* was selected as the most suitable internal reference gene since it was found to have exhibited from MAS 5.0 pivot data (not shown) the most stable level of expression, of all the transcripts which are routinely assessed. Mean cycle threshold (Ct) values for post-SPIA™ amplified material were significantly lowered for *ACTB* [pre-SPIA™ 19.278 (n=12) and post-SPIA™ measurements 10.801 (N=8); ⇩1.80-fold (p<0.001***)] but remained reasonable consistent for *HBA2* [pre-



		Pre-SPIA™			Post-SPIA™			
		N	*mean Ct*	*SEM*	*N*	*mean Ct*	*SEM*	*p-value*
ACTB	BLDPAT'S	6	19.417	0.243	4	12.498	1.001	0.012
	BLDCON'S	6	19.138	0.150	4	9.105	0.357	2.56E-05
	ALL	12	19.278	0.142	8	10.801	0.808	2.23E-05
HBA2	BLDPAT'S	6	11.713	0.457	4	10.258	0.170	0.031
	BLDCON'S	6	11.955	4.881	3	8.870	1.610	0.147
	ALL	12	11.834	0.271	7	9.663	0.676	0.030

Figure 3.12 Pre- and Post-SPIA™ qRT-PCR Measurements of *HBA2* mRNA Transcript Levels Relative to *ACTB* Using the NuGEN Ovation® Whole Blood Solution Mean and SEM cycle threshold (Ct) values (y-axis) for haemoglobin, alpha 2 (*HBA2*) (■) and the internal reference control gene actin, beta (*ACTB*) (🟥) are provided for each treatment group (x-axis). The bar chart in the uppermost panel was created in GraphPad Prism® software version 5.04 © 1992-2014 (GraphPad Software, Inc. CA USA). Probability values were determined at the 5% significance threshold ($p<0.05$) with a paired student's t-test applied in Microsoft Excel 2010 (Microsoft Corporation UK).

Abbreviations: BLDCON - blood control, BLDPAT - blood patient, mRNA - messenger RNA, *N* - number, qRT-PCR - quantitative real-time polymerase chain reaction, SEM - standard error of the mean and SPIA™ - single primer isothermal amplification

SPIA™ 11.833 (n=12) and post-SPIA™ measurements 9.663 (N=7); ⇩1.20-fold ($p< 0.05$*)]; an observation that also held true when the different sample types were interpreted individually [Blood control (BLDCON): *ACTB* ⇩2.10-fold ($p<0.001$***) and *HBA2* ⇩1.40-fold (p-value not significant) and Blood patient (BLDPAT): *ACTB* ⇩1.60-fold ($p<0.05$*) and *HBA2* ⇩1.10-fold ($p<0.05$*) (Figure 3.12)]. These findings suggest that the NuGEN Ovation® Whole Blood Solution, which utilises a unique DNA/RNA chimeric primer and proprietary whole blood reagent, has been successful in limiting the amplification of globin mRNA relative to other transcripts, in this case *ACTB,* that are also contained within the sample in order to reduce interference on the microarray (Wright et al 2008).

3.5 Peripheral Whole Blood Gene Expression Data

Direct comparisons were drawn between the JB NuGEN Ovation® and RR Ambion® GLOBINClear™ (Raman 2011) strategies for performing GEP from peripheral whole blood using identical, age and as far as possible, gender matched patient (BLDPAT) and control (BLDCON) samples which were collected at the same time in PAXgene® Blood RNA Collection Tubes and stored at -20^{0}C for up to three years prior to being processed (Table 2.1) (Section 2.3.1.1).

3.5.1 GeneSpring GX v11.5.1

3.5.1.1 Normalisation

Affymetrix® CEL files with the exclusion of BLDCON07, which was reported to have failed a number of the QC parameters (Section 3.3.2.1 and 3.3.2.6) assessed by Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd, UK), were uploaded into GeneSpring GX v11.5.1 analysis suite (Agilent Technologies Genomics Ltd., UK). Raw expression values were log2 transformed and a PLIER16 estimation algorithm applied (Section 2.3.1.9.2) without the need for performing a baseline conversion to the median of all the samples (Figure 3.13). Normalised signal intensities (Figure 3. 14) were visualised on a profile plot in which each of the 54,675 probesets that are present on Human Genome U133 Plus 2.0 GeneChip® Arrays, is represented under different experimental conditions (i.e. healthy versus disease status) by a single coloured line where red, yellow and blue indicates whether the corresponding transcript has a high, intermediate or low abundance (Figure 3.14).

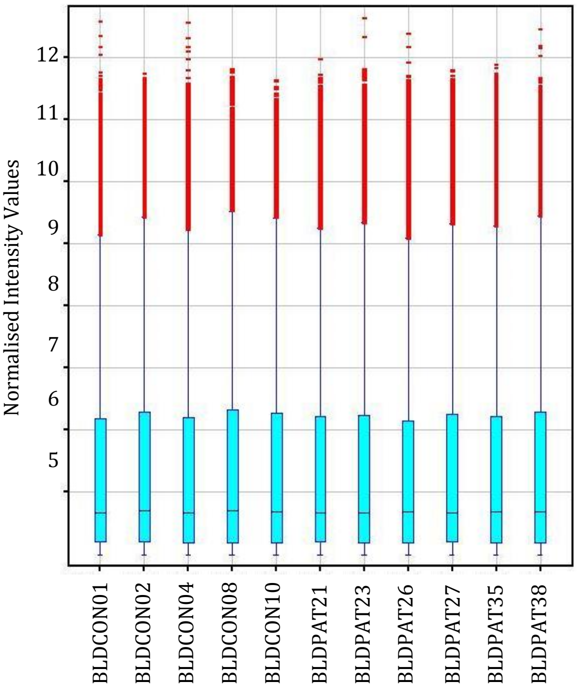


Figure 3.13 PLIER 16 Normalised Distribution of Relative Log2 Transformed Signal Intensity Values for Samples in the NuGEN Ovation® Whole Blood Study Box and Whisker plot generated using GeneSpring GX v11.5.1 (Agilent Technologies Genomics Ltd., UK). BLDCON07 was omitted on the basis that it had failed several of the QC parameters assessed in Expression Console™ software version 1.3.0.187.

Abbreviations: BLDCON - blood control, BLDPAT - blood patient, PLIER - Probe Logarithmic Intensity Error and QC - quality control.

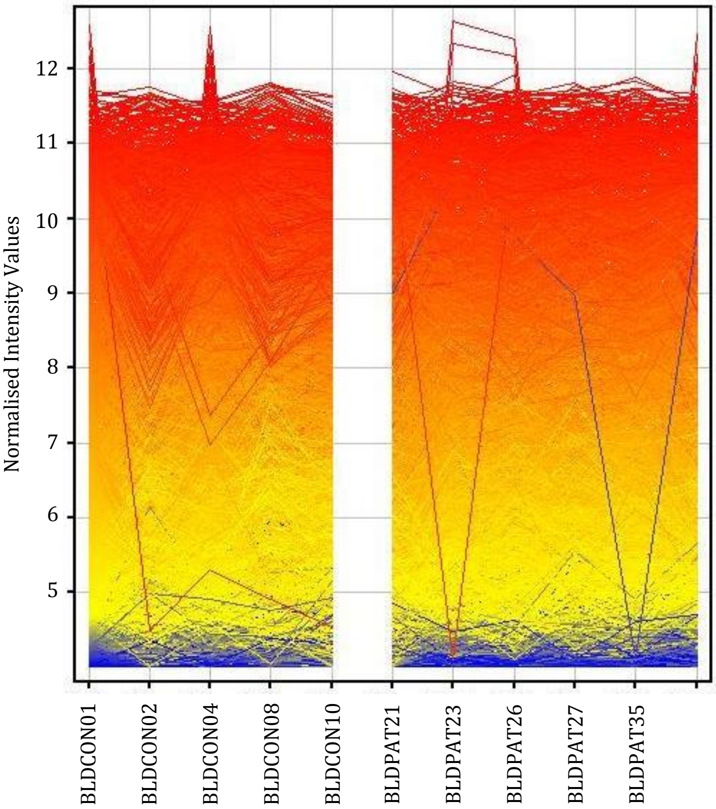


Figure 3.14 Profile Plot of PLIER 16 Normalised Signal Intensity Values for Samples in the NuGEN Ovation® Whole Blood Study Mean absolute expression values which are displayed along the y-axis are represented under different experimental conditions (x-axis) [i.e. healthy (left panel) versus disease (right panel) status] for each of the 54,675 probesets on the Affymetrix® Human Genome U133 Plus 2.0 GeneChip® Arrays. Red, yellow and blue lines signify high, intermediate and low expressing transcripts, respectively. The plot was generated using GeneSpring GX software version 11.5.1 (Agilent Technologies Genomics Ltd., UK) with BLDCON07 having already been excluded on the basis that it failed several QC parameters assessed by Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK).

Abbreviations: BLDCON - blood control, BLDPAT - blood patient, PLIER - Probe Logarithmic Intensity Error and QC - quality control.

3.5.1.2 Detection of Differentially Expressed Transcripts

DE transcripts were detected at the 5% significance level in GeneSpring GX v11.5.1 using an unpaired student's t-test with an FDR corrected p<0.05 and FC threshold of ≥ ±1.50 (Section 2.3.1.9.2).

3.5.1.2.1 JB NuGEN Ovation® Dataset

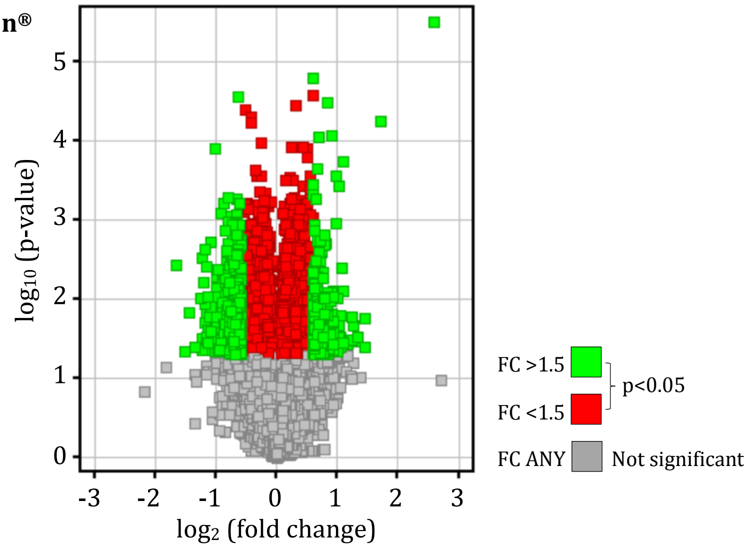
Analysis of the JB NuGEN Ovation® dataset identified 706 DE transcripts [unpaired student's t-test FDR p<0.05, FC ≥ ±1.50]; considerably fewer than would ordinarily be expected by chance (n=2,733) (Figure 3.15). These included 239 genes (33.9%) that were significantly up-regulated (⇧) and a further 467 genes (66.1%) which were significantly down-regulated (⇩) [APPENDIX TABLE A1].

3.5.1.2.2 RR Ambion® GLOBINClear™ Dataset

In contrast, analysis of the RR Ambion® GLOBINClear™ dataset (Dr Rohini Raman) identified a substantially greater proportion of transcripts (n=4,520) (Figure 3.15) as being DE [unpaired student's t-test FDR p<0.05, FC ≥ ±1.50]. These included 3,440 genes (76.1%) that were significantly up-regulated (⇧) and a further 1,080 genes which were significantly down-regulated (⇩) [APPENDIX TABLE A2].

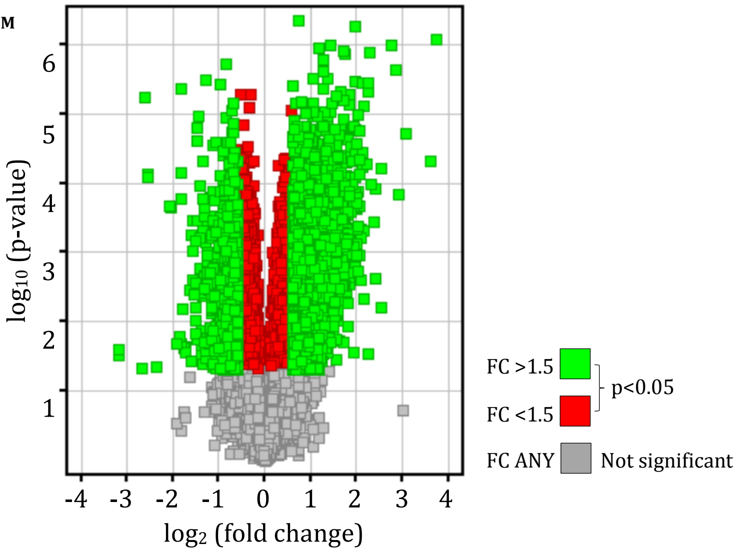
3.5.1.2.3 JB NuGEN Ovation® and RR Ambion® GLOBINClear™ Comparison

a) JB NuGEN Ovation®



	ALL	p<0.05	p<0.02	p<0.01	p<0.005	p<0.001
ALL	54,675	3,785	1,449	728	371	81
FC>1.1	22,242	3,426	1,325	685	351	78
FC>1.5	1,643	706	296	161	82	22
FC>2.0	74	50	27	16	11	5
FC>3.0	6	3	3	3	3	2
Expected by Chance		2,733	1,093	546	273	54

b) RR GLOBINClear™



	ALL	p<0.05	p<0.02	p<0.01	p<0.005	p<0.001
ALL	54,675	11,103	7,064	4,983	3,473	1,389
FC>1.1	33,707	11,072	7,055	4,982	3,473	1,389
FC>1.5	5,560	4,520	3,611	2,869	2,246	1,074
FC>2.0	1,264	1,213	1,126	986	833	492
FC>3.0	198	192	180	176	172	132
Expected by Chance		2,733	1,093	546	273	54

Figure 3.15 Volcano Plots of the 706 and 4,520 Gene Lists Detected in GeneSpring GX v11.5.1 Between JB NuGEN Ovation® and RR GLOBINClear™ Datasets

Abbreviations: FC - fold change, JB - Joanna Bury generated CEL files and RR - Dr Rohini Raman generated CEL files.

A GeneVenn diagram depicted in Figure 3.16, of the formerly discussed JB NuGEN Ovation® and RR Ambion® GLOBINClear™ (Section 3.5.1.2.1 and 3.5.1.2.2) datasets revealed substantial differences between the 706 and 4,520 lists. Only a handful of transcripts (n=82) (Table 3.3) representing just 11.6 or 1.8% of genes, respectively were shared in common with the majority of these disease related changes found to occur in opposing directions.

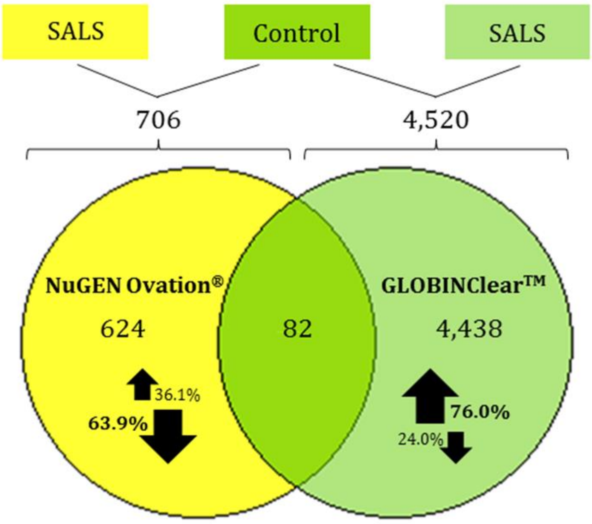


Figure 3.16 GeneVenn of JB NuGEN Ovation® and RR GLOBINClear™ Datasets DE transcripts were detected at the 5% significance level using an unpaired student's test (p<0.05) and applying a FC threshold of ≥ ±1.50 in GeneSpring GX software version 11.5.1 (Agilent Technologies Genomics Ltd., UK). The Venn diagram was created using the GeneVenn application that is freely available online at genevenn.sourceforge.net (University of Southern Mississippi, USA) (Pirooznia et al 2007).

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, DE - differentially expressed, FC - fold-change, JB - Joanna Bury generated CEL files, RR - Dr Rohini Raman generated CEL files and S - sporadic.

3.5.1.3 Clustering Analysis

Clustering analysis conducted at the 5% significance threshold in GeneSpring GX v1 1.5.1 applying the 706 (Section 3.5.1.2.1) and 4,520 (Section 3.5.1.2.2) filtered gene lists [unpaired student's t-test FDR p<0.05, FC ≥ ±1.50] demonstrated more distinct patient (BLDPAT) (blue) and control (BLDCON) (red) groupings on the PCA plot and hierarchically clustered HeatMap for the RR Ambion® GLOBINClear™ (Figure 3.17) dataset in comparison to the JB NuGEN Ovation® (Figure 3.18) dataset.

Transcript	Symbol	Gene Name	JB NuGEN Ovation® FC	p-value	RR GLOBINClear™ FC	p-value
206697_s_at	*HP*	haptoglobin	⇧ 2.40-fold	0.021	⇧ 2.69-fold	2.48E-03
211781_x_at	---	---	⇧ 2.34-fold	0.033	⇧ 1.97-fold	0.020
219359_at	*ATHL1*	ATH1, acid trehalase-like 1 (yeast)	⇧ 2.09-fold	4.06E-03	⇧ 1.75-fold	0.021
208470_s_at	*HP*	haptoglobin	⇧ 2.05-fold	0.031	⇧ 1.98-fold	0.046
238591_at	*HEXDC*	hexosaminidase (glycosyl hydrolase family 20, catalytic domain) containing	⇧ 1.83-fold	0.028	⇧ 1.59-fold	0.030
1559128_at	*HSDL2*	hydroxysteroid dehydrogenase like 2	⇧ 1.71-fold	9.18E-03	⇧ 1.86-fold	8.87E-04
226322_at	*TMTC1*	transmembrane and tetratricopeptide repeat containing 1	⇧ 1.69-fold	0.026	⇧ 4.47-fold	4.55E-03
203326_x_at	*COL5A1*	collagen, type V, alpha 1	⇧ 1.58-fold	0.014	⇧ 1.97-fold	4.61E-04
221996_s_at	*CLTB*	clathrin, light chain (Lcb)	⇧ 1.57-fold	8.79E-03	⇧ 1.91-fold	5.91E-04
213457_at	*MFHAS1*	malignant fibrous histiocytoma amplified sequence 1	⇧ 1.56-fold	8.95E-03	⇧ 1.66-fold	0.048
229392_s_at	*PIK3R2*	phosphoinositide-3-kinase, regulatory subunit 2 (beta)	⇧ 1.54-fold	6.70E-03	⇧ 2.04-fold	8.85E-04
1558739_at	*DUSP16*	dual specificity phosphatase 16	⇧ 1.53-fold	0.042	⇧ 1.80-fold	3.07E-03
206237_s_at	*NRG1*	neuregulin 1	⇧ 1.51-fold	0.041	⇧ 1.59-fold	0.046
218978_s_at	*SLC25A37*	solute carrier family 25, member 37	⇧ 1.51-fold	0.046	⇧ 1.95-fold	0.047
205215_at	*RNF2*	ring finger protein 2	⇩ 1.50-fold	0.027	⇧ 1.93-fold	6.58E-03
206544_x_at	*SMARCA2*	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 2	⇩ 1.50-fold	0.025	⇩ 3.06-fold	5.37E-04
241242_at	*FAM120A*	family with sequence similarity 120A	⇩ 1.51-fold	3.96E-03	⇧ 1.94-fold	5.62E-03
226109_at	*C21ORF91*	chromosome 21 open reading frame 91	⇩ 1.52-fold	0.048	⇧ 1.52-fold	0.032
222313_at	*CNOT2*	CCR4-NOT transcription complex, subunit 2	⇩ 1.52-fold	0.038	⇧ 2.04-fold	0.014
1555199_at	*GOSR1*	golgi SNAP receptor complex member 1	⇩ 1.53-fold	0.011	⇧ 1.62-fold	1.72E-03
200806_s_at	*HSPD1*	heat shock 60kDa protein 1 (chaperonin)	⇩ 1.53-fold	0.015	⇩ 2.87-fold	5.53E-04
223254_s_at	*G2E3*	G2/M-phase specific E3 ubiquitin ligase	⇩ 1.55-fold	0.026	⇧ 1.89-fold	0.041
242760_x_at	*PIGB*	phosphatidylinositol glycan anchor biosynthesis, class B	⇩ 1.55-fold	0.026	⇧ 1.70-fold	0.018
1555977_at	*LOC727918*	hypothetical LOC727918	⇩ 1.55-fold	0.043	⇧ 2.00-fold	1.98E-03
216072_at	---	---	⇩ 1.55-fold	0.039	⇧ 1.56-fold	4.89E-04
240248_at	*C10ORF46*	chromosome 10 open reading frame 46	⇩ 1.57-fold	0.045	⇧ 2.35-fold	0.036
201409_s_at	*PPP1CB*	protein phosphatase 1, catalytic subunit, beta isoform	⇩ 1.57-fold	0.048	⇧ 1.73-fold	0.027
229966_at	*EWSR1*	Ewing sarcoma breakpoint region 1	⇩ 1.57-fold	0.048	⇧ 2.13-fold	2.88E-03
202412_s_at	*USP1*	ubiquitin specific peptidase 1	⇩ 1.57-fold	2.42E-03	⇧ 2.50-fold	4.91E-03
217608_at	*SFRS12IP1*	SFRS12-interacting protein 1	⇩ 1.58-fold	0.015	⇧ 1.73-fold	0.018
200889_s_at	*SSR1*	signal sequence receptor, alpha	⇩ 1.58-fold	5.27E-04	⇩ 1.92-fold	2.71E-03
235009_at	*BOD1L*	biorientation of chromosomes in cell division 1-like	⇩ 1.60-fold	0.014	⇧ 2.41-fold	2.80E-03

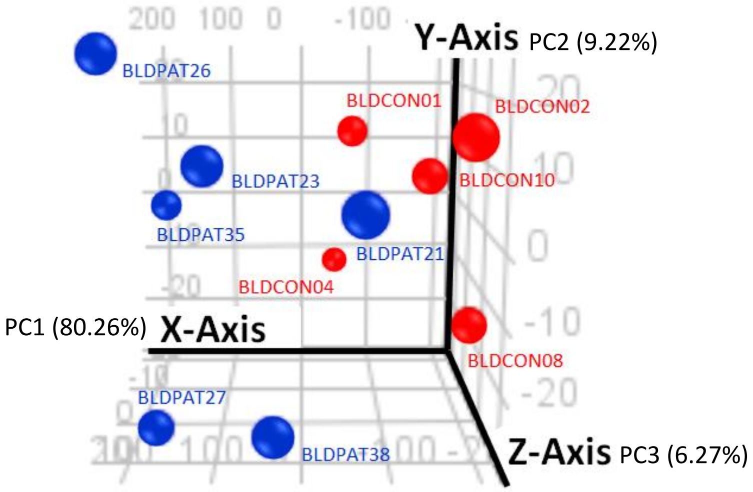
1560017_at	*TMTC3*	transmembrane and tetratricopeptide repeat containing 3	⇩ 1.60-fold	0.049	⇧ 1.58-fold	5.54E-04
1555439_at	*GTF3C3*	general transcription factor IIIC, polypeptide 3, 102kDa	⇩ 1.61-fold	0.043	⇧ 1.67-fold	5.84E-03
241294_at	*AP1G1*	adaptor-related protein complex 1, gamma 1 subunit	⇩ 1.62-fold	0.023	⇧ 1.78-fold	0.011
225980_at	*C14ORF43*	chromosome 14 open reading frame 43	⇩ 1.62-fold	0.027	⇩ 1.72-fold	7.84E-03
202068_s_at	*LDLR*	low density lipoprotein receptor	⇩ 1.63-fold	0.045	⇩ 1.83-fold	5.36E-03
222850_s_at	*DNAJB14*	DnaJ (Hsp40) homolog, subfamily B, member 14	⇩ 1.63-fold	0.047	⇧ 2.84-fold	4.39E-03
241610_x_at	*PACS1*	phosphofurin acidic cluster sorting protein 1	⇩ 1.64-fold	3.51E-03	⇧ 4.94-fold	1.01E-04
1569302_at	*KIAA1731*	KIAA1731	⇩ 1.64-fold	0.033	⇧ 1.84-fold	0.017
229353_s_at	*NUCKS1*	nuclear casein kinase and cyclin-dependent kinase substrate 1	⇩ 1.65-fold	0.027	⇧ 3.10-fold	2.90E-03
236752_at	*PKP4*	plakophilin 4	⇩ 1.66-fold	1.12E-03	⇧ 1.97-fold	0.011
232311_at	*B2M*	Beta-2-microglobulin	⇩ 1.67-fold	0.019	⇧ 3.33-fold	3.07E-04
212479_s_at	*RMND5A*	required for meiotic nuclear division 5 homolog A (*S. cerevisiae*)	⇩ 1.67-fold	0.023	⇧ 1.87-fold	1.23E-03
213518_at	*PRKCI*	protein kinase C, iota	⇩ 1.67-fold	0.047	⇧ 2.36-fold	6.86E-04
1561015_at	*KLF3*	Kruppel-like factor 3 (basic)	⇩ 1.68-fold	0.014	⇧ 1.67-fold	0.011
235060_at	*LOC100190986*	hypothetical LOC100190986	⇩ 1.68-fold	0.029	⇧ 1.67-fold	0.016
202006_at	*PTPN12*	protein tyrosine phosphatase, non-receptor type 12	⇩ 1.69-fold	0.020	⇩ 1.77-fold	0.038
222111_at	*FAM63B*	family with sequence similarity 63, member B	⇩ 1.71-fold	0.013	⇧ 1.57-fold	0.016
243233_at	*RNU6-1*	RNA, U6 small nuclear 1	⇩ 1.72-fold	0.021	⇧ 2.41-fold	6.03E-03
1554241_at	*COCH*	coagulation factor C homolog, cochlin (*Limulus polyphemus*)	⇩ 1.72-fold	0.048	⇧ 3.13-fold	4.26E-05
242576_x_at	*N4BP2L2*	NEDD4 binding protein 2-like 2	⇩ 1.72-fold	5.97E-03	⇧ 2.89-fold	2.11E-03
220369_at	*SMEK1*	SMEK homolog 1, suppressor of mek1 (*Dictyostelium*)	⇩ 1.72-fold	0.024	⇧ 1.75-fold	0.016
244679_at	*STK38*	serine/threonine kinase 38	⇩ 1.72-fold	0.025	⇧ 2.23-fold	0.017
211352_s_at	*NCOA3*	nuclear receptor coactivator 3	⇩ 1.73-fold	0.032	⇧ 1.80-fold	0.033
218294_s_at	*NUP50*	nucleoporin 50kDa	⇩ 1.73-fold	0.016	⇧ 2.10-fold	0.013
200751_s_at	*HNRNPC*	heterogeneous nuclear ribonucleoprotein C (C1/C2)	⇩ 1.73-fold	5.38E-03	⇩ 1.90-fold	1.32E-03
201299_s_at	*MOBKL1B*	MOB1, Mps One Binder kinase activator-like 1B (yeast)	⇩ 1.75-fold	0.037	⇧ 1.50-fold	0.016
238317_x_at	*RBMS1*	RNA binding motif, single stranded interacting protein 1	⇩ 1.75-fold	0.027	⇧ 2.62-fold	1.03E-03
227259_at	*CD47*	CD47 molecule	⇩ 1.76-fold	6.15E-03	⇧ 1.85-fold	7.84E-03
1563975_at	*RNF130*	ring finger protein 130	⇩ 1.76-fold	5.12E-04	⇧ 1.56-fold	0.016
242844_at	*PGGT1B*	protein geranylgeranyltransferase type I, beta subunit	⇩ 1.77-fold	2.46E-03	⇧ 1.82-fold	0.022
237461_at	*NLRP7*	NLR family, pyrin domain containing 7	⇩ 1.85-fold	0.020	⇩ 1.79-fold	0.019
214352_s_at	*KRAS*	v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog	⇩ 1.85-fold	8.23E-03	⇧ 2.45-fold	2.60E-03
201407_s_at	*PPP1CB*	protein phosphatase 1, catalytic subunit, beta isoform	⇩ 1.86-fold	0.044	⇧ 2.01-fold	1.11E-03
227364_at	*CAPZA1*	capping protein (actin filament) muscle Z-line, alpha 1	⇩ 1.86-fold	0.039	⇧ 2.16-fold	6.57E-03
1558747_at	*SMCHD1*	structural maintenance of chromosomes flexible hinge domain containing 1	⇩ 1.88-fold	0.036	⇧ 2.61-fold	3.44E-03

233898_s_at	*FGFR1OP2*	FGFR1 oncogene partner 2	⇩ 1.89-fold	0.036	⇧ 1.79-fold	0.037
212418_at	*ELF1*	E74-like factor 1 (ets domain transcription factor)	⇩ 1.94-fold	0.025	⇩ 1.75-fold	5.43E-03
224778_s_at	*TAOK1*	TAO kinase 1	⇩ 1.98-fold	0.041	⇧ 2.01-fold	2.71E-03
222409_at	*CORO1C*	coronin, actin binding protein, 1C	⇩ 1.98-fold	7.03E-03	⇧ 1.94-fold	0.025
230180_at	*DDX17*	DEAD (Asp-Glu-Ala-Asp) box polypeptide 17	⇩ 1.99-fold	0.017	⇧ 1.71-fold	0.047
215635_at	*PDE8A*	phosphodiesterase 8A	⇩ 1.99-fold	0.037	⇧ 2.05-fold	0.021
228471_at	*ANKRD44*	ankyrin repeat domain 44	⇩ 2.06-fold	0.033	⇧ 3.12-fold	1.62E-05
239957_at	*SETD5*	SET domain containing 5	⇩ 2.14-fold	0.026	⇧ 2.03-fold	8.30E-03
1552480_s_at	*PTPRC*	protein tyrosine phosphatase, receptor type, C	⇩ 2.19-fold	0.035	⇧ 1.99-fold	0.026
219978_s_at	*NUSAP1*	nucleolar and spindle associated protein 1	⇩ 2.23-fold	3.82E-03	⇧ 2.01-fold	0.014
228222_at	*PPP1CB*	protein phosphatase 1, catalytic subunit, beta isoform	⇩ 2.25-fold	0.030	⇧ 3.34-fold	1.34E-03
1552552_s_at	*CLEC4C*	C-type lectin domain family 4, member C	⇩ 2.28-fold	2.31E-03	⇩ 2.27-fold	0.018
201237_at	*CAPZA2*	capping protein (actin filament) muscle Z-line, alpha 2	⇩ 2.36-fold	0.031	⇧ 2.53-fold	0.019
1555687_a_at	*CLEC4C*	C-type lectin domain family 4, member C	⇩ 2.73-fold	0.015	⇩ 2.15-fold	0.018
231484_at	*ATP8A1*	ATPase, aminophospholipid transporter (APLT) class I, type 8A, member 1	⇩ 2.84-fold	0.046	⇧ 3.82-fold	0.028

Table 3.3 JB NuGEN Ovation® and RR GLOBINClear™ GeneSpring Common List (n=82) [unpaired student's t-test $p<0.05$, FC ≥ ±1.50] Affymetrix® transcript IDs are ranked in order of fold-change (FC) for whole blood samples in the JB NuGEN Ovation® dataset and corresponding values for the same BLDCON and BLDPAT cases are provided in the adjacent columns for the RR GLOBINClear™ dataset. Unannotated transcripts as determined using the NetAffx™ Analysis Centre, which is freely available at affymetrix.com/analysis/index.affx (Affymetrix® Ltd, UK) (Liu et al 2003), were represented by three dashed lines under the 'Symbol' and 'Gene Name' headings. Arrows were used to indicate the direction of change [up-regulation (red) and down-regulation (green)]. Transcripts with the same direction of change for both datasets are highlighted in grey.

Abbreviations: ATH1 - acid trehalase 1, ATP - adenosine triphosphate, BLDCON - blood control, BLDPAT - blood patient, CCR4 - chemokine (C-C motif) receptor 4, FGFR - fibroblast growth factor receptor, JB - Joanna Bury generated CEL files, NEDD - neural precursor cell expressed, developmentally down-regulated, NLR - NOD-like receptor, RR - Dr Rohini Raman generated CEL files, SNAP - snRNA activating protein, snRNA - small nuclear RNA and TAO - Thousand and One Amino Acid Protein.

a) PCA plot



b) Hierarchically Clustered HeatMap

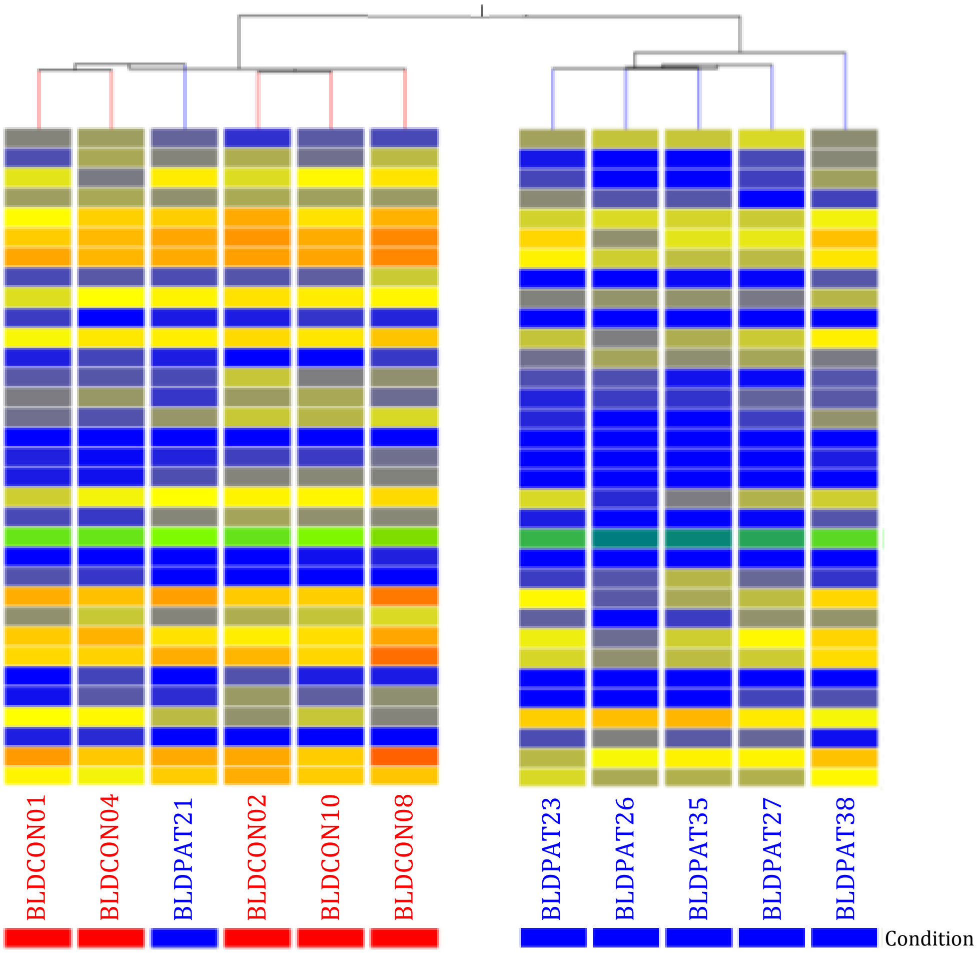
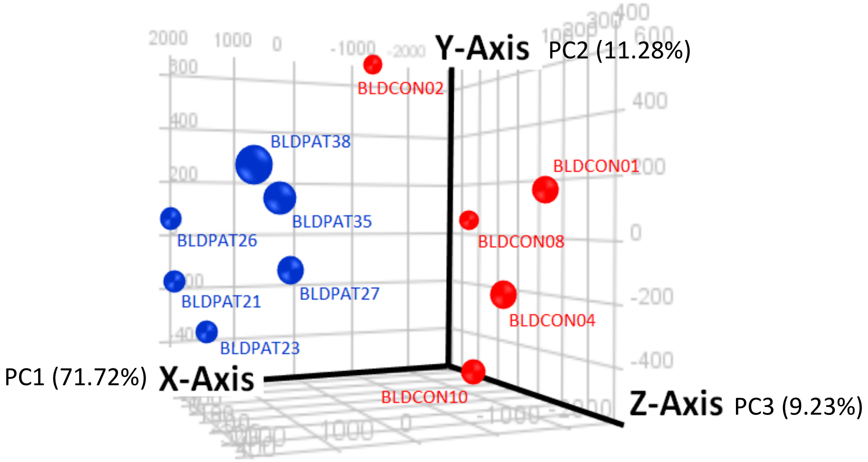


Figure 3.17 Clustering Analysis of the JB NuGEN Ovation® Dataset Applying the 706 Gene List in GeneSpring GX v11.5.1 [unpaired student's t-test FDR p<0.05, FC ≥ ± 1.50]

Abbreviations: BLDCON - blood control, BLDPAT - blood patient, FC - fold change, JB - Joanna Bury generated CEL files and PCA - principal components analysis.

a) PCA plot



b) Hierarchically Clustered HeatMap

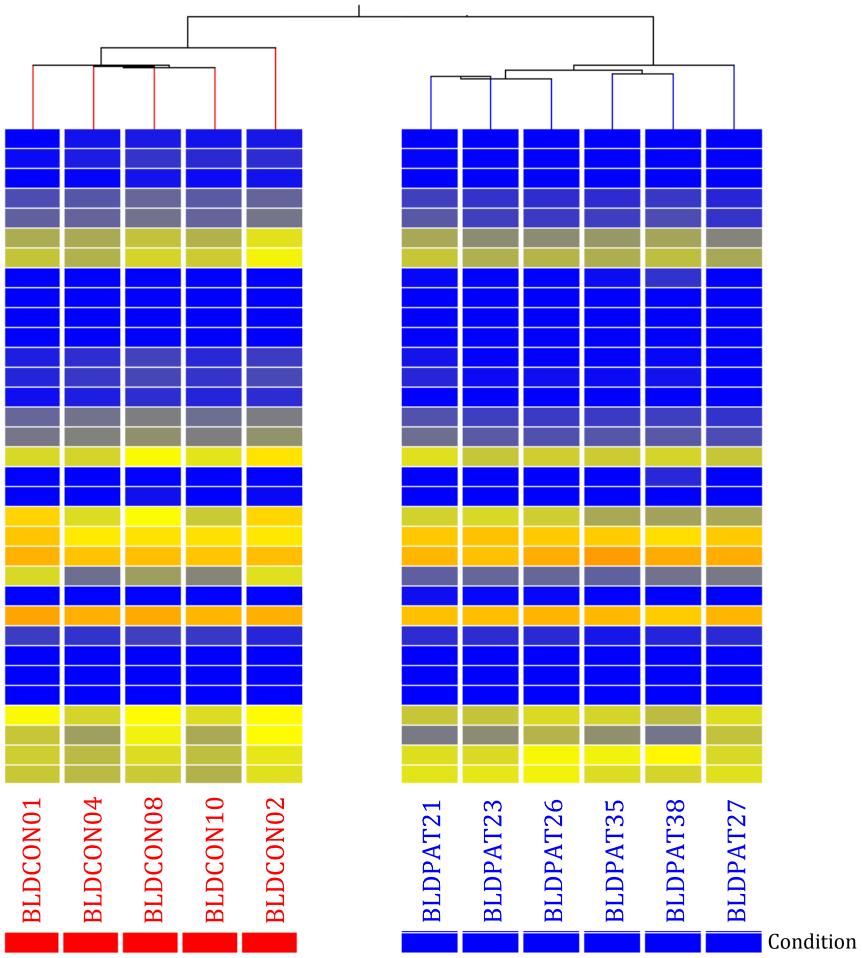


Figure 3.18 Clustering Analysis of the RR GLOBINClear™ Dataset Applying the 4,520 Gene List in GeneSpring GX v11.5.1 [unpaired student's t-test FDR p<0.05, FC ≥ ± 1.50]

Abbreviations: BLDCON - blood control, BLDPAT - blood patient, FC - fold change, PCA - principal components analysis and RR - Dr Rohini Raman generated CEL files.

3.5.1.4 DAVID Functional Annotation Enrichment Analysis

The GeneSpring GX v11.5.1 generated 706 and 4,520 gene lists [unpaired student's t-test FDR p<0.05, FC ≥ ±1.50] pertaining to JB NuGEN Ovation® (Section 3.5.1.2.1) and RR Ambion® GLOBINClear™ (Section 3.5.1.2.2) datasets could also be imported into DAVID bioinformatics resource version 6.7 (Huang da et al 2009a, Huang et al 2009b). Functional annotation clustering analysis was subsequently performed on GOTERM_BP_FAT and GOTERM_MF_FAT gene ontology (GO) terms applying a *Homo sapiens* background and filtering using 'Medium' classification stringency (Section 2. 3.1.8.3). Note that for the analysis of the RR Ambion® GLOBINClear™ dataset the 4, 520 list was necessarily trimmed to include only the top ranking 3,000 probeset IDs as determined by probability value since this represents the upper limit which the software is capable of handling in each run. Categories with a minimum EASE score above 1.30 and Benjamini-Hochberg FDR corrected p<0.05 were considered statistically significant. In total, DAVID mapped 686 (97.2%) of 706 [230 genes ⇧ and 456 genes ⇩] and 2,692 (89.7%) of 3,000 (4,520) [2,130 genes ⇧ and 562 genes ⇩] Affymetrix® probeset IDs identified from each comparison.

3.5.1.4.1 JB NuGEN Ovation® Dataset

The 706 list of DE transcripts in GeneSpring GX v11.5.1 [unpaired student's t-test FDR p<0.05, FC ≥ ±1.50] from the JB NuGEN Ovation® dataset was enriched for GO categories associated with protein serine/threonine kinase activity, enzyme binding, intracellular transport as well as the regulation of gene transcription from the RNA polymerase II promoter (Table 3.4).

#	GO term	Functional Category	EASE	Count	Benjamini
1	GO:0004674	protein serine/threonine kinase activity	4.40	39	8.30E-05
2	GO:0019899	enzyme binding	3.66	38	5.60E-03
3	GO:0046907	intracellular transport	2.48	44	0.030
4	GO:0006357	regulation of transcription from RNA polymerase II promoter	2.47	47	0.028
5	GO:0003702	RNA polymerase II transcription factor activity	1.33	21	0.019

Table 3.4 JB NuGEN Ovation® DAVID Functional Annotation Clustering Analysis

Abbreviations: # - rank, DAVID - Database of Annotation, Visualisation and Integrated Discovery, EASE - enrichment score, GO - gene ontology and JB - Joanna Bury generated CEL files.

3.5.1.4.2 RR Ambion® GLOBINClear™ Dataset

Conversely, the 3,000 highest ranking genes in the GeneSpring GX v11.5.1 4,520 list of DE transcripts from the RR Ambion® GLOBINClear™ dataset [unpaired student's t-test FDR p<0.05, FC ≥ ±1.50] were found to be enriched for GO categories that are associated with chromosome organisation, nucleotide binding, mRNA metabolism, protein transport and negative regulation of gene transcription (Table 3.5).

#	GO term	Functional Category	EASE	Count	Benjamini
1	GO:0051276	chromosome organization	5.60	95	4.80E-04
2	GO:0016071	mRNA metabolic process	4.17	70	0.014
3	GO:0015031	protein transport	4.05	126	0.016
4	GO:0045892	negative regulation of transcription, DNA -templated	3.22	80	0.029
5	GO:0000166	nucleotide binding	3.17	321	1.90E-03
6	GO:0009057	macromolecular catabolic process	2.80	121	0.049
7	GO:0051173	negative regulation of nitrogen compound metabolic process	2.50	103	0.049
8	GO:0006351	transcription, DNA-templated	2.28	291	0.031
9	GO:0051169	nuclear transport	2.05	35	0.038

Table 3.5 RR GLOBINClear™ DAVD Functional Annotation Clustering Analysis

Abbreviations: # - rank, DAVID - Database for Annotation, Visualisation and Integrated Discovery, EASE - enrichment score, GO - gene ontology, mRNA - messenger RNA and RR - Dr Rohini Raman generated CEL files.

3.5.1.4.3 JB NuGEN Ovation® and RR Ambion® GLOBINClear™ Comparison

The DAVID comparative analyses of functionally enriched GO categories which are summarised in Table 3.4 and 3.5 highlighted very few commonalities, with perhaps the exception of gene transcription, between the JB NuGEN Ovation® (Section 3.5.1.4.1) and RR Ambion® GLOBINClear™ (Section 3.5.1.4.2) datasets. EASE scores of 5.6 or below coupled with relatively low gene counts suggest that both methodologies assessed here for GEP from peripheral whole blood in ALS are highly variable.

3.5.1.5 KEGG Pathway Analysis

KEGG pathway analysis also conducted in DAVID (Huang da et al 2009a, Huang et al 2009b) identified six shared pathways common to both the JB NuGEN Ovation® and RR Ambion® GLOBINClear™ datasets including MAPK signalling (Section 3.5.1.5.1)

[Rank 1 (13), count 20 (46), 3.2% (2.0%) uncorrected p<0.001*** (Table 3.6 and 3.7)], Non-small cell lung cancer, T cell receptor signalling, chronic myeloid leukemia and gonadotropin releasing hormone (GnRH) signalling. In the following two sections, JB NuGEN Ovation® related gene expression changes which are associated with the top two most significant KEGG pathways, namely the MAPK (Section 3.5.1.5.1) and neurotrophin (Section 3.5.1.5.2) signalling cascades, are discussed further.

#	KEGG Pathway	Count	%	p-value	Benjamini
1	MAPK signalling pathway	20	3.2	1.60E-03	0.210
2	Oocyte meiosis	11	1.8	4.00E-03	0.250
3	Long-term potentiation	8	1.3	7.90E-03	0.320
4	Neurotrophin signalling pathway	11	1.8	9.20E-03	0.280
5	Non-small cell lung cancer	7	1.1	9.50E-03	0.240
6	T cell receptor signalling pathway	10	1.6	0.011	0.230
7	RNA degradation	7	1.1	0.012	0.230
8	Chronic myeloid leukemia	8	1.3	0.013	0.210
9	NOD-like receptor signalling pathway	7	1.1	0.018	0.250
10	Endometrial cancer	6	1.0	0.031	0.360
11	GnRH signalling	8	1.3	0.048	0.480

Table 3.6 JB NuGEN Ovation® KEGG Pathway Analysis Highlighted in yellow JB NuGEN Ovation® and RR Ambion® GLOBINClear™ common pathways.

Abbreviations: # - rank, GnRH - gonadotropin releasing hormone, JB - Joanna Bury generated CEL files, KEGG - Kyoto Encyclopaedia of Genes and Genomes, MAPK - mitogen activated protein kinase, NOD - nucleotide binding oligomerization domain and RR - Dr Rohini Raman generated CEL files.

3.5.1.5.1 MAPK Signalling Cascade

The mitogen-activated protein kinases (MAPK's) (otherwise known as extracellular signal-regulated kinases (ERK's)) are a family of serine/threonine/tyrosine specific kinases which are responsible for the phosphorylation of cytoplasmic components and nuclear transcription factors (NTF's) that regulate gene expression in response to a diverse array of extracellular stimuli including growth factors [classical MAPK cascade], pro-inflammatory cytokines, osmotic stress, heat shock and UV radiation [c-Jun N-terminal kinase (JNK)/p38 MAPK cascade] (Murai et al 2010, Strniskova et al 2002).

Upon ligand binding to the receptor tyrosine kinases of the classical MAPK cascade autophosphorylation is triggered in order to attract protein complexes containing SOS [*SOS2* (son of sevenless homolog 2 (*Drosophila*)) ⇧1.71-fold SALS, p<0.05] and

#	KEGG Pathway	Count	%	p-value	Benjamini
1	Fc gamma R-mediated phagocytosis	23	1.0	8.50E-04	0.140
2	Glioma	17	0.8	1.50E-03	0.130
3	Endocytosis	36	1.6	1.50E-03	0.090
4	Chronic myeloid leukemia	19	0.8	1.60E-03	0.071
5	B cell receptor signalling pathway	19	0.8	1.60E-03	0.071
6	Insulin signalling pathway	28	1.2	2.50E-03	0.087
7	Adipocytokine signalling pathway	17	0.8	3.00E-03	0.089
8	Ubiquitin mediated proteolysis	28	1.2	3.10E-03	0.078
9	Neurotrophin signalling pathway	26	1.2	3.10E-03	0.070
10	Phosphatidylinositol signalling system	18	0.8	3.50E-03	0.069
11	Spliceosome	26	1.2	3.90E-03	0.070
12	VEGF signalling pathway	18	0.8	4.00E-03	0.066
13	MAPK signalling pathway	46	2.0	4.40E-03	0.066
14	Renal cell carcinoma	17	0.8	4.80E-03	0.066
15	ErbB signalling pathway	19	0.8	8.60E-03	0.110
16	RNA degradation	14	0.6	0.011	0.120
17	Adherens junction	17	0.8	0.012	0.130
18	Pathways in cancer	52	2.3	0.013	0.130
19	GnRH signalling pathway	20	0.9	0.014	0.140
20	Pancreatic cancer	16	0.7	0.015	0.140
21	T cell receptor signalling pathway	21	0.9	0.020	0.170
22	Leukocyte transendothelial migration	22	1.0	0.026	0.200
23	Natural killer cell mediated cytotoxicity	24	1.1	0.028	0.210
24	Jak-STAT signalling pathway	27	1.2	0.028	0.210
25	Acute myeloid leukemia	13	0.6	0.029	0.200
26	Fc epsilon R1 signalling pathway	16	0.7	0.029	0.200
27	mTOR signalling pathway	12	0.5	0.031	0.200
28	Progesterone-mediated oocyte maturation	17	0.8	0.033	0.210
29	Inositol phosphate metabolism	12	0.5	0.040	0.230
30	Non-small cell lung cancer	12	0.5	0.040	0.230
31	Regulation of actin cytoskeleton	34	1.5	0.047	0.260

Table 3.7 RR Ambion® GLOBINClear™ KEGG Pathway Analysis Highlighted in yellow JB NuGEN Ovation® and RR Ambion® GLOBINClear™ common pathways.

Abbreviations: # - rank, ErbB - epidermal growth factor receptor, GnRH - gonadotropin releasing hormone, JAK - Janus kinase, JB - Joanna Bury generated CEL files, KEGG - Kyoto Encyclopaedia of Genes and Genomes, MAPK - mitogen activated protein kinase, mTOR - mammalian target of rapamycin, RR - Dr Rohini Raman generated CEL files, STAT - signal transducers and activators of transcription and VEGF - vascular endothelial growth factor.

the GRB2 [*GAPT* (growth factor receptor-bound protein 2 (GRB2) binding adaptor protein, transmembrane) ⇩1.60-fold SALS, p<0.05] adaptor molecule to the plasma membrane which, in turn, leads to the activation of Ras [*KRAS* (Kirsten rat sarcoma viral oncogene homolog) ⇩1.85-fold SALS, p<0.01 accompanied by the inhibitory regulator *RASA1* (RAS p21 protein activator GTPase activating protein 1) ⇩1.51-fold S ALS, p<0.05].

In the presence of the guanine nucleotide exchange factor, RasGRP [*RASGRP2* (Ras guanyl releasing protein 2 (calcium and DAG-related) ⇧1.55-fold SALS, p<0.05] Ras directly, or indirectly via protein kinase C, activates Raf1, B-Raf and the oncogene homolog Mos which leads to the sequential phosphorylation of MAP2K1 (⇩1.56-fold SALS, $p<0.05$), MAPK1, RPS6K [*RPS6KA2/A5* (ribosomal protein S6 kinase, 90 kDa) ⇧1.96-fold SALS, $p<0.001$ and ⇩1.86-fold SALS, $p<0.05$ for the second and fifth polypeptide respectively] and cyclic adenosine monophosphate (cAMP) response element binding transcription factor CREB (Di Giacomo et al 2009, Lu et al 2010) in order to promote cell differentiation and survival (Figure 3.19). Furthermore, MAPK1 that is negatively regulated by DUSP16 [*DUSP16* (dual specific phosphatase 16) ⇧1.53-fold SALS, $p<0.05$] is known to phosphorylate the calcium independent phospholipase PLA2G [*PLA2G4C* (phospholipase A2, group IVC (cytosolic, calcium-indepen dent) ⇧1.81-fold SALS, $p<0.01$ and *PLA2G6* (phospholipase A2, group VI (cytosolic, calcium-independent) ⇧1.76-fold SALS, $p<0.05$]; a molecule considered essential for normal lipid metabolism (Murakami et al 2011) which may also play an important role in FasL mediated apoptosis (Figure 3.19) (Section 1.2.4.8) (Atsumi et al 1998). An overall down-regulation in Ras GTPase activity observed on the 3' IVT expression arrays in the peripheral whole blood of SALS patients recruited to the NuGEN Ovation® Whole Blood Study is expected to lead to a reduction in the levels of mitochondrial membrane associated B-cell CLL/lymphoma 2 protein (Bcl2) [*BCLAF1* (BCL2-associated transcription factor 1) ⇩1.77-fold SALS, $p<0.01$; *BCL2L13* (BCL2-like 13 (apoptosis facilitator)) ⇩1.59-fold SALS, $p<0.01$], which under normal physiological conditions, is known to suppress cell death signals by binding to apoptotic peptidase activating factor 1 (APAF1) and blocking cytochrome c release (Brunet et al 2001, Hockenbery et al 1990, Liu et al 1996, Ruvolo et al 2001). A significant depletion in the abundance of Bcl2 lifts its inhibition of apoptosis-related cysteine peptidase activation [*CASP5* (caspase 5) ⇧2.03-fold SALS, $p<0.05$] thereby inducing programmed cell death (Kuranaga 2012, Momeni et al 2013).

Several components of the JNK/p38 MAPK cascades, responsible for mediating cell cycle arrest and inducing potent pro-apoptotic signals upon detecting DNA damage (Ghosh et al 2009, Kim et al 2011, Ryazantseva et al 2008, Tamagno et al 2003, Van Laethem et al 2006), were also found to be dysregulated in the peripheral whole venous blood of SALS patients compared to controls. These include protein LAK1 [*NLK* (nemo-like kinase) ⇩1.82-fold SALS, $p<0.05$], TAO1/2 [*TAOK1* (Thousand And One amino acid protein kinase) ⇩1.98-fold SALS, $p<0.05$], TGFR-2 [*TGFBR2* (transforming growth factor, beta receptor II (70/80kDa)) ⇩1.82-fold SALS, $p<0.05$], p58 [*PAK2* p 21 protein Cdc42/Rac associated kinase 2) ⇩1.60-fold SALS, $p<0.05$], MEKK1 [*MAP 3K1* ⇩1.70-fold SALS, $p<0.05$], MEKK7 [*MAP3K7* ⇩ 1.61-fold SALS, $p<0.05$] and MAP 3K7 interacting protein 1 (TAB1) [*MAP3K7IP1* (TGF-beta activated kinase 1) ⇧1.59-fold SALS, $p<0.05$].

3.5.1.5.2 Neurotrophin Signalling Cascade

The neurotrophic factors NT-3 (neurotrophin-3), NT-4/5 (neurotrophin-4/5), NGF (nerve growth factor) and BDNF represent a family of small secreted proteins which are responsible for promoting cell survival and cell death signals in the developing sensory/MN's and microglial cells of the mammalian CNS (Ernsberger 2009). Their engagement of tropomyosin-related tyrosine kinase receptors, namely TrkA, TrkB and TrkC, induces receptor dimerization and autophosphorylation which attracts a whole plethora of signal transducing molecules to the plasma membrane (Chao et al 2006, Skaper 2008). Of particular relevance were the SHC (Src homology 2 domain, containing) and SH2-B (SH2 domain containing signalling mediator) adaptor proteins which are involved in the recruitment of GRB2 (⇩1.60-fold SALS, $p<0.05$) and SOS2 (⇧1.71-fold SALS, $p<0.05$) complexes that leads to the activation of Ras (⇩1.85-fold SALS, $p<0.01$); a small GTPase important for a diverse array of processes including cellular differentiation, retrograde axonal transport, neurite outgrowth and synaptic plasticity (Figure 3.19) (Bhattacharyya et al 1997, Feig 2011, Stornetta & Zhu 2011, Tartaglia & Gelb 2010). The Ras proteins K, N and H function as molecular switches which exert their effects via several intracellular signalling cascades including MAP K (Section 3.5.1.5.1) and the PI3K-AKT pathways [*PIK3R2* (phosphoinositide-3-kinase (PI3K) regulatory subunit 2, beta) ⇧1.54-fold SALS, $p<0.01$ which enhances AKT (alternative name protein kinase B (PKB)) inhibition of forkhead box O3a (*FBXO3*) ⇩ 1.54-fold, $p<0.05$ and glycogen synthase kinase 3, beta (*GSK3B*) proteins (Leger et al 2006)]. Increases in PI3K-mediated phosphorylation of the serine/threonine specific kinase, AKT (Brunet et al 1999), is expected to block the translocation of FOXO3a into the nucleus; thereby preventing the subsequent activation of FasL gene transcription to promote cell survival (Zheng et al 2002, Zheng & Quirion 2004).

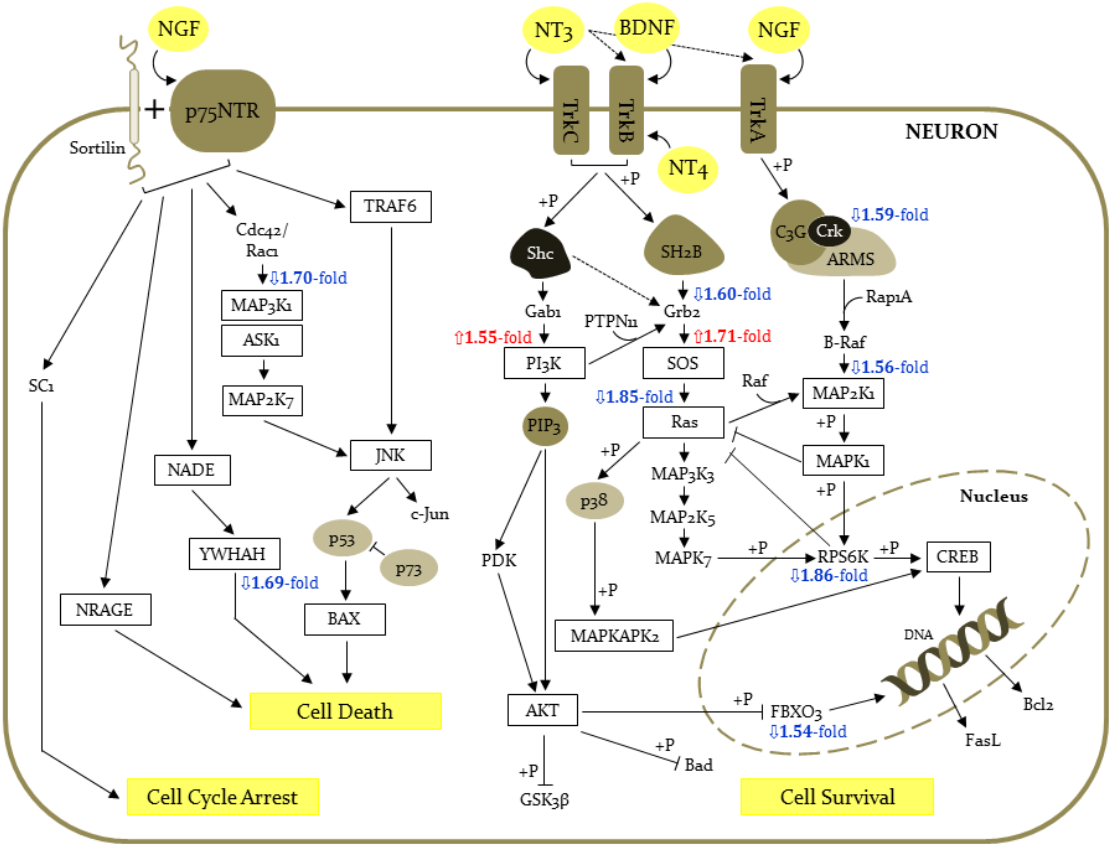


Figure 3.19 KEGG Pathway Schematic of Neurotrophin Signalling Cascade

Abbreviations: +P - phosphorylation, (⇧) - up-regulated, (⇩) - down-regulated, AKT - v-akt murine thymoma viral oncogene homolog, ARMS - ankyrin repeat rich membrane spanning, ASK - associated X protein, Bcl2 - B-cell CLL/lymphoma 2, BDNF - brain derived neurotrophic factor, B-Raf - v-raf murine sarcoma viral oncogene homolog B, C3G - guanine nucleotide releasing protein, Cdc42 - cell division control protein 42 homolog, CREB - cyclic adenosine monophosphate (cAMP) responsive element binding protein, Crk - v-crk avian sarcoma virus CT10 oncogene homolog, Fas - first apoptosis signal, FasL - Fas ligand, FBXO3 - forkhead box O3, Gab - GRB2 associated binding protein, GRB2 - growth factor receptor bound protein 2, GSK3β - glycogen synthase kinase 3, beta, JNK - c-Jun N-terminal kinase, KEGG - Kyoto Encyclopaedia of Genes and Genomes, MAPK - mitogen activated protein kinase, NADE - p75NTR associated cell death executor, NGF - nerve growth factor, NRAGE - neurotrophin receptor interacting melanoma antigen gene (MAGE) homolog, NTR - neurotrophin receptor, PI3K - phosphoinositide 3 kinase, PTPN11 - tyrosine protein phosphatase non-receptor type 11, Rap1A - Ras related protein, RPS6K - ribosomal protein S6 kinase, SC1 - Schwann cell factor 1, SH2B - SH2 domain containing signalling mediator, Shc - Src homology 2 domain containing, SOS - son of sevenless, TRAF6 - TNF receptor associated factor 6, E3 ubiquitin protein ligase, TNF - tumour necrosis factor, Trk - tyrosine kinase receptor and YWHAH - tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta.

Additionally, Ras is also known to interact with the Raf family of serine/threonine specific kinases that are known to mediate MAP2K1 (⇩1.56-fold SALS, $p<0.05$) and RPS6K activity (⇧1.96-fold SALS, $p<0.001$ and ⇩1.86-fold SALS, $p<0.05$ for the second and fifth polypeptides, respectively (Gysin et al 2011)). Rap1A, a member of the Ras oncogene family, and its binding partner RASSF5 [*RASSF5* (Ras association (Ral

GDS/AF-6) domain family member 5) ⇩1.59-fold SALS, p<0.01] exert a similar function which is initiated by the establishment of long lived complexes several additional adaptor molecules including C3G (guanine nucleotide releasing protein), SHP-2 (protein tyrosine phosphatase, non-receptor type 11 (PTPN11)), GAP2 (glycosylation-associated protein 2) and the v-crk avian sarcoma virus CT10 oncogene homolog (Gotoh et al 1995) [*CRK* ⇩1.59-fold SALS, p<0.05].

NGF bound to the type I transmembrane protein sortilin (*SORT1*) is also a common ligand of the p75 neurotrophin receptor (p75NTR); a member of the TNF-receptor superfamily which activates several intracellular signalling cascades including the MAP3K1/JNK/p53/Bax [*MAP3K1* (mitogen-activated protein kinase kinase kinase 1, E3 ubiquitin protein ligase) ⇩1.70-fold SALS, p<0.01 (Figure 3.19)], NADE/YWHAH [*YWHAH* (tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta) ⇩1.69-fold SALS, p<0.001] and NRAGE [neurotrophin receptor-interacting MAGE (melanoma antigen gene) homolog] pathways that can induce cell cycle arrest and programmed cell death. An overall down-regulation in the expression of a number of these transcripts detected in the peripheral whole venous blood of SALS patients compared to controls would be expected to further promote signals which enhance cell survival (Arnett et al 2007, Chen et al 2008, Feng et al 2010, Fortress et al 2011, Nykjaer et al 2004, Teng et al 2005).

3.6 DISCUSSION

In ALS the tissue which is primarily affected remains inaccessible during life. There are also a number of limitations (Section 1.3.2) (Cooper-Knock et al 2012a, Sharp et al 2006a, Sutherland at al 2011) associated with the use of human post-mortem SC and brain specimens; not least of all that the GEP's generated from such material is only representative of the terminal stages of disease progression at which point the majority of vulnerable neuronal cell populations will have already been lost from the system. In more recent years a wide range of peripheral tissues (Section 1.3.1 and 1.3.2) including whole venous blood [Chapter 3: 'Whole Blood Study'] and immortalised EBV-transformed B-lymphocytes (LCL's) [Chapter 5: '*C9ORF72* GEP Study' and Chapter 6: '*C9ORF72* Survival Study'] have been observed, by many, to recapitulate the pathogenesis of a number of neurodegenerative and neuropsychiatric conditions including ALS (Saris et al 2009) (Section 1.4.1.1), SCHIZ and BPD (Tsuang et al 2005) (Section 1.4.1.2.4 and 1.4.2.2.1-2), ALZ (Maes et al 2007) (Section 1.4.1.2.3), HD (Borovecki et al 2005) (Section 1.4.1.2.1) and PD (Scherzer et al 2007) (Section 1.4.1.2.2) that have been reviewed briefly in Chapter 1: 'Introduction' and elsewhere in the literature by Borovecki & Habek (2010), Cooper-Knock et al (2012c), Mohr & Liew (2007), Sharp et al (2006b) and Woelk et al (2011).

Blood offers a particularly attractive source of material for microarray applications owing to good standardization of technical procedures, non-invasive collection and longitudinal sampling in large volumes (Table 1.4) (Burczynski & Dorner 2006). At least 80% of the genes which are routinely expressed in the CNS are also detectable in the transcriptome profile of circulating blood (Liew et al 2006). Additionally, the majority of disease causative genes in ALS have been reported to be ubiquitously expressed (Cooper-Knock et al 2012c). Quantifiably changes in the mRNA levels of these transcripts in response to perturbations in the micro- or macroenvironment, therefore, is suggestive of blood constituting a rich biosensor pool which has the potential to act as a sentinel of the neurodegenerative disease process (Kennedy et al 2008, Pahl 2005, Staratschek-Jox et al 2009). It has become apparent, however, that the sheer abundance (Raghavachari et al 2009, Winn et al 2010) of erythrocyte derived alpha (α) and beta (β) haemoglobin transcripts, comprising up to 70% of total RNA species isolated from peripheral whole blood preparations, could be producing interference on the microarray that is masking the detection of other, less abundant transcripts of equal biological importance within the sample (Section 1.3.3) (Feezor et al 2004, Kam et al 2012, Wright et al 2008). In order to overcome this challenge, and to improve the overall reliability and sensitivity of such studies, several globin reduction strategies have been developed (Vartanian et al 2009) including Ambion® GLOBINClear™ (Raman 2011) which utilises selective hybridization and a magnetic bead based separation method of depletion (Field et al 2007) and NuGEN Technologies Inc., UK patented SPIA™ system that uses a proprietary reagent in the Ovation® Whole Blood Solution for generating ss-cDNA targets, from as little as 5ng starting material (Dafforn et al 2004); which have proven less prone to non-specific hybridizations owing to the higher fidelity of DNA-DNA as opposed to RNA-DNA (Barker et al 2005, Debey et al 2006, Eklund et al 2006, Parrish et al 2010, Tian et al 2009) interactions. Previously obtained results using the Ambion GLOBINClear™ protocol in combination with the PAXgene® Blood RNA collection tubes (Dumeaux et al 2008, Li et al 2008a, Liu et al 2006) demonstrated high interindividual variability, low sample integrity and poor reproducibility (Raman 2011); with inconsistencies between microarray findings and subsequent qRT-PCR validation experiments.

The initial aim of the PhD was to evaluate the NuGEN Ovation® Whole Blood Solution as a suitable alternative for the generation of robust gene expression data from peripheral whole blood. For direct comparability, patient and control samples were recruited to the study from the Raman (2011) cohort with specimens collected at the same time in different PAXgene® Blood RNA Collection Tubes (Section 2.3.1.1) and stored at -20^{0}C for a maximum of 3 years prior to being processed. Although storage times differed considerably between the RR Ambion® GLOBINClear™ and the JB NuGEN Ovation® datasets, PreAnalytiX does advocate that intracellular RNA should remain stable for up to 8 years without a significant degree of degradation occurring *ex vivo* (preanalytix.com). The achievement of comparable RNA concentrations and yields that produced similar ratios of absorbencies at 260/280nm wavelengths and high RNA integrity values [RIN's 7.5 or above (Section 2.3.1.3)] on the Agilent 2100 Bioanalyzer is supportive of this statement. The electropherogram traces are illustrative of good quality, intact RNA having been extracted using the PAXgene® Blood RNA Isolation Kits (Section 2.3.1.2) (Figure 3.1) and post-hybridization QC measures assessed using Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK) were also relatively consistent between the two (Table 3.8) with reduced noise (Raw Q), lower background (bgrd) signal intensities and higher %P calls associated with the JB NuGEN Ovation® dataset.

Circulating blood is classified as a fluid connective tissue that is in a permanent state of renewal and is known to play a pivotal role in physiological homeostasis, cellular immunity and inflammation. It is composed of a mixed cell population that contains plasma (55%), erythrocytes (43%), leukocytes (<1%) [neutrophils, lymphocytes (T-cells, B-cells and natural killer or NK cells), monocytes, basophils and eosinophils] and platelets (1.5%) which continuously permeates and interacts with every other tissue and organ of the mammalian body (Joehanes et al 2012, Mohr & Liew 2007).

a) JB NuGEN Ovation® dataset

	RNA Yield	$A_{260/280}$	RIN	Bgrd	Raw(Q)	SF	%P	GAPDH 3'-5' ratio
BLDCON01	3.89 µg	2.23	8.4	27.3	0.643	2.3	51	1.70
BLDCON02	6.23 µg	2.21	7.7	25.6	0.598	8.3	42	3.09
BLDCON04	2.82 µg	2.46	8.8	27.4	0.637	2.2	52	1.72
BLDCON07	3.71 µg	2.16	7.7	25.6	0.643	19.7	31	1.94
BLDCON08	8.10 µg	2.23	8.8	26.4	0.605	3.6	48	3.54
BLDCON10	6.44 µg	2.12	7.9	26.8	0.596	6.6	43	2.61
BLDPAT21	3.77 µg	2.28	8.4	26.6	0.613	8.6	40	3.27
BLDPAT23	9.32 µg	2.15	7.5	27.5	0.670	1.5	54	1.64
BLDPAT26	6.21 µg	2.12	8.0	27.5	0.654	1.3	53	1.97
BLDPAT27	6.44 µg	2.14	8.1	26.7	0.665	1.9	53	3.19
BLDPAT35	3.64 µg	2.25	8.8	27.5	0.660	2.1	51	1.82
BLDPAT38	3.91 µg	2.14	7.7	27.3	0.692	1.1	56	2.68
Mean	**5.37 µg**	**2.21**	**8.2**	**26.9**	**0.640**	**3.6**	**49**	**2.43**

b) RR Ambion GLOBINClear™ dataset

	RNA Yield	$A_{260/280}$	RIN	Bgrd	Raw(Q)	SF	%P	GAPDH 3'-5' ratio
BLDCON01	1.44 µg	2.11	8.5	51.6	1.800	0.5	45	3.57
BLDCON02	1.91 µg	2.20	8.1	38.9	1.100	0.9	49	3.60
BLDCON04	1.47 µg	2.05	8.4	61.9	2.100	0.6	43	2.70
BLDCON07	2.10 µg	2.20	8.8	39.6	1.200	0.9	45	3.04
BLDCON08	4.18 µg	2.18	8.9	38.7	1.100	1.0	44	3.68
BLDCON10	1.89 µg	2.17	8.8	45.4	1.400	0.8	43	2.30
BLDPAT21	1.89 µg	2.09	8.4	65.3	2.200	0.6	44	2.30
BLDPAT23	4.35 µg	2.13	8.8	84.5	2.800	0.5	44	1.99
BLDPAT26	1.72 µg	2.13	8.9	74.5	2.400	0.4	46	2.02
BLDPAT27	1.70 µg	2.14	8.7	73.6	2.400	0.4	47	4.30
BLDPAT35	1.68 µg	2.08	8.8	55.8	1.800	0.6	47	3.09
BLDPAT38	1.90 µg	1.99	8.8	58.2	1.900	0.5	47	2.94
Mean	**2.19 µg**	**2.12**	**8.7**	**57.3**	**1.850**	**0.6**	**42**	**2.96**

Table 3.8 Summary of JB NuGEN Ovation® and RR Ambion® GLOBINClear™ QC Parameters RNA purity, as determined by absorbance ratios at 260/280nm ($A_{260/280}$) wavelengths, and yield were measured using the NanoDrop™ 1000 Spectrophotometer (Thermo Fisher Scientific® Inc., UK). RNA integrity numbers (RIN's) were computed on a scale of zero (undetectable, completely degraded) to ten (high quality, intact RNA) using the Agilent 2100 Bioanalyzer (Agilent Technologies Ltd., UK). Mean values recorded across the JB NuGEN Ovation® (top) or RR Ambion® GLOBIN Clear™ (bottom) datasets are represented in bold. Affymetrix® QC parameters including noise (Raw Q), average background (bgrd) signal intensities, scaling factor (SF), percentage presence (%P) calls and *GAPDH* 3'-5' ratio were assessed in Expression Console™ software version 1.3. 0.187 (Affymetrix® Ltd., UK). Significant outliers removed from subsequent downstream analyses are highlighted in red.

Abbreviations: 3' - three prime, 5' - five prime, BLDCON - blood control, BLDPAT - blood patient, *GAPDH* - glyceraldehyde 3-phosphate dehydrogenase, JB - Joanna Bury generated CEL files, QC - quality control and RR - Dr Rohini Raman generated CEL files.

Consequentially, a distinct possibility exists that there are a number of potentially confounding environmental covariates which may also influence the transcriptome profile of circulating blood (Dumeaux et al 2010, Leonardson et al 2010). To control for the variability introduced by such factors: a) Individuals were matched as far as possible for their age, gender and ethnicity; b) BLDPAT donors were all on a stable dose of Riluzole (50mg twice daily); c) BLDCON donors were recruited from patient partners or unrelated carers; d) Samples were collected by venepuncture between the hours of 8.00am and 11.00am and e) The subjects were fasted overnight prior to phlebotomy. One limitation of the study, however, still remained. Since a full blood count was not performed at the time the tissue was donated (Raman 2011) it is not possible to determine the extent to which differences in the relative abundance of different cell populations is having on the resultant GEP's (Bennett et al 2003, Jiang et al 2005, Whitney et al 2003).

The efficiency of the NuGEN Technologies Inc., UK patented linear SPIA™ system in limiting the amount of amplified globin cDNA relative to other, less abundant transcripts also contained within the sample, which are of equal biological importance (in this case the standard housekeeping control, beta actin) was assessed in a qRT-PCR assay with the size of the amplified products having been confirmed by agarose gel electrophoresis (Section 3.4) [APPENDIX FIGURE A3]. Across the cohort mean cycle threshold (Ct) values were shown to be significantly lowered for *ACTB* [pre-SPIA™ 19.278 (n=12) versus post-SPIA™ 10.801 (n=8) measurements; ⇩1.80-fold ($p<0.001$***)] but had remained reasonably consistent for *HBA2* [pre-SPIA™ 11.833 (n=12) versus post-SPIA™ 9.663 (n=7) measurements; ⇩1.20-fold ($p<0.05$*) (Figure 3.12)]; suggesting, initially, that the NuGEN Ovation® Whole Blood Solution had been succussful in reducing the levels of globin. However, despite multiple attempts Ct values could not be recorded for more than 40% of the post-SPIA™ samples analysed, as demonstrated by a sizeable reduction in *N* (Figure 3.12). The reason for this is unclear, although it is plausible, given the uncharacteristic nature of the amplification plots which were generated using Stratagene Brilliant II [APPENDIX FIGURE A1] or Roche FastStart Universal [APPENDIX FIGURE A2] Master Mix, that NuGEN's proprietary reagent may not be compatible with the SYBR® Green fluorescence based detection method deployed in this study and alternatives, such as TaqMan probes, would need to be trialled. There is also evidence in the literature that *ACTB* may not be the most suitable candidate for use as an endogenous control when analysing whole blood and other genes, including peptidylpropyl isomerase B (*PPIB*), for example, would also need to be considered alongside the more traditional choices (Pachot et al 2004). In Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK) MAS 5.0 normalised pivot data for Affymetrix® Human Genome U133 Plus 2.0 Gene Chip® Arrays found mean probeset signal intensities for *HBA2* and *ACTB* to be comparable, but both were substantially higher than either *GAPDH* or *18SrRNA* (Figure 3.20).

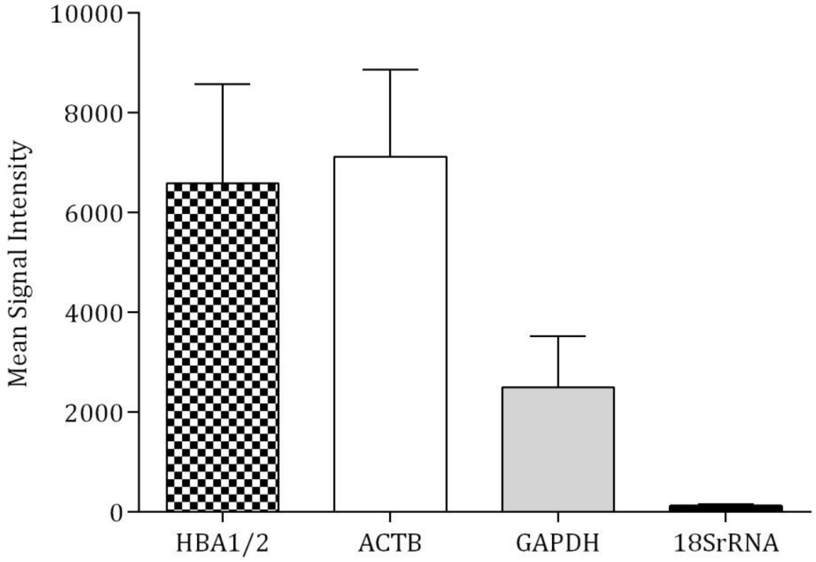


Figure 3.20 MAS 5.0 Signal Intensities for HBA1/2 Transcripts and the Housekeeping Genes ACTB, GAPDH and 18SrRNA Mean probeset signal intensity values for the JB NuGEN Ovation® Human Genome U133 Plus 2.0 GeneChip® Arrays normalised in Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK) using Microarray Suite 5.0 (MAS 5.0) and plotted in GraphPad Prism® software version 5.04 © 1992-2014 (GraphPad Software Inc., CA USA). Error bars represent SEM (standard error of the mean).

Abbreviations: *ACTB* - actin beta, *GAPDH* - glyceraldehyde 3-phosphate dehydrogenase, *HBA1/2* - haemoglobin alpha 1/2, JB - Joanna Bury generated CEL files and rRNA - ribosomal RNA.

An overall down-regulation in the level of gene transcription was apparent in the JB NuGEN Ovation® dataset (Figure 3.15) (Section 3.5.1.2.1) with 467 (66.1%) of the 706 DE transcripts in GeneSpring GX v11.5.1 [unpaired student's t-test FDR p<0.05, FC ≥ ±1.50] exhibiting a significant decrease in expression in the peripheral whole venous blood of SALS patients (n=6) compared to equal numbers of neurologically normal, healthy control subjects. A similar trend has also been observed in cultured skin fibroblasts derived from a second cohort of SALS patients and controls (n=12) in which a total of twenty-eight commonly dysregulated transcripts were identified including zinc finger DNA binding protein 652 (*ZNF652*) [JB NuGEN Ovation® ⇩2.30 -fold SALS, $p<0.01$; RR Fibroblast ⇩2.04, $p<0.05$] and protein tyrosine phosphatase, receptor type, C (*PTPRC*) [JB NuGEN Ovation® ⇩2.20-fold, $p<0.05$; RR Fibroblast ⇩ 1.12-fold, $p<0.05$] (Raman et al 2014). ZNF652 interacts with the putative breast tumor suppressor core-binding factor runt domain alpha subunit 2; translocated to 3 (CBFA2T3) to inhibit transcription of the HeLa E-box binding protein (HEB) which has important implications for myogenesis and haematopoiesis (Kumar et al 2008). PTPRC may be associated with apoptosis (Yi et al 2011) and has been shown to play a pivotal role in maintaining intracellular Ca^{2+} homeostasis (Duplay et al 1996, Lane et al 1991, Qin & Chock 2002) which could link it to the induction of excitotoxicity; a major mechanism contributing to the degeneration and loss of MN's in ALS (Section 1.2.4.2) (Grosskreutz et al 2010). Aberrations in the *PTPRC* gene have also conferred increased susceptibility for developing certain autoimmune diseases including MS (Do et al 2006, Schwinzer et al 2003) and rheumatoid arthritis (Miterski et al 2004, Plant et al 2012). Moreover, loss of CD45 function in a mouse model of ALZ induces widespread microglial activation and the formation of Aβ plaques (Zhu et al 2011); a pathological hallmark of this disease (Section 1.4.1.2.3).

In contrast, an overall up-regulation in the level of gene transcription was apparent in the RR Ambion GLOBINClear™ dataset (Figure 3.15) with 3,440 (76.1%) of 4,520 DE transcripts in GeneSpring GX v11.5.1 [unpaired student's t-test FDR $p<0.05$, FC ≥ ±1.50] exhibiting a significant increase in expression in the peripheral whole venous blood of SALS patients compared to controls (Section 3.5.1.2.2). This percentage was even higher (86.9%) in an analysis of the top 1,215 hits, ranked by probability value, with an FC ≥ ±2.0. It is also of interest to note that despite the use of identical age, gender & ethnicity matched donor samples there was more than a 6-fold difference in the number of DE transcripts in GeneSpring GX v11.5.1 [unpaired student's t-test FDR $p<0.05$, FC ≥ ±1.50] between the JB NuGEN Ovation® (n=706) and RR Ambion GLOBINClear™ (n=4,520) datasets with 2,733 expected to occur by chance (Figure 3.14). It can be speculated, therefore, that the latter may provide a more sensitive approach to GEP in blood. Alternatively, it could also signify a greater proportion of false positive outcomes which is supported by a lack of qRT-PCR validation of gene targets identified in the RR Ambion GLOBINClear™ dataset (Raman 2011).

Very few of the aforementioned transcriptional changes detected in the peripheral blood of SALS patients compared to controls were shared in common between the JB NuGEN Ovation® and RR Ambion GLOBINClear™ datasets (Figure 3.15) with only a third (34.2%) of these 82 transcripts (encoding 78 unique genes) reported to occur in the same direction of change (Table 3.3). These included: haptoglobin (*HP*), a risk factor for idiopathic PD (Alberio et al 2013, Costa-Mallen et al 2008) which confers protection against elevated levels of OS (Section 1.2.4.1) and has been shown to play an important role in iron (Fe^{2+}) homeostasis (Arguelles et al 2010); the ER adaptor molecule transmembrane tetratricopeptide repeat containing 1 (*TMTC1*) (Sunryd et al 2014); neuregulin 1 (*NRG1*), a possible candidate gene of SCHIZ and BPD (Deng et al 2013a, Walker et al 2010) that promotes skeletal muscle fibre development and maintains synaptic plasticity in the hippocampus during learning and memory (Liu et al 2011, Mei & Xiong 2008, Neddens et al 2009) and *DUSP16,* a key regulator of T helper (Th) cell differentiation (Musikacharoen et al 2011) that has been shown to interact with the MAPK signalling cascade (Section 3.5.1.5.1) which were up-regulated in addition to the type II transmembrane glycoprotein C-type lectin domain family, 4 member C (*CLEC4C*) implicated in the innate immune response and inflammation (Riboldi et al 2011); protein tyrosine phosphatase, non-receptor type 12 (*PTPN12*), a potent tumor suppressor critical for cell adhesion and migration (Luo et al 2014); signal sequence receptor, alpha (*SSR1*) responsible for protein translocation across the ER membrane (Mesbah et al 2006); molecular chaperone heat shock 60kDa protein 1 (*HSPD1*), a rare cause of hereditary spastic paraplegia (SPG13) (Hansen et al 2002, Hewamadduma et al 2008) which is essential for the correct folding and assembly of newly imported proteins into the mitochondria (Magnoni et al 2014) as well as the RNA processing gene heterogeneous nuclear ribonucleoprotein C (*HNRNPC*) (Romano & Buratti 2013) which were shown to be consistently down-regulated.

KEGG pathway analysis produced better enrichment using the DAVID bioinformatics resource version 6.7 than functional annotation clustering performed on GO terms (Section 3.5.1.4 and 3.5.1.5), although Benjamini-Hochberg FDR corrected p-values did not reach the 5% significance threshold. Commonly dysregulated pathways (n= 7) included the MAPK (Section 3.5.1.5.1) [Rank #1 (13), count 20 (46), percentage 3.2 (2.0), p=1.60E-03 (4.40E-03)] and Neurotrophin (Section 3.5.1.5.2) [Rank #4 (9) count 11 (26), percentage 1.8 (1.2), p=9.20E-03 (3.10E-03)] signalling cascades with oocyte meiosis, NOD-like receptor signalling, endometrial cancer and LTP (long term potentiation) specific to the JB NuGEN Ovation® dataset (Table 3.6) and endocytosis, ubiquitin-mediated proteolysis, phosphatidylinositol signalling, spliceosome, ErbB signalling, VEGF signalling and regulation of the actin cytoskeleton specific to the RR Ambion GLOBINClear™ dataset (Table 3.7). *PIK3R2*, which is associated with four of these pathways, was identified as the only DE transcript [JB NuGEN Ovation® ⇧ 1.54-fold, p<0.01; RR Ambion GLOBINClear™ ⇧2.04-fold, p<0.001] with a direction of change that correlated between the two methodologies (Table 3.3). This enzyme was found to be significantly up-regulated in the blood of SALS patients compared to controls and is considered to be important in regulating DNA replication and cell survival (Marques et al 2009). However, it remains unclear as to the reasons why so many other transcripts including *PTPRC* [JB NuGEN Ovation® ⇩2.19-fold, p<0.05; RR Ambion GLOBINClear™ ⇧1.99-fold, p<0.05] and the v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog (*KRAS*) [JB NuGEN Ovation® ⇩1.85-fold, p<0.05; RR Ambion GLOBINClear™ ⇧2.45-fold, p<0.05] appear to exert apposing regulatory effects in blood specimens derived from identical patient and control samples. Dysregulation of the MAPK signalling cascade is, nevertheless, an interesting finding that warrants further investigation (Limviphuvadh et al 2007). Previously elevated levels of p38 MAPK have been observed in the ventral horn MN's and microglia of the SOD1^{G93A} transgenic mouse model of the disease which is linked to the induction of apoptosis (Veglianese et al 2006) and genes of the same pathway have also been shown to be significantly altered in ALS patients carrying a *CHMP2B* mutation (Section 1.2.5.2.8) (Cox et al 2010).

In conclusion, a lack of consistency between the JB NuGEN Ovation® and RR Ambion GLOBINClear™ datasets analysed in this chapter suggests that the abundance of α and β globin transcripts still remains a contentious issue which will require further clarification. Given the problems outlined above (i.e. blood is composed of a mixed cell population not directly affected by the neurodegenerative disease process and is influenced by environmental covariates) there is good rationale in the alternative use of immortalised EBV-transformed B-lymphocytes (LCL's) (Section 1.3.2) which eliminate the need for re-sampling, are a genetically homogeneous cell population and can be cultured *in vitro* to support downstream functional assays (Gladkevich et al 2004, Hu et al 2011, Min et al 2010, Shtilbans et al 2011).

CHAPTER 4: CHARACTERISATION OF LCL'S

The focus of this methodological chapter was to characterise the large bank of LCL's in the ECACC discovery and replication cohorts, which were being screened as part of a wider project (N^0 259867) funded by EuroMOTOR (FP7/2007-2013), under the Seventh Framework Health Cooperation Programme. Due to time constraints, it was not possible to include all cases and controls in the scope of the PhD. Instead specific subsets of LCL's were selected, according to strict criteria (e.g. matched for age and gender), in order to perform the subsequent downstream comparative analyses outlined in 'Chapter 5: *C9ORF72* GEP Study' and 'Chapter 6: *C9ORF72* Survival Study'. A detailed summary of the clinical and genetic information of each cohort is provided (Section 4.1.1 and 4.1.2), along with measures of RNA yield (Section 4.2) and microarray QC parameters, as assessed by the Affymetrix® Expression Console™ (Section 4.3).

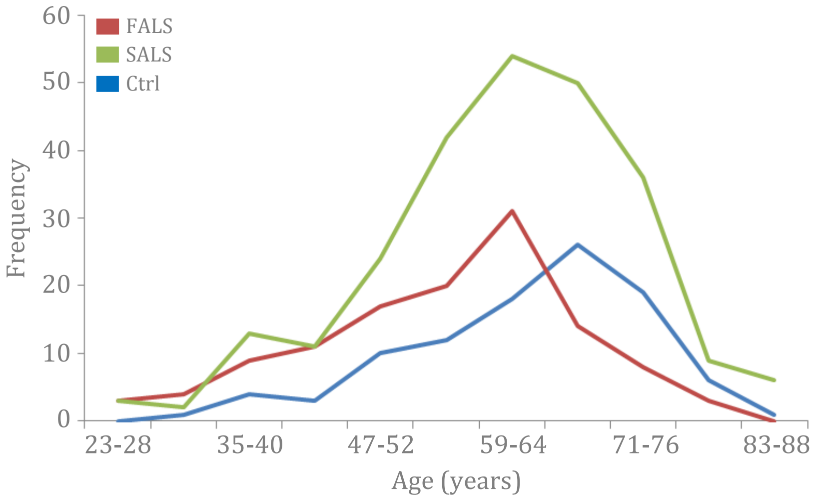
4.1 ECACC EBV-Transformed B-Lymphocytes

4.1.1 ECACC Discovery Cohort

4.1.1.1 Clinical Characteristics

4.1.1.1.1 Control Cases

Neurologically normal, healthy control LCL's (n=100) [63-M, 37-F] were largely recruited to the ECACC discovery cohort (Section 2.1.2) from patient partners or their unrelated carers in the National MNDA DNA Bank. These were comprised of 27 Birmingham (27.0%) cases including one from Belfast City Hospital [C020-(BBe0006)], one from Oxford [C090-(BOx0073)] and eight from Liverpool [C02-(BLi0245), C039 -(BLi0169), C065-(BLi0123), C083-(BLi 0269), C086-(BLi0217), C093-(BLI0196), C 096-(BLi0029) and C097-(BLi0083)]; 26 London (26.0%) cases including two from Cambridge [C019-(LCa0022) and C021-(LCa0076)], three from Poole General Hospital [C05-(LPo0033), C017-(LPo0027) and C053-(LPo0062)] and four from Southampton General Hospital [C012-(LSh0025), C015-(LSh0032), C038-(LSh0022) and C046-(LSh0023)] and 47 Sheffield (47.0%) cases including three from Nottingham [C048-(SNt0005), C052-(SNt0073) and C024-(SNt0035)], four from Manchester [C01-(SMa0033), C033-(SMa0183), C036-(SMa0156) and C077-(SMa0047)], one from Durham [C013-(SDu0012)], five from Preston [C08-(SPr0050), C010-(SPr0014), C022-(SPr0086), C072-(SPr0048) and C074-(SPr0068)] and eleven from Newcastle [C04-(SNc0091), C07-(SNc0038), C09-(SNc0103), C011-(SNc0045), C019-(SNc0096), C025-(SNc0218), C029-(SNc0023), C044-(SNc0041), C047-(SNc0149), C076-(SNc0106106) and C085-(SNc0035)]. Age at consultation ranged between 33 and 84 years with a mean of 63.2±11yrs. The M:F ratio was 1.70:1 (Figure 4.1) [APPENDIX TABLE B1].



	FALS	SALS	Control
M:F	1.45:1	1.43:1	1.70:1
Age	55.4±12yrs	60.6±12yrs	63.2±11yrs
Total	**120**	**250**	**100**

Figure 4.1 Age Frequency Distribution of Patient and Control LCL's in the ECACC Discovery Cohort (n=470)

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, Ctrl - control, ECACC - European Collection of Cell Cultures, F - familial, F - female, LCL - lympho-blastoid cell line, M - male and S - sporadic.

4.1.1.1.2 Familial Cases

FALS patient derived LCL's (n=120) [71-M, 49-F] recruited to the ECACC discovery cohort were comprised of 31 Birmingham (25.8%) cases including one from Oxford

	----------- Replication Cohort -----------		-------------------------------------- Discovery Cohort --------------------------------------			
	SALS	**CTRL**	**SALS**	**FALS**	**ALL**	**CTRL**
M:F	2.17:1	1.78:1	1.43:1	1.45:1	1.43:1	1.70:1
Age						
range	31-87yrs	35-83yrs	22-86yrs	23-82yrs	22-86yrs	33-84yrs
mean	60yrs	63yrs	61yrs	55yrs	59yrs	63yrs
Onset						
Limb	161 (64.4%)	n/a	146 (58.4%)	57 (47.5%)	203 (54.9%)	n/a
Bulbar	60 (24.0%)	n/a	76 (30.4%)	38 (31.7%)	114 (30.8%)	n/a
Mixed	20 (8.0%)	n/a	23 (9.2%)	17 (14.1%)	40 (10.8%)	n/a
Respiratory	4 (1.6%)	n/a	5 (2.0%)	2 (1.7%)	7 (1.9%)	n/a
unknown	5 (2.0%)	n/a	0 (0.0%)	6 (5.0%)	6 (1.6%)	n/a
Diagnosis						
ALS	242 (96.8%)	n/a	234 (93.6%)	111 (92.6%)	345 (93.2%)	n/a
ALS+FTLD	0 (0.0%)	n/a	3 (1.2%)	1 (0.8%)	4 (1.1%)	n/a
ALS+PD	1 (0.4%)	n/a	0 (0.0%)	1 (0.8%)	1 (0.3%)	n/a
PBP	5 (2.0%)	n/a	12 (4.8%)	6 (5.0%)	18 (4.8%)	n/a
PLS	2 (0.8%)	n/a	0 (0.0%)	1 (0.8%)	1 (0.3%)	n/a
PMA	0 (0.0%)	n/a	1 (0.4%)	0 (0.0%)	1 (0.3%)	n/a
ALSFRS-R						
range	0-48	n/a	0-48	0-48	0-48	n/a
mean	34	n/a	33	32	33	n/a
Survival						
range	0.4-10.3yrs	n/a	0.3-7.7yrs	0.5-18.7yrs	0.3-18.7yrs	n/a
mean	3.7yrs	n/a	2.8yrs	2.9yrs	2.8yrs	n/a
Total	**250 (249)**	**100 (100)**	**250 (244)**	**120 (118)**	**370 (362)**	**100 (97)**

Table 4.1 Clinical Summary of Patient and Control LCL's in the ECACC Discovery (n=470) and Replication (n=350) Cohort Highlighted in red are the final sample numbers obtained following assessment of QC metrics in Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK).

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, CTRL - control, ECACC - European Collection of Cell Cultures, F - familial, F - female, FRS-R - Revised Functional Rating Scale, FTLD - frontotemporal lobar degeneration, LCL - lymphoblastoid cell line, M - male, n/a - not available, PBP - Progressive Bulbar Palsy, PD - Parkinson's disease, PLS - Primary Lateral Sclerosis, PMA - Progressive Muscular Atrophy, QC - quality control and S - sporadic.

[F078-(BOx0029)], one from Bristol Frenchay Hospital [F48-(BBr0015)] and seven from Liverpool [F020-(BLi0236), F038-(BLi0249), F045-(BLi0254), F072-(BLi0251), F074-(BLi0272), F094-(BLi0246) and F103-(BLi0265)]; 48 London (40.0%) cases including one from Southampton General Hospital [F102-(LSh0038)], one from Plymouth Derriford Hospital [F029-(LPy0018)], one from Poole General Hospital [F058-(LP0036)] and two from Cambridge [F014-(LCa0111) and F052-(LCa0026)] and 44 Sheffield (34.2%) cases including three from Preston [F010-(SPr0085), F025-(SPr0059) and F101-(SPr0026)], five from Newcastle [F027-(SNc0204), F064-(SNc0063), F071-(SNc0031), F109-(SNc0202) and F118-(SNc0189)] and five from Manchester [F028-(SMa0020), F081-(SMa0006), F095-(SMa0008), F108-(SMa0078) and F117-(SMa0166)]. The M:F ratio was 1.45:1 (Figure 4.1) [APPENDIX TABLE B2].

The majority of FALS patients, 94.2% (n=113/120) were diagnosed according to the World Federation of Neurology's amended EEC of 1998 (Section 1.1.3) (Figure 1.1) with either definite (n=57/113) or probable ALS (n=56/113) (Table 4.1) including one incidence of concomitant FTLD [F115-(SP3118)] and another of concomitant PD [F114-(SP3560)] (Section 1.2.1). Of the remaining 5.8% (n=7/120) of patients, one was diagnosed with PLS [F087-(SP3216)] (Section 1.2.2.2) and six were diagnosed with PBP [F029-(LPy0018), F041-(LP0440), F052-(LCa0026), F058-(LPo0036), F100-(SP3070) and F118-(SNc0189)] (Section 1.2.2.1). Age at symptom onset ranged between 23 and 82 years with a mean of 55.4±12yrs. Survival ranged from 6 months to 18 years and 8 months in 81.7% of cases (n=98/120) with a mean of 2.92±2.3yrs. For 14.2% of FALS (n=17/120) this information was not available and in the remaining 4.1% of cases (n=5/120) the individual was still reported to be alive as of June 2013 with a minimum disease duration of either 4 [F047-(BP6502)], 6 [F013-(BP6494)], 9 [F054-(SP3048) and F119-(SP3218)] or 11 years [F015-(LP0460)], respectively. Limb or spinal onset at 47.5% (n=57/120) [56-FALS, 1-PLS (familial)] was more prominent than the onset of bulbar weakness 31.7% (n=38/120) [32-FALS and 6-PBP (familial)], a mixed presentation 14.2% (n= 17/120) [17-FALS] or the onset of respiratory muscle dysfunction 1.7% (n=2/120) [2-FALS]. Information regarding presentation was unavailable for the remaining 4. 9% (n=6/120) [6-FALS] of the cohort. Revised ALS Functional Rating Scale (ALSFRS-R) scores ranged between 0 (severe disability) and 48 (normal function) (Castrillo-Viguera et al 2010, Cedarb aum et al 1999, Gordon & Cheung 2006, Kollewe et al 2008) with an average of 31.8±13 for 99.0% of FALS (n=199/120) (Figure 4.2).

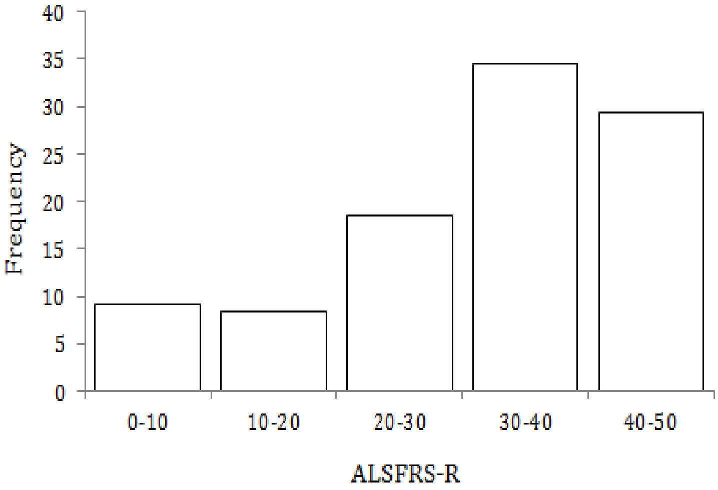


Figure 4.2 ALSFRS-R Frequency Distribution of FALS (n=120) Recruited to the ECACC Discovery Cohort. Revised ALS Functional Rating Scale scores on a scale of 0 to 48 where zero represents severe disability and a score of forty-eight signifies that normal function is preserved. Mean ALSFRS-R plotted along the x-axis is computed based on measurements that are incorporated from a series of twelve questions relating to the patient's ability to perform common daily tasks including but not limited to: speech, salivation, swallowing, dressing & hygiene, walking, climbing stairs, handwriting and shortness of breath (SOB) (Cedarbaum et al 1999). Relative counts or frequencies along the y-axis were calculated as a percentage of the total number of FALS (n=119/120) in the ECACC discovery cohort for which this information was available.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, ECACC - European Collection of Cell Cultures, F - familial and FRS-R - Functional Rating Scale Revised.

For the Sheffield cases some additional clinical information could be extracted from the local database. Of these, 7.3% (n=3/41) [2-FALS and 1-PLS (familial)] were prone to EL, a further 2.4% (n=1/41) [1-FALS] suffered from excessive salivation or hypersialorrhea and approximately a fifth (n=8/41) [8-FALS] reported dyspnoea with 37.5% of these latter cases requiring NIPPV support (n=3/8) [3-FALS] (Section 1.1.4). Dysarthria and dysphagia was also apparent in 29.3% (n=12/41) [10-FALS, 1-FALS+PD and 1-PBP (familial)] of the cohort with PEG feeding becoming a necessary intervention in four of these latter cases [3-FALS and 1-FALS+PD]. One in ten (n=4/41) [3-FALS and 1-FALS+PD] patients were non-ambulant and a further 17.1% (n=7/41) [7-FALS] were unable to walk without assistance. Current smokers comprised 7.3% (n=3/41) [2-FALS and 1-PBP (familial) of the cohort, ex-smokers who had not smoked a cigarette in the last 18 years 2.4% (n=1/41) [1-FALS] and non-smokers a further 46.3% (n=19/41) [18-FALS and 1-FALS+PD]. For the remaining 43.9% (n=18/41) [13-FALS and 5-PBP (familial)] of cases this information was not disclosed.

A strong family history of dementia was associated with up to 4.9% of the Sheffield pedigrees (n=2/41) [F089-(SP3331) and F115-(SP3118)]. There were also reports of at least one other neurological condition occurring in a first degree relative of an additional 12.2% of kindreds (n=5/41). These included one incidence of ALZ [F089-(SP3331)] (Section 1.3.1.3.1) and another of hereditary PD (Section 1.2.1) [F114-(SP3560)].

4.1.1.1.3 Sporadic Cases

SALS patient derived LCL's (n=250) [147-M, 103-F] recruited to the ECACC discovery cohort were comprised of 40 Birmingham (16.0%) cases including three from Liverpool [S074-(BLi0048), S098-(BLi0037) and S181-(BLi0039)] and eight from Belfast City Hospital [S05-(BBe0007), S09-(BBe0018), S052-(BBe0016), S058-(BBe0001), S087-(BBe0009), S122-(BBe0014), S196-(BBe0013) and S248-(BBe0003)]; 45 London (18.0%) cases including one from Poole General Hospital [S035-(LPo0010)] and 165 Sheffield (66.0%) cases including twenty-one from Newcastle [S012-(SNc0022), S046-(SNc0001), S077-(SNc0042), S088-(SNc0086), S089-(SNc0053), S105-(SNc0018), S106-(SNc0077), S130-(SNc0010), S134a-(SNc0016), S141-(SNc0071), S152-(SNc0090), S155-(SNc0055), S156-(SNc0029), S182-(SNc0008), S193-(SNc0024), S203-(SNc0059), S209-(SNc0012), S212-(SNc0002), S223-(SNc0095), S225-(SNc0092) andS232-(SNc0051) and twelve from Nottingham [S036-(SNt0031), S067-(SNt0038), S075-(SNt0034), S096-(SNt0001), S115-(SNt0004), S129-(SNt0024), S138b-(SNt0017), S140-(SNt0020), S158-(SNt0006), S198-(SNt0016), S219-(SNt0036) and S240-(SNt0030)]. The M:F ratio was 1.43:1 (Figure 4.1) [APPENDIX TABLE B3].

The majority of SALS patients, 94.8% (n=237/250) were diagnosed with either definite (n=110/237) or probable ALS (n=127/237) (Section 1.1.3) (Figure 1.1) (Table 4.1) including three incidences of concomitant FTLD [S093-(SP3049), S178-(SP3145) and S191-(SP3042)] (Section 1.2.1). Of the remaining 5.2% of the cohort (n=13/250), one patient was diagnosed with PMA [S069-(SP3230)] (Section 1.2.2.3) and twelve were diagnosed with PBP [S040-(SP3271), S044-(SP3329), S045-(SP3289), S105-(SNc0018), S106-(SNc0077), S129-(SNt0024) and S232-(SNc0051)] (Section 1.2.2.1). Age at symptom onset ranged between 22 and 86 years with a mean of 60. 6±12yrs (Table 4.1). Survival ranged from 4 months to 7 years and 8 months with a mean of 2.75±1.3yrs. Limb onset 58.4% (n=146/250) [145-SALS, 1-PMA (sporadic)] was more prominent than the onset of bulbar weakness 30.4% (n=76/250) [64-SALS and 12-PBP (sporadic)], a mixed presentation 9.2% (n=23/250) [23-SALS] or onset in the respiratory muscles 2.0% (n=5/250) [5-SALS] combined. ALSFRS-R scores ranged between 0 (severe disability) and 48 (normal function) (Figure 4.3) with an average of 33.1±10 for 84.0% of SALS (n=210/250).

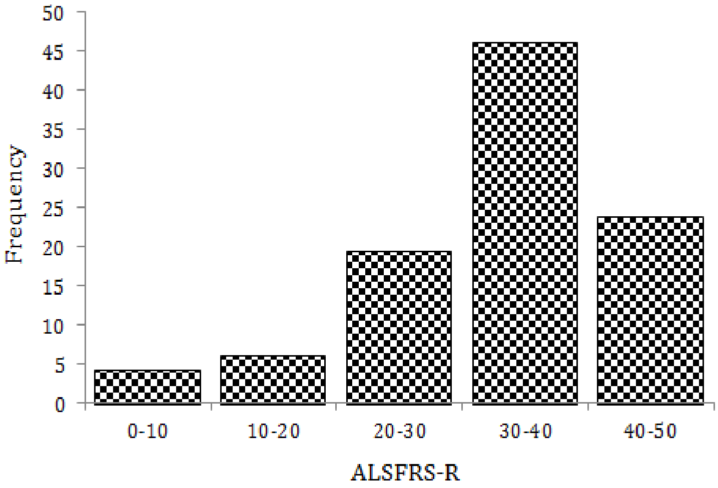


Figure 4.3 ALSFRS-R Frequency Distribution of SALS (n=250) Recruited to the ECACC Discovery Cohort. Revised ALS Functional Rating Scale scores on a scale of 0 to 48 where zero represents severe disability and a score of forty-eight signifies that normal function is preserved. Mean ALSFRS-R plotted along the x-axis is computed based on measurements that are incorporated from a series of twelve questions relating to the patient's ability to perform common daily tasks including but not limited to: speech, salivation, swallowing, dressing & hygiene, walking, climbing stairs, handwriting and shortness of breath (SOB) (Cedarbaum et al 1999). Relative counts or frequencies along the y-axis were calculated as a percentage of the total number of SALS (n=210/250) in the ECACC discovery cohort for which this information was available.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, ECACC - European Collection of Cell Cultures, F - familial and FRS-R - Functional Rating Scale Revised.

For the Sheffield cases some additional clinical information could be extracted from the local database. Of these 12.7% (n=21/165) [19-SALS and 2-PBP (sporadic)] were prone to EL, a further 1.2% (n=2/165) [2-SALS] suffered from hypersialorrhea and almost a quarter (n=39/165) [36-SALS and 3-PBP (sporadic)] displayed symptoms of dyspnoea, with 33.3% of these latter cases (n=13/39) [13-SALS] requiring NIPPV support (Section 1.1.4). Dysarthria and dysphagia was also apparent in 31.5% (n=52/165) [49-SALS an d3-PBP (sporadic)] of the cohort with PEG feeding becoming a necessary intervention in eighteen of these latter cases [17-SALS and 1-PBP (sporadic)]. Four individuals presented with the rare FA variant of the disease (Section 1.1.5.1) [S015-(SP3299), S042-(SP3122), S060-(SP3338) and S223-(SNc0095)] and two additional cases presented with a clinical history of depression [S113-(SP3347) and S116-(SP3351)]. One in twenty-five patients were non-ambulant (n=7/165) [7-SALS] with a further 18.2% (n=30/165) unable to walk without assistance. Current smokers comprised 3.6% of the cohort (n=6/165) [6-SALS], ex-smokers who had not smoked a cigarette for a minimum of 12 months (mean 21.4±9yrs) (n=17/165) [16-SALS and 1-PMA (sporadic)] a further 10.3% and non-smokers 55.8% (n=92/165) [87-SALS and 5-PBP (sporadic)]. For the remaining 30.3% (n=50/165) [43-SALS and 7-PBP (sporadic)] of cases this information was not disclosed.

There were reports of at least one other neurological condition occurring in a first degree relative of 7.3% (n=12/165) of apparently sporadic, Sheffield ALS kindreds including ALZ (Section 1.3.1.3.1) [S010-(SP3275), S054-(SP3179), S060-(SP3338), S069-(SP3230), S112-(SP3363), S121-(SP3420), S162-(SP3326) and S247-(SP3353)], PD (Section 1.2.1) [S146-(SP3132), S148-(SP3368), S167-(SP3327) and S227-(SP3043)] and Multiple Sclerosis (MS) (Etemadifar et al 2012, Ismail et al 2013) [S148-(SP3368), S153-(SP3423) and S236-(SP3286)]. A family history of dementia [S08-(SP3111), S042-(SP3122), S078-(SP3140), S116-(SP3351), S172-(SP3067), S191-(SP3042) and S227-(SP3043)] was also associated with up to 4.2% (n=7/165) of cases. In addition, cancer affected a further 11.5% (n=19/165) [12-colon, 2-throat, 4-stomach and 1-other], cerebrovascular disease (CVA) 1.2% (n=2/165), inflammatory bowel disease (IBD) 0.6% (n=1/165) and depression/strokes 1.2% (n=2/165) of Sheffield pedigrees.

4.1.1.2 Therapeutics Used to Treat the Cohort

4.1.1.2.1 Familial Cases

Riluzole, administered at a dose of 50mg twice daily, was being used to treat 76.7% of FALS (n=92/120) [89-FALS, 1-FALS+PD and 2-PBP] with two additional patients waiting to commence treatment at the time of biosample collection. Vitamin C/E or multivitamin supplements were collectively being taken by 15.8% (n=19/120) [19-FALS] of the cohort. As well as the Riluzole therapy, several patients (n=3/120) [3-FALS] were also participants of the BDNF [F091-(SP3534)], minocycline [F073-(BP 6165)] or lithium carbonate (LiCALS) [F053-(SP3610)] drug trials [APPENDIX TAB LE B4]. In contrast, 14.2% (n=17/120) [14-FALS, 2-PBP (familial) and 1-PLS (familial)] chose not to receive any kind of disease modifying therapy and for the remaining 7.5% of FALS (n=9/120) [7-FALS and 2-PBP (familial)] this information was not available.

4.1.1.2.2 Sporadic Cases

Riluzole was also used to treat 88.0% of SALS patients (n=220/250) [205-SALS, 3-SALS+FTLD, 11-PBP and 1-PMA (sporadic)]. In a small number of cases, approximately 1.8% (n=4/220) [3-SALS and 1-PBP (sporadic)] the individual experience adverse side effects and the medication was withdrawn. Vitamin C/E and multivitamin supplements were collectively being taken by 40.8% (n=102/250) [93-SALS, 1-SAL S+FTLD, 6-PBP and 1-PMA (sporadic)] of the cohort. As well as the Riluzole therapy several patients (n=12/250) [12-SALS] were also participants of the glatiramer acetate (Copaxone®) [S176-(SP3385)], ONO-2506 (Arundic acid) [S118-(SP3030), S1 32-(SP3413), S149-(SP3391), S168-(LP0001), S203-(SNc0059) and S237-(BP6008)] or minocycline [S050-(SP3023), S121-(SP3420), S157-(LP0015), S164-(LP0053) and S212-(SNc0002)] drug trials [APPENDIX TABLE B4]. In contrast, 11.6% (n=29/ 250) [28-SALS and 1-PBP (sporadic)] chose not to receive any kind of disease modifying therapy and for the remaining 0.4% (n=1/250) [1-SALS] of SALS this information was not available.

4.1.1.3 Genetic Status of the Cohort

At the beginning of the project the genetic status of the majority of LCL's was unknown. However, upon the discovery, in October 2011, of a pathogenic non-coding G_4

C_2 hexanucleotide repeat expansion (Renton et al 2011, DeJesus-Hernandez et al 2011) in intron 1 of the previously uncharacterised *C9ORF72* gene (Section 1.2.5.4), a further 40.8% of FALS (n=49/120) [42-FALS, 1-FALS+PD and 6-PBP] and 10.0% of SALS (n=25/250) [24-SALS and 1-PBP (sporadic)] cases have now been genetically assigned.

4.1.1.3.1 Familial Cases

All familial index cases in the ECACC discovery cohort for which DNA was available in the local Sheffield or National MNDA DNA Bank were screened for genetic defects in *SOD1*, *TARDBP* and *FUS* prior to the commencement of this study. *SOD1* mutations occurred at a frequency of 4.4% (n=5/115) (Section 1.2.5.1.1). These were primarily clustered in exon 4 and included the single base substitutions c.305A>G (p.D102G) [F120-(SP3218)], c.335G>A (p.C111Y) [F103-(BLi0265)] and c.341T>C (p.I114T) [F031-(SP3526) and F053-(SP3610)]. For London individual [F068-(LP0075)] the amino acid change was not known. Rarer pathological changes were also described in exon 6 of *TARDBP* including c.1043G>T (p.G348V) [F092-(SP3154)] and c.1009A>G (p.M337V) [F015-(LP0460), F040-(SP3068) and F067-(SP3086)] and in exon 15 of *FUS* including c.1555C>G (p.Q519E) [F086-(LP0051)] and c.1562G>A (p.R521H) [F036-(LP0193) and F03-(LP0048)]; accounting for ~3.8% (n=4/106) (Section 1.2.5.2.1) or 2.9% (n=3/103) (Section 1.2.5.2.2) of FALS cases, respectively. In a more recent screening of the *C9ORF72* gene (Cooper-Knock et al 2012b), repeat-primed PCR detected >30 copies of the G_4C_2 repeat in 48.4% (n=15/31) of Birmingham, 39.6% (19/48) of London and 36.6% (n=15/41) of Sheffield FALS cases. There was also one example of oligogenic inheritance: Patient sample [F056-(SP3462)], in addition to carrying the expansion in *C9ORF72*, was also known to harbour a heterozygous c.964G>A (p.E322K) missense substitution in exon 10 of the *OPTN* gene (Section 5.3.2.1) (Bury et al 2015) (Table 4.2).

4.1.1.3.2 Sporadic Cases

Of the sporadic cases, patient samples [S166-(SP3082) and S146-(SP3132)] carry a SNP in the first [c.85A>G (p.I29V)] or third [c.618A>C (p.Q206H)] exon of *CHMP2B*, respectively (Section 1.2.5.2.8) (Cox et al 2010). Another individual [S062-(SP3301)]

			Birmingham	London	Sheffield	ALL
Familial						
SOD1	exon 4	p.D102G	0	0	1	
		p.C111Y	1	0	0	
		p.I114T	0	0	2	
	not known	not known	0	1	0	4.4%
TARDBP	exon 6	p.G348V	0	1	1	
		p.M337V	0	0	2	1.2%
FUS	exon 15	p.Q519E	0	1	0	
		p.R521H	0	1	0	
		p.R522G	0	1	0	3.0%
C9ORF72	non-coding	G_4C_2 repeat	15	19	15	40.8%
C9ORF72+OPTN	exon 10	p.E322K	0	0	1	0.8%
Total			**16**	**24**	**21**	**50.8%**
Sporadic						
ANG	exon 2	p.K54E	0	0	1	0.4%
C9ORF72	non-coding	G_4C_2 repeat	2	2	21	10.0%
CHMP2B	exon 1	p.I29V-SNP	0	0	1	
	exon 3	p.Q206H-SNP	0	0	1	0.8%
Total			**2**	**2**	**24**	**11.2%**

Table 4.2 Summary of Genetic Variants Reported in the ECACC Discovery Cohort

Abbreviations: *ANG* - angiogenin, *C9ORF72* - chromosome 9 open reading frame 72, *CHMP2B* - charged multivesicular protein 2B, ECACC - European Collection of Cell Cultures, *FUS* - fused in sarcoma, *OPTN* - optineurin, SNP - single nucleotide polymorphism, *SOD1* - copper/zinc superoxide dismutase 1 and *TARDBP* - transactive response (TAR) DNA binding protein.

was heterozygous for a c.232A>G (p.K54E) missense substitution in exon 2 of *ANG* (Section 1.2.5.2.3) (Kirby et al 2013). An additional 5.0% (n=2/40) of Birmingham, 4.4% (n=2/45) of London and 12.7% (n=21/165) of Sheffield SALS cases were also known to harbour the G_4C_2 repeat expansion in *C9ORF72* (Table 4.2).

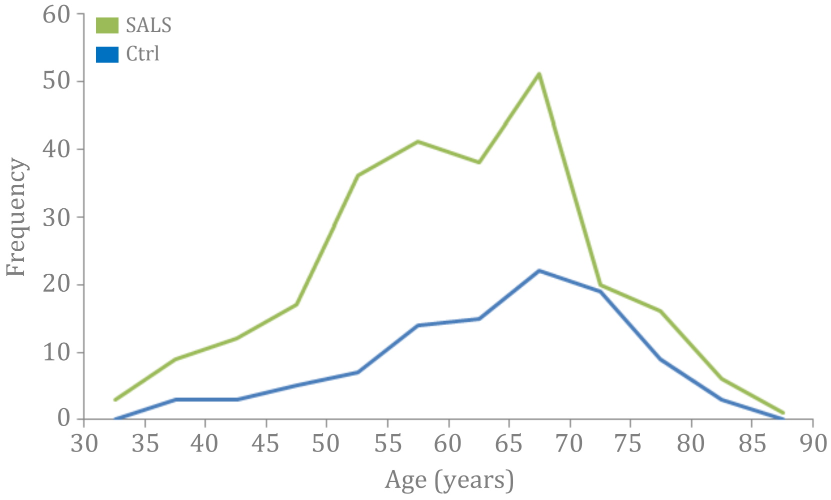
4.1.2 ECACC Replication Cohort

4.1.2.1 Clinical Characteristics

4.1.2.1.1 Control Cases

Neurologically normal, healthy control LCL's (n=100) [64-M, 36-F] were largely recruited to the ECACC replication cohort from patient partners and their unrelated carers in the National MNDA DNA Bank (Section 2.1.2). These were comprised of 31

Birmingham (31.0%) cases including nine from Liverpool [C117-(BLi0224), C130-(BLi0105), C148-(BLi0259), C160-(BLi0032), C162-(BLi0198), C175-(BLi0021), C185-(BLi0240), C188-(BLi0074) and C195-(BLi0204)], one from Oxford [C110-(BOx0008)], one from Belfast City Hospital [C153-(BBe0002)] and one from Bristol Frenchay Hospital [C150-(BBr0020)]; 28 London (28.0%) cases including two from Poole General Hospital [C119-(LPo0059) and C122-(LPo0087)], two from Cambridge [C189-(LCa0093) and C190-(LCa0134)] and one from Plymouth Derriford Hospital [C125-(LPy0011)] and 41 Sheffield (41.1%) cases including six from Newcastle [C102-(SNc0201), C109-(SNc0158), C135-(SNc0125), C144-(SNc0078), C146-(SNc0167) and C157-(SNc0015)], ten from Manchester [C111-(SMa0096), C124-(SMa0227), C133-(SMa0009), C139-(SMa0188), C151-(SMa0050), C163-(SMa0054), C167-(SMa0203), C170-(SMa0232), C171-(SMa0133) and C194-(SMa0013)], one from Preston [C104-(SPr0016)], one from Nottingham [C177-(SNt0075)] and two from Durham [C197-(SDu0009) and C120-(SDu0007)]. Age at consultation ranged between 35 and 83 years with a mean of 63.4±10yrs. The M:F ratio was 1.78:1 (Figure 4.4) [APPENDIX TABLE B5].



	SALS	**Control**
M:F	2.17:1	1.78:1
Age	59.7±11yrs	63.4±10yrs
Total	**250**	**100**

Figure 4.4 Age Frequency Distribution of Patient and Control LCL's in the ECACC Replication Cohort (n=350)

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, Ctrl - control, ECACC - European Collection of Cell Cultures, F - female, LCL - lymphoblastoid cell line, M - male and S - sporadic

4.1.2.1.2 Sporadic Cases

SALS patient derived LCL's (n=250) [171-M, 79-F] recruited to the ECACC replication cohort were comprised of 107 Birmingham (42.8%) cases including one from Belfast City Hospital [S432-(BBe0015)]; 96 London (38.4%) cases including four from Southampton General Hospital [S322-(LSh0002), S326-(LSh0016), S405-(LSh0028) and S473-(LSh0004)] and nine from Poole General Hospital [S289-(LPo0003), S298-(LPo0001), S349-(LPo0016), S362-(LPo0019), S383-(LPo0018), S394-(LPo0009), S429-(LPo0039), S485-(LPo0005) and S489-(LPo0017)] and 47 Sheffield (18.8%) cases including two from Preston [S446-(SPr0005) and S456-(SPr0001)], two from Durham [S327-(SDu0001) and S476-(SDu0005)], seven from Nottingham [S274-(SNt0008), S359-(SNt0012), S407-(SNt0042), S427-(SNt0021), S463-(SNt0013), S464-(SNt0040) and S492-(SNt0019)] and five from Newcastle [S299-(SNc0028), S305-(SNc0043), S380-(SNc0049), S420-(SNc0057) and S466-(SNc0020)]. The M:F ratio was 2.17:1 (Figure 4.4) [APPENDIX TABLE B6].

The majority of SALS patients, 97.2% (n=243/250) were diagnosed (Section 1.1.3) (Figure 1.1) with either definite (n=81/243) or probable ALS (n=162/243) including one incidence of concomitant PD (Section 1.2.1) [S455-(BP6152)] (Table 4.1). Of the remaining 2.8% (n=7/250) of the cohort, two patients were diagnosed with PLS (Section 1.2.2.2) [S301-(SP3402) and S497-(SP3234)] and five were diagnosed with PBP (Section 1.2.2.1) [S272-(SP3253, S299-(SNc0028), S308-(BP6328), S349-(BP6100) and S359-(SNt0012)]. Age at symptom onset ranged between 31 and 87 years with a mean of 59.7±11yrs. Survival ranged from 5 months to 10 years and 3 months in 80.0% (n=200/250) of cases with a mean of 3.72±2.0yrs. For 14.8% (n=37/250) of SALS this information was not available and in the remaining 5.2% (n=13/250) of cases the individual was still reported to be alive as of June 2013 with minimum disease duration of either 7 [S281-(LP0482) and S304-(LP0400)], 8 [S298-(LPo0001), S326-(LSh0016), S351-(LP0451), S452-(LP0195), S453-(LP0380) and S454-(LP0364)], 9 [S311-(LP0086), S334-(LP0442) and S395-(LP0109)], 10 [S321-(LP0003)] or 12 years [S300-(LNh0020)], respectively. Onset occurred focally in at least 90.0% (n=225/250) of cases. Of these, 71.5% (n=161/225) [150-SALS and 2-PLS (sporadic)] presented with asymmetric weakness in the upper and/or lower limbs, 26.7% (n=60/225) [55-SALS and 5-PBP (sporadic)] experienced bulbar symptoms and a further 1.8% (n=4/225) [4-SALS] had impaired respiratory function. The remaining 10.0% (n=25/250) of the cohort comprised 20 SALS cases of mixed presentation and five incidences where the site of onset was not known. ALSFRS-R scores ranged between 0 (severe disability) and 48 (normal function) with an average of 3 4.2±10 for 55.6% of SALS (n=139/250) (Figure 4.5).

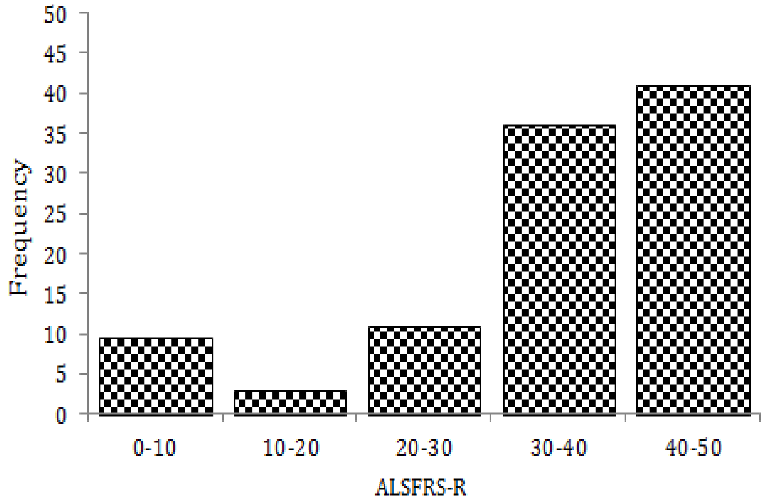


Figure 4.5 ALSFRS-R Frequency Distribution of SALS (n=250) Recruited to the ECACC Replication Cohort Revised ALS Functional Rating Scale scores on a scale of 0 to 48 where zero represents severe disability and a score of forty-eight signifies that normal function is preserved. Mean ALSFRS-R plotted along the x-axis is computed based on measurements that are incorporated from a series of twelve questions relating to the patient's ability to perform common daily tasks including but not limited to: speech, salivation, swallowing, dressing and hygiene, walking, climbing stairs, handwriting and shortness of breath (SOB) (Cedarbaum et al 1999). Relative counts or frequencies along the y-axis were calculated as a percentage of the total number of SALS (n=139/250) in the ECACC replication cohort for which this information was available.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, ECACC - European Collection of Cell Cultures, FRS-R - Revised Functional Rating Scale and S - sporadic.

For the Sheffield cases some additional clinical information could be extracted from the local database. Of these 4.3% (n=2/47) [2-SALS] were prone to EL, 10.6% (n=5 /47) [5-SALS] suffered pronounced dyspnoea with a fifth in need of NIPPV support (Section 1.1.4) and one individual presented with the rarer FA variant (Section 1.1. 5.1) [S467-(SP3198)]. Dysarthria and dysphagia were also apparent in 23.4% (n=11 /47) [10-SALS and 1-PBP (sporadic)] of the cohort with PEG feeding becoming a necessary intervention in the case the PBP patient. Three individuals were non-ambulant with a further 12.8% (n=6/47) [6-SALS] unable to walk without assistance. Current smokers comprised 10.6% (n=5/47) [5-SALS] of the cohort, ex-smokers who had not smoked a cigarette in the last 8 years a further 4.3% (n=2/47) [2-SALS] and non-smokers 42.6% (n=20/47) [19-SALS and 1-PBP (sporadic)]. For the remaining 42.5% (n=20/47) [13-SALS, 1-SALS+PD, 4-PBP (sporadic) and 2-PLS (sporadic)] of cases this information was not disclosed.

There were reports of at least one other neurological condition occurring in a first degree relative of 8.5% (n=4/47) of Sheffield pedigrees which received a diagnosis of SALS in the ECACC replication cohort including PD (Section 1.2.1) [S306-(SP343 9) and S482-(SP3367)], HD (Section 1.4.1.2.1) [S284-(SP3069)], tremor [S461-(SP3 107)] and ALZ (Section 1.3.1.3.1) [S272-(SP3253)]. Incidences of cancer affecting 6 .4% (n=3/47) [1-bowel, 1-breast and 1-other], strokes 2.1% (n=1/47) or post-viral motor/immune disorder 2.1% (n=1/47) were also reported.

4.1.2.2 Therapeutics Used to Treat the Cohort

Riluzole, administered at a dose of 50mg twice daily, was being used to treat 88.4% of SALS cases (n=221/250) [213-SALS, 1-SALS+PD, 4-PBP and 2-PLS (sporadic)]. In a small number of instances, approximately 3.6% (n=8/221) [8-SALS] the individual experienced adverse side effects and the medication was withdrawn. Vitamin C/E or multivitamin supplements were collectively being taken by 26.4% (n=66/250) [63-SALS, 2-PBP and 1-PLS (sporadic)] of the cohort. As well as the Riluzole therapy, several patients (n=4/250) [4-SALS] were also participants of the Novartis [S450-(LP 0014)], ONO-2506 (Arundic acid) [S413-(LP0019)], minocycline [S253-(BP6180)] or glatiramer acetate (Copaxone®) [S333-(LP0432)] drug trials [APPENDIX TABLE B4]. In contrast, 14.0% (n=35/250) [34-SALS and 1-PBP (sporadic)] chose not to receive any kind of disease modifying therapy and for the remaining 0.8% (n=2/250) [2-SALS] of the cohort this information was not available.

4.1.2.3 Genetic Status of the Cohort

TARDBP mutations were reported in the ECACC replication cohort at a frequency of 1.2% (n=3/250). They included a c.269C>T (p.A90V) SNP in exon 3 [S412-(SP3147)] and two single base substitutions, namely c.859G>A (p.G287S) [S461-(SP3107)] and c.962C>T (p.A321V) [S352-(SP3484)] in exon 6. In addition, 5.6% (n=6/107) of Birmingham, 9.4% (n=9/104) of London and 2.1% (n=1/48) of Sheffield SALS carried a minimum of thirty copies of the G_4C_2 repeat expansion in *C9ORF72.* There was also one example of oligogenic inheritance (Section 5.3.2.2) involving patient sample [S352-(SP3484)] which was *C9ORF72+* and also found to harbour a heterozygous missense c.962C>T (p.A321V) mutation in exon 6 of *TARDBP* (Kirby et al 2010) (Table 4.3).

			Birmingham	**London**	**Sheffield**	**ALL**
TARDBP	exon 3	p.A90V-SNP	0	0	1	
	exon 6	p.G287S	0	0	1	0.8%
C9ORF72	non-coding	G_4C_2 repeat	6	9	1	6.4%
C9ORF72+TARDBP	exon 6	p.A321V	0	0	1	0.4%
Total			**6**	**9**	**3**	**7.2%**

Table 4.3 Summary of Genetic Variants Reported in the ECACC Replication Cohort

Abbreviations: *C9ORF72* - chromosome 9 open reading frame 72, ECACC - European Collection of Cell Cultures, SNP - single nucleotide polymorphism and *TARDBP* - transactive response (TAR) DNA binding protein.

4.2 QIAGEN Extraction of Total RNA

Having assigned LCL samples from the National MNDA DNA Bank to each of the two cohorts described above in Section 4.1.1 and 4.1.2, aliquots of frozen stocks, preserved in RNA*later*™, were requested from ECACC (Section 2.2.1.2). One Sheffield control [C200-(SC3479)] and three SALS patients including two from Birmingham [S498-(BP6326) and S499-(BP6272)] and one from Belfast City Hospital [S248-(BBe0003)] were no longer available. These samples failed the EBV-transformation process and, following two unsuccessful attempts, were removed from our study design.

Using QIAGEN's RNeasy® Mini Kit (Section 2.3.2.2), total RNA was isolated from 469 (99.8%) of 470 LCL samples [120-FALS, 249-SALS and 100-CTRL] in the ECACC discovery cohort and 347 (99.1%) of 350 LCL samples [248-SALS and 99-CTRL] in the ECACC replication cohort. Collectively, 617 patients [120-FALS and 497-SALS] and 199 age and, as far as possible, gender matched neurologically normal, healthy control subjects yielded between 800ng and 20µg total RNA. Concentrations (Section 2.

3.1.3) on the NanoDrop™ 1000 Spectrophotometer were reasonably consistent across cohorts, with respective means and standard deviations of 171.37±64.9ng/µL (Section 4.1.1) and 140.51±46.3ng/µL (Section 4.1.2). Consistency was also observed across the different sample types [Discovery: 145.84±48.2ng/µL CTRL, 172.67± 64.4ng/µL FALS and 181.72±68.4ng/µL SALS versus Replication: 130.39±42.5ng/µL CTRL and 144.56±47.3ng/µL SALS (Figure 4.6)], extraction batches (Table 4.4 and Figure 4.8) and kits (Figure 4.7). Absorbance ratios at 260/280nm wavelengths ranged 1.8 and 2.2 in 99.3% (n=810/816) of cases [APPENDIX TABLE B7].

RNA integrity was assessed on the Agilent 2100 Bioanalyzer. Distinct separation of the 18S and 28S ribosomal peaks was observed on the electropherogram trace with rRNA ratios [28S/18S] of around 2.2 (Figure 4.9). Average RIN scores were 8.3 for samples in the ECACC discovery cohort and 7.4 for samples in the ECACC replication cohort (Figure 4.6). These remained reasonably consistent across the different sample types within each cohort [Discovery: 8.1 CTRL, 8.3 FALS and 8.3 SALS versus Replication: 7.0 CTRL and 7.6 SALS] but steadily declined over time when examined by extraction batch (Table 4.4 and Figure 4.8) or kit (Figure 4.7). Despite the reduction, mean values did not fall below the previously accepted threshold of 7.0 (Raman et al 2009, Strand et al 2007, Thompson et al 2007) that is considered to be of sufficient quality, in order to, reliably proceed with microarray profiling and downstream GE analyses.

Samples of poor quality (RIN scores below 5.0) were DNase treated to remove any potentially contaminating genomic DNA. This additional processing step had failed to improve the purity of the isolated material (Figure 4.10) and what's more, in the majority of instances, performing repeat extractions from frozen LCL pellets using a fresh QIAGEN RNeasy® Mini Kit also had little impact on the RNA quality and yield that was achieved (Table 4.5).

4.3 Human Exon 1.0ST GeneChip® Array Profiling

4.3.1 Affymetrix® WT Sense-Target Labelling Assay

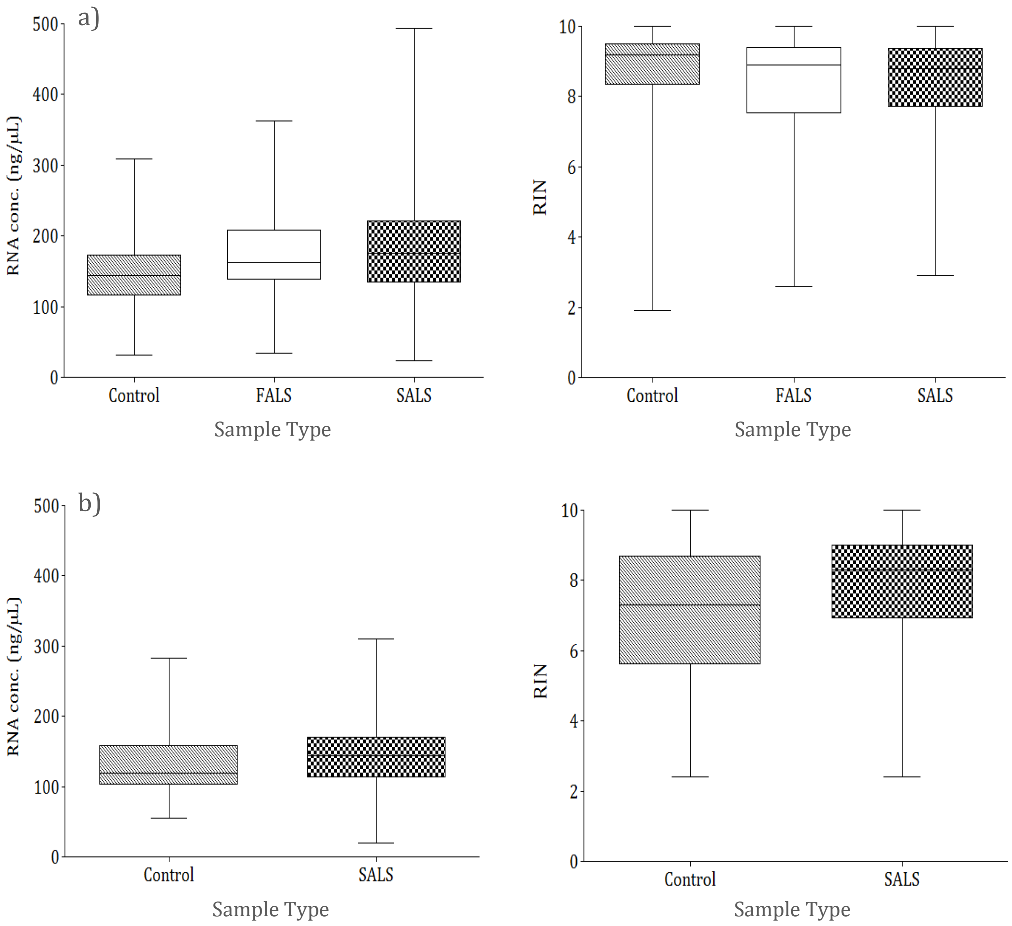


Figure 4.6 ECACC RNA Extraction Boxplots Grouped by Sample Type Summary plots produced using GraphPad Prism® software version 5.04. Whiskers represent minimum and maximum RNA concentrations measured on the NanoDrop™ 1000 Spectrophotometer (left panels) or RNA integrity values (RIN) as determined by the Agilent 2100 Bioanalyzer (right panels) that were achieved for control, familial ALS (FALS) and sporadic ALS (SALS) samples in the ECACC Discovery (a) or Replication (b) cohort.

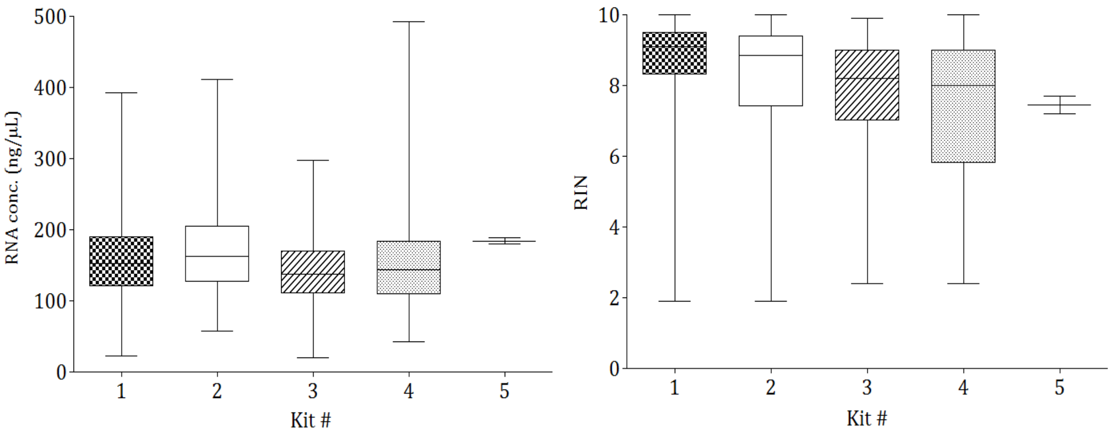


Figure 4.7 ECACC RNA Extraction Boxplots Grouped by QIAGEN RNeasy® Mini Kit Summary plots produced using GraphPad Prism® software version 5.04. Whiskers represent minimum and maximum RNA concentrations measured on the NanoDrop™ 1000 Spectrophotometer (left panel) or RNA integrity values (RIN's) as determined on a scale of 0 (undetectable, completely degraded) to 10 (high quality, intact RNA) by the Agilent 2100 Bioanalyser (right panel).

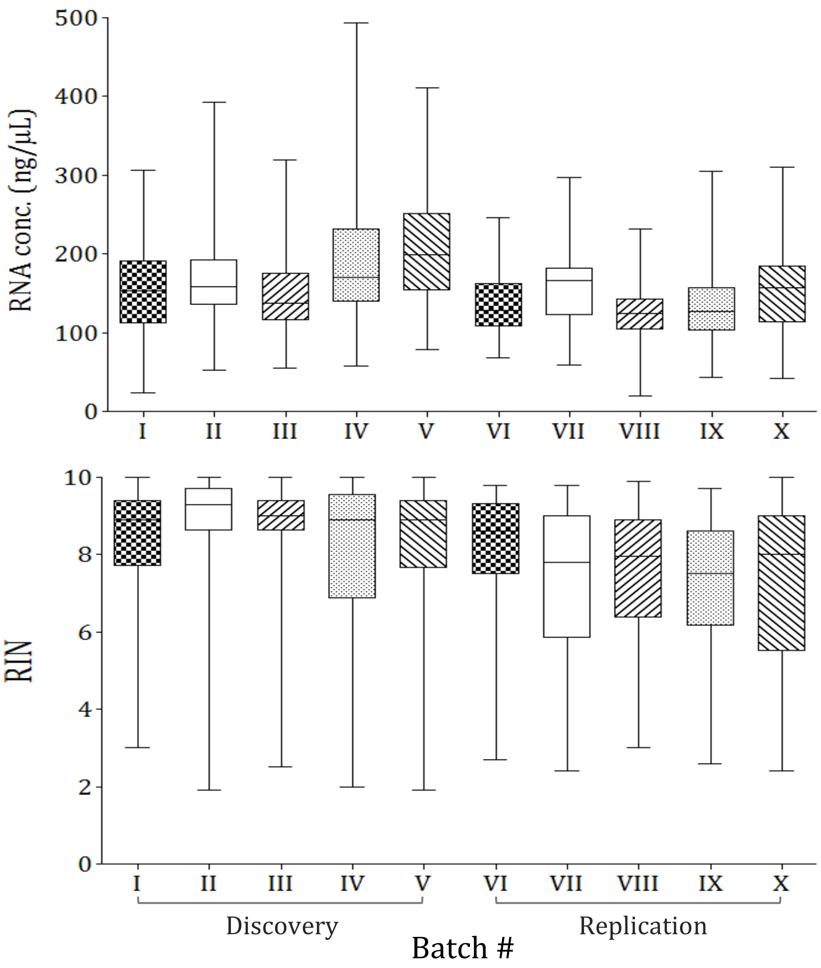


Figure 4.8 ECACC RNA Extraction Boxplots Grouped by Batch Summary plots produced using GraphPad Prism® software version 5.04. Whiskers represent minimum and maximum RNA concentrations measured on the NanoDrop™ 1000 Spectrophotometer (upper) or RNA integrity values (RIN's) as determined by the Agilent 2100 Bioanalyzer (lower) which were achieved for each batch of lymphoblastoid cell lines in the ECACC Discovery (left) [I-V] and Replication (right) [VI-X] cohorts.

	ECACC Batch number (#)				
	I	II	III	IV	V
FALS	F1-24	F25-48	F49-72	F73-96	F97-120
SALS	S1-50	S51-100	S101-149	S150-199	S200-248
Control	C1-20	C21-40	C41-60	C61-80	C81-100

	ECACC Batch number (#)				
	VI	VII	VIII	IX	X
SALS	S249-299	S300-349	S350-399	S400-449	S450-499
Control	C101-120	C121-140	C141-160	C161-180	C181-200

Table 4.4 ECACC LCL Batches Cell pellets were preserved in RNA*later*™ and shipped on dry ice. Dispatch dates and freezer code a) Discovery Cohort I 15/11/2011 [D-ORANGE], II 22/11/2011 [D-GREEN], III 29/11/2011 [D-BLUE], IV 6/12/2011 [D-YELLOW], V 13/12/2011 [D-PINK] and b) Replication Cohort VI 20/12/2011 [R-ORANGE], VII 11/01/2012 [R-GREEN], VIII 24/01/2012 [R-BLUE], IX 31/01/2012 [R-YELLOW], X 7/02/2012 [R-PINK]. For the purposes of this study each sample was assigned a unique reference number with the prefixes: C - control, F - familial patient or S - sporadic patient.

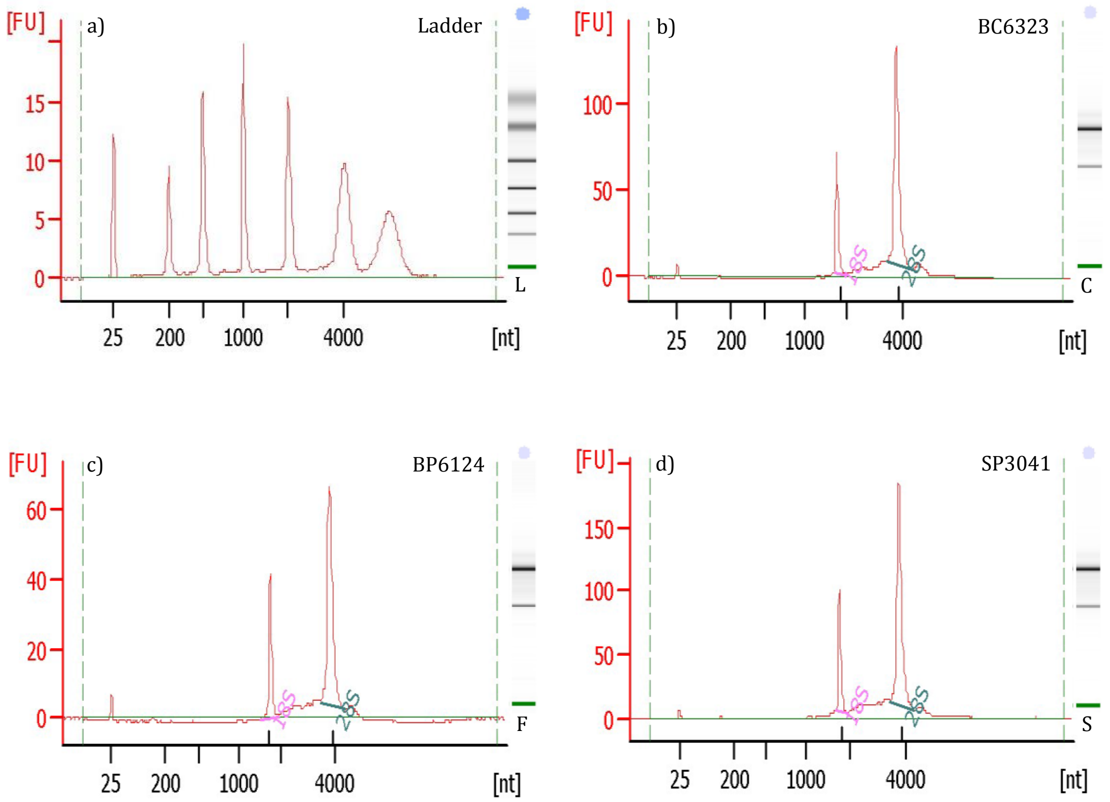


Figure 4.9 Agilent 2100 Bioanalyzer Assessment of LCL RNA Integrity External standard a) RNA 6000 Nano Ladder with a 25nt molecular weight marker and 0.2kb, 0.5kb, 1kb, 2kb, 4kb and 6kb fragments at a total concentration of 150ng/µL. Representative electropherogram traces and corresponding electrophoresis gel images for b) control samples c) familial patient samples and d) sporadic patient samples in the ECACC Discovery and Replication cohort

Abbreviations: BC - Birmingham control, BP - Birmingham patient, [FU] - fluorescent units, [nt] - nucleotide, S - sedimentation coefficient and SP - Sheffield patient

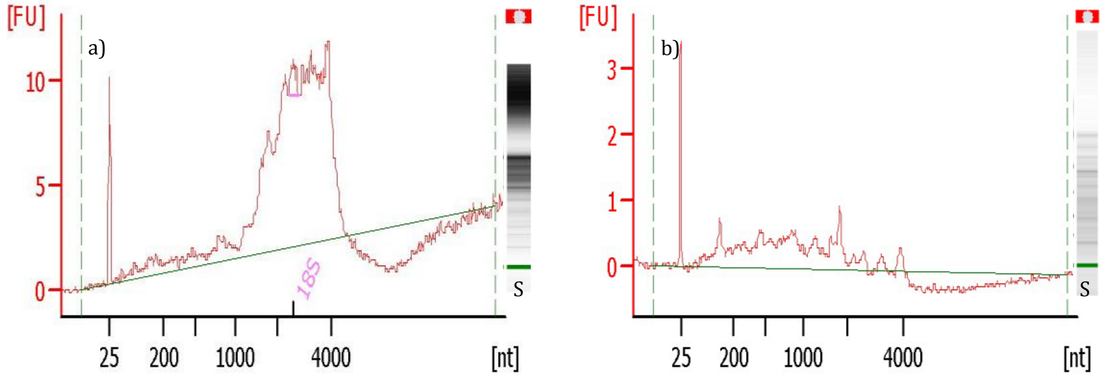


Figure 4.10 Agilent 2100 Bioanalyzer Assessment of DNase Treated Samples of Low Quality Representative electropherogram traces and corresponding electrophoresis gel images for poor quality RNA isolated from pelleted lymphoblastoid cell lines derived from sporadic sample S227 (SP3043) in the ECACC Discovery cohort a) pre DNase treatment and b) post DNase treatment.

Abbreviations: [FU] - fluorescent units, [nt] - nucleotide, S - sedimentation coefficient and SP - Sheffield patient.

	First Extraction				Second Extraction			
	260/280	260/230	RNA Yield	RIN	260/280	260/230	RNA Yield	RIN
C084	1.99	2.07	3.68	-	2.02	1.65	4.44	6.6
C087	2.02	1.23	4.31	2.6	2.05	2.23	4.86	2.5
C091	2.09	2.12	4.99	-	2.06	0.82	3.21	-
F094	2.06	1.50	8.57	5.2	2.07	2.09	7.33	3.3
F096	1.96	0.60	3.40	-	2.06	1.73	7.19	7.7
F100	2.04	2.25	12.52	2.9	2.06	1.23	9.25	4.8
S153	2.05	2.16	12.52	3.0	2.08	1.67	13.86	-
S154	2.06	2.13	13.36	2.8	2.09	2.24	7.52	-
S220	2.06	1.59	3.95	-	2.06	1.77	6.77	-
S227	2.09	2.02	8.77	-	2.09	2.19	12.09	2.4
S244	2.02	2.06	6.73	1.9	2.06	2.25	5.69	2.6

Table 4.5 QIAGEN RNeasy® Mini Kit Repeat RNA Extractions from Frozen LCL Pellets Concentrations and absorbance (A) ratios at 260/280nm and 260/230nm wavelengths were recorded on the NanoDrop™ 1000 Spectrophotometer. Total yield was calculated in micrograms (µg) and the RNA integrity number (RIN) computed on a scale of zero (undetectable, completely degraded) to ten (intact, high quality RNA) by the Agilent 2100 Bioanalyzer. Green shading indicates improved yield and/or quality of the isolated material when the extraction procedure was repeated. Conversely, red represents samples that produced equally poor or even lower quality RNA following the second extraction.

Abbreviations: C - control, F - familial, LCL - lymphoblastoid cell line, RIN - RNA integrity number and S - sporadic.

4.3.1 Affymetrix® WT Sense-Target Labelling Assay

4.3.1.1 Linearly Amplified Material

4.3.1.1.1 Anti-Sense cRNA

The isolated material was *in vitro* transcribed (Section 2.3.2.3.1), following the first step of linear amplification, into as-cRNA using the Ambion® Whole Transcriptome (WT) Expression Kit [APPENDIX TABLE B7]. Concentrations of between 395.64ng/µL and 3,498.70ng/µL were achieved from an input of 312.7±36.5ng total RNA with minimum and maximum yield of 16µg and 140µg, respectively. Samples comprised all of the LCL's that were received in the ECACC discovery cohort (n=469/470) [100 -CTRL, 120-FALS and 249-SALS], plus an additional seven *C9ORF72+* SALS patients in the ECACC replication cohort which met the criteria for inclusion into the long (≥ 4yrs) versus short (<2yrs) survival study [S268-(BP6107), S319-(LP0203), S368-(LP0454), S373-(LP0359), S352-(SP3484), S440-(BP6297) and S438-(LP0411)]. Measurements on the NanoDrop™ 1000 Spectrophotometer were found to be consistent across the different sample types with means and standard deviations of 1,883.

40±739.33ng/μL, 1,832.27±674.18ng/μL and 1,933.25±608.71ng/μL for CTRL, FALS and SALS, respectively. Absorbance ratios at 260/280nm wavelengths ranged between 1.97 and 2.32 (Figure 4.11).

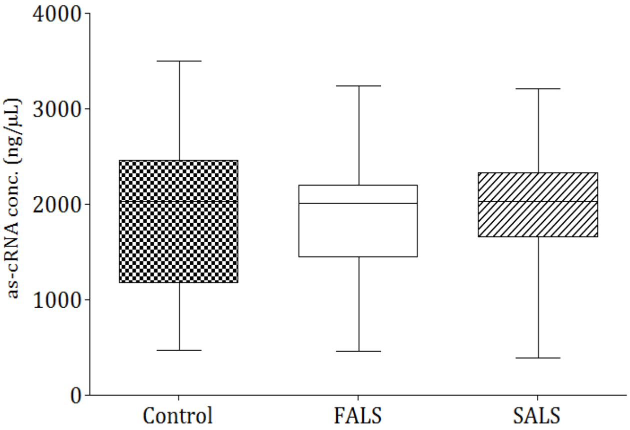


Figure 4.11 ECACC as-cRNA Amplification Boxplot Grouped by Sample Type Summary plots produced using GraphPad Prism® software version 5.04 copyright © 1992-2014 (GraphPad Prism® Inc., USA). Whiskers represent minimum and maximum anti-sense copy RNA (as-cRNA) concentrations achieved on the NanoDrop™ 1000 Spectrophotometer for linearly amplified material derived from control (CTRL), familial ALS (FALS) and sporadic ALS (SALS) samples in the final ECACC LCL microarray cohort (n=476/470) [100-CTRL, 120-FALS and 256-SALS].

4.3.1.1.2 Single-Stranded cDNA

Following the second step of linear amplification using the Ambion® WT Expression Kit (Section 2.3.2.3.1) an input of 10μg purified as-cRNA yielded between 5.79μg and 12.98μg of newly synthesised ss-cDNA. Measurements on the NanoDrop™ 1000 Spectrophotometer were consistent across the different sample types with means and standard deviations of 269.80±35.14ng/μL, 268.25±30.30ng/μL and 270.84±26.25 ng/μL for CTRL, FALS and SALS, respectively. Absorbance ratios at 260/280nm wavelengths ranged between 1.95 and 2.10 (Figure 4.12) [APPENDIX TABLE B7].

4.3.1.2 Fragmented ss-cDNA

Sense-strand cDNA targets were generated from 451 (94.8%) of 476 LCL samples [96-CTRL, 116-FALS and 239-SALS] comprising the final microarray cohort, with the remaining 25 (5.2%) samples [4-CTRL, 4-FALS and 17-SALS] failing to amplify. Ap-

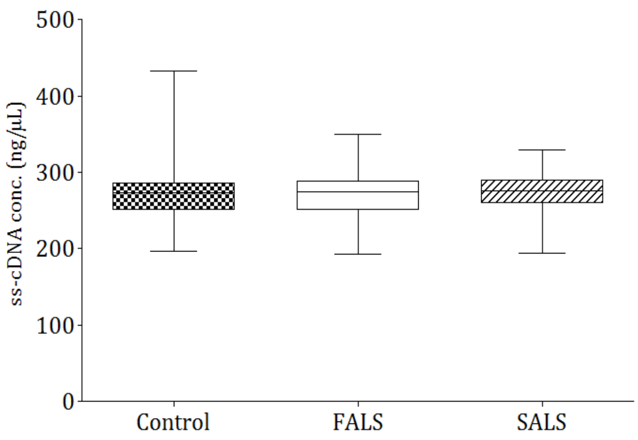


Figure 4.12 ECACC ss-cDNA Amplification Boxplot Grouped by Sample Type Summary plots produced using GraphPad Prism® software version 5.04 copyright © 1992 to 2014 (GraphPad® Software Inc., CA USA). Whiskers represent the minimum and maximum single-stranded complementary DNA (ss-cDNA) concentrations on the NanoDrop™ 1000 Spectrophotometer that were achieved for linearly amplified material derived from control (CTRL), familial ALS (FALS) or sporadic ALS (SALS) samples in the final ECACC LCL microarray cohort (n=476/470) [100-CTRL, 120-FALS and 256-SALS].

plication of the Affymetrix GeneChip® WT Fragmentation and Terminal Labelling Kit produced fragments of ~40 to 70nt in length. Size distribution analysis of a randomly selected subset of pre- and post-fragmented nucleic acid products was performed on the Agilent 2100 Bioanalyzer. Representative traces and their corresponding gel images are illustrated in Figure 4.13 (Section 2.3.1.3).

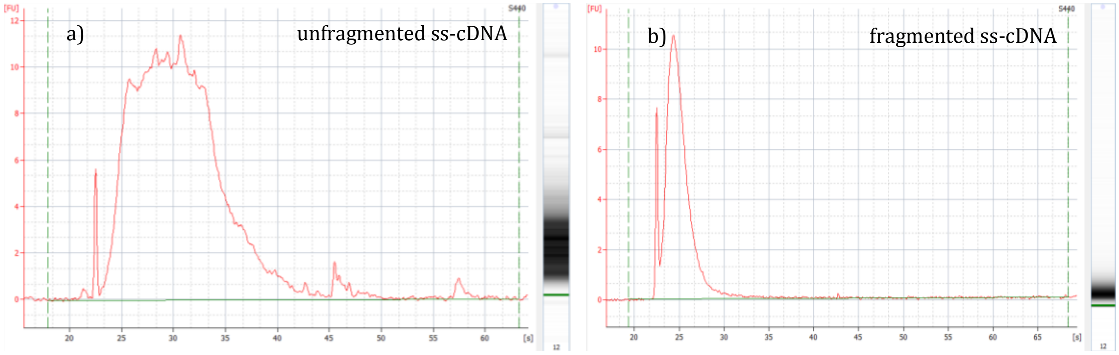


Figure 4.13 Agilent 2100 Bioanalyzer Size Distribution Analysis of Fragmented ss-cDNA Microarray Targets Representative electropherogram traces and corresponding gel images for a) pre-fragmented and b) post-fragmented single-stranded complementary DNA (ss-cDNA) amplified from sporadic sample [S440-(BP6297)] in the ECACC replication cohort using the Affymetrix GeneChip® Whole Transcriptome (WT) Fragmentation and Terminal Labelling Kit.

Abbreviations: BP - Birmingham patient, ECACC - European Collection of Cell Cultures, [FU] - fluorescent units, [nt] - nucleotides, [s] - seconds, S - sedimentation coefficient

4.3.1.3 Biotinylation of Sense-Strand Targets

The biotinylation efficiency (Section 2.3.2.3.4) of the labelling process was assessed on randomly selected ECACC control, FALS and SALS LCL samples from each of the amplification batches by performing an electrophoretic mobility shift assay (EMSA) as depicted in Figure 4.14. Fragmented sense-strand cDNA targets were incubated in the presence or absence of the biotin-binding protein, NeutrAvidin™ before being loaded onto 4 to 20% gradient polyacrylamide gels and electrophoresed at 150v for approximately 1 hour. Negative controls containing unbound biotin-tagged cDNA in lanes 3, 5, 7, 9 and 11 ran close to the dye front. In the NeutrAvidin™ positive samples in lanes 2, 4, 6, 8, 10 and 12 nucleic acid-protein complexes (~60kDa) formed of a substantially larger molecular weight which migrate through the non-denaturing gel matrix at a slower rate; resulting in the detection of a shifted band at around 300 to 400bp (red arrow). Staining with a 0.001% ethidium bromide solution for 30 to 40 minutes permits this change in banding pattern between NeutrAvidin™ positive (+) and NeutrAvidin™ negative (-) lanes (Figure 4.14) to be visualised under a UV light source using the Syngene GENi Gel Documentation System.

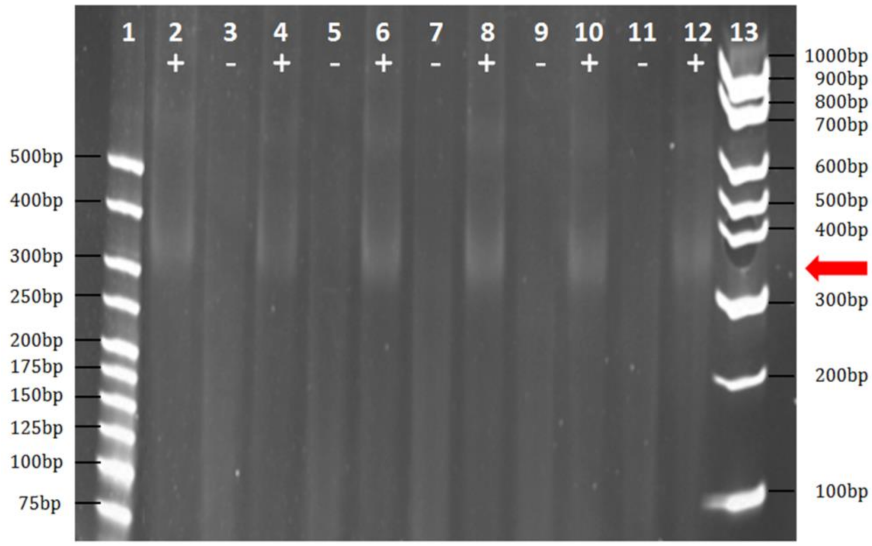


Figure 4.14 Electrophoretic Mobility Shift Assay (EMSA) Representative electrophoresis gel image assessing labelling efficiency of fragmented sense-strand cDNA targets generated from LCL's in the final microarray cohort (n=451/476) [96-CTRL, 116-FALS and 239-SALS]. Samples incubated in the presence (+) or absence (-) of biotin-binding protein NeutrAvidin™ were run with DNA markers of 25bp molecular weight (HyperLadder™ V) in lane 1 and 100bp (HyperLadder™ IV) molecular weight in lane 13 on 4 to 20% gradient polyacrylamide gels at 150v for approximately 1 hour, stained in a 0.001% Ethidium Bromide solution for 20 to 30 minutes and visualised under a ultraviolet (UV) light source using the Syngene GENi Gel Documentation System.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, CTRL - control, bp - base pairs, cDNA - complementary DNA, EMSA - electrophoretic mobility shift assay, F - familial, LCL - lymphoblastoid cell line and S - sporadic.

4.3.2 Affymetrix® Expression Console™ QC Metrics

4.3.2.1 Eukaryotic Hybridization Controls

Three genes of the *E. coli* biotin synthesis pathway (BioB, BioC and BioD) in addition to the recombinase gene from the P1 bacteriophage (CreX) (Section 2.3.2.4.2) were spiked in at increasing concentrations [1.5pM, 5pM, 25pM and 100pM, respectively] of the hybridization reaction. Since it is anticipated that these targets will not cross-hybridize with samples of a non-bacterial or non-viral origin, the intensity pattern for these controls should be seen to mimic the increase in target concentration [i.e. BioB<BioC<BioD<CreX] described above. For the ECACC LCL's this proved to be the case in all but one instance (Figure 4.15) involving familial sample [F042-(SP3303)] which is represented by the red line in plot b) of Figure 4.16.

BioB, at a concentration of 1.5pM, represents the absolute limit of detection. In the Affymetrix® Expression Console™ software version 1.3.0.187 at least one probeset pertaining to this endogenous control was flagged as present for each array which is a strong indicator of having achieved good overall sensitivity.

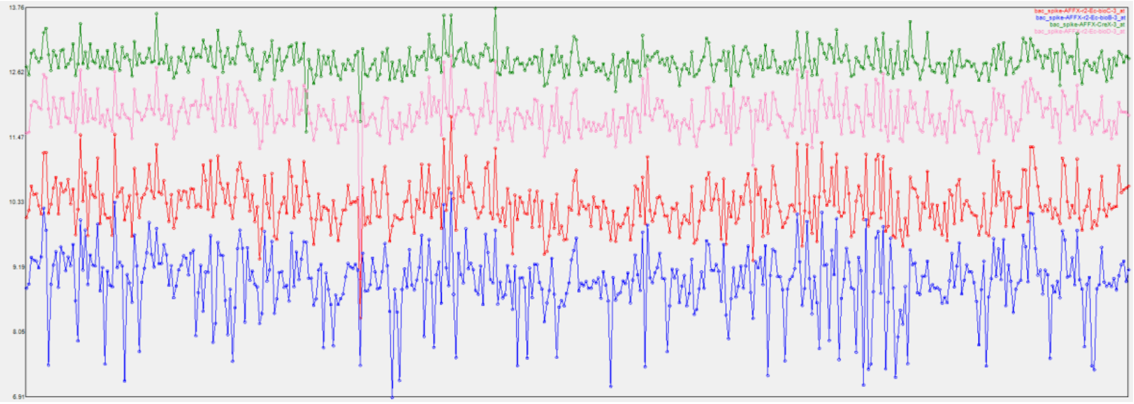


Figure 4.15 Eukaryotic Hybridization Controls Bacterial spike in controls [*E. coli* derived genes of the biotin synthesis pathway BioB (blue), BioC (red), BioD (pink) and the recombinase gene CreX (green) from the P1 bacteriophage] at staggered concentrations of 1.5pM (representing the limit of detection), 5pM, 25pM and 100pM, respectively. Assessment of Affymetrix® quality control metrics was performed using the Expression Console™ software version 1.3.0.187.

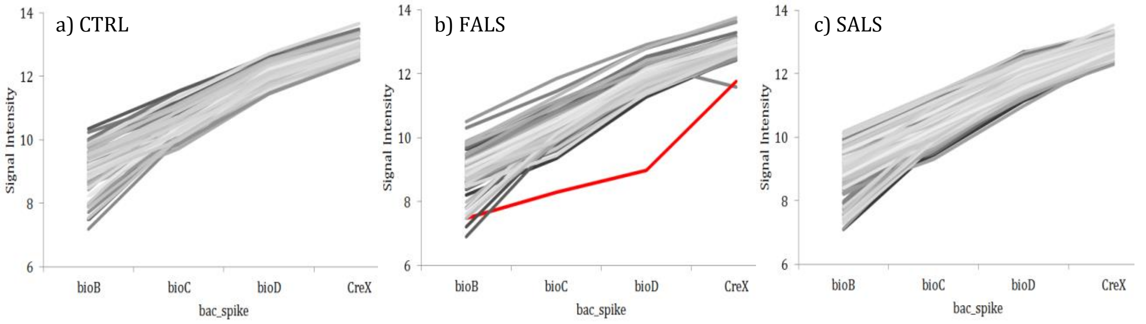


Figure 4.16 Bacterial Spike in Controls Mean signal intensities of BioB, BioC, BioD and CreX probesets on the Affymetrix Human Exon 1.0ST GeneChip® Arrays for a) control (CTRL), b) familial (FAL S) and c) sporadic (SALS) samples in the final microarray cohort [95-CTRL (C73 failed to scan), 116-FALS and 239-SALS]. Each line represents a single array with outliers highlighted in red [F042-(SP 3303)]. Assessment of Affymetrix® QC metrics performed using the Expression Console™ software version 1.3.0.187.

4.3.2.2 Overall Signal Quality

4.3.2.2.1 Average Background

Average background signal intensities ranged between 80.566 and 367.741 for the 450 GeneChips® [95-CTRL, 116-FALS and 239-SALS] in the final microarray cohort which excluded one Birmingham control [C073-(BC6091)] that failed to scan. Values were comparable across the different sample types with means and standard deviations of 191.448±45.92, 204.245±45.03 and 204.609±45.88 for controls, FALS and SALS, respectively (Figure 4.17).

Tukey defined outliers with significantly higher (n=5/450) [1-CTRL, 2-FALS and 2-SALS] or lower (n=3/450) [3-SALS] average background signal intensities included one female control [C031-(SC3709)], five FALS patients (3-M, 2-F) [F01-(LP0137), F08-(BP6074), F076-(SP3670), F079-(SP3508) and F099-(LP0073)] and two SALS patients (2-F) [S033-(SP3045) and S203-(SNc0059)].

4.3.2.2.2 Average Percentage Presence Calls

On average, 63.1% (n=181,305) of the 287,329 'core' metaprobesets annotated by RefSeq which are incorporated onto the Affymetrix® Human Exon 1.0ST GeneChip® Arrays were flagged as present (P) (Figure 4.18). This percentage proved reasonably consistent across the different sample types with means and standard deviations of

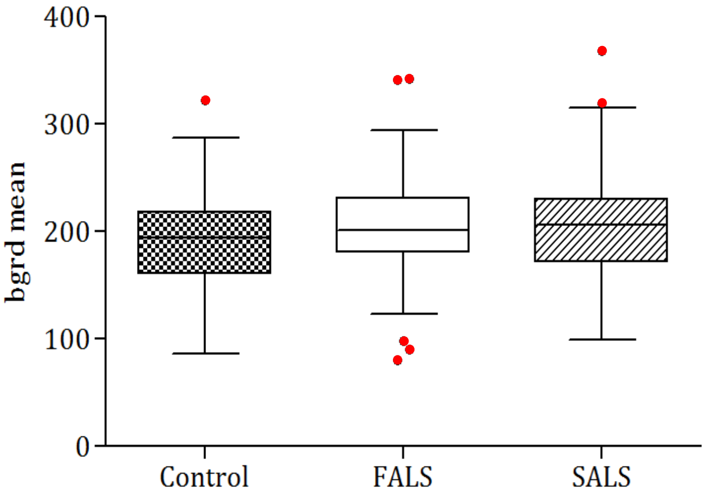


Figure 4.17 Mean Background Signal Intensities Across LCL Sample Types Summary box and whisker plots were generated in GraphPad® Prism software version 5.04 copyright © 1992-2014 (GraphPad® Software Inc., CA USA) applying a Tukey multiple comparison test. Samples of significantly higher or lower mean background (bgrd) signal intensities (outliers) were highlighted in red (n=8/450) [1-CTRL, 5-FALS and 2-SALS]. Assessment of Affymetrix® QC metrics performed using Expression Console™ software version 1.3.0.187.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, CTRL - control, F - familial, LCL - lymphoblastoid cell line, QC - quality control and S - sporadic.

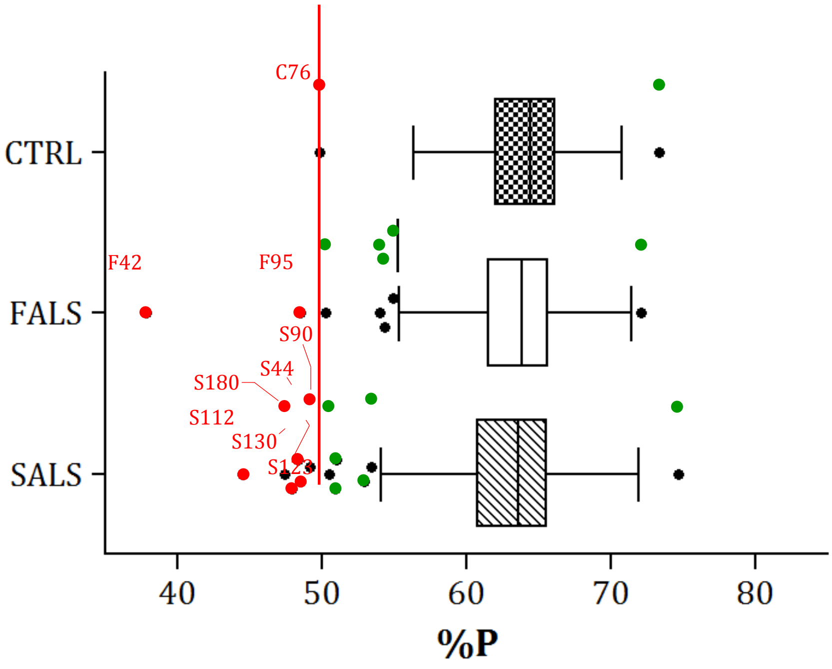


Figure 4.18 Average Percentage Presence (%P) Calls Across LCL Sample Types Summary box and whisker plots produced in GraphPad Prism® software version 5.04 copyright © 1992-2014 (GraphPad® Software Inc., CA USA) applying a Tukey multiple comparisons test. Outliers of insufficient quality with fewer than 143,665 'core' meta-probesets called as present (P) on Affymetrix® Human Exon 1.0ST GeneChip® Arrays are highlighted in red (n=9/450) [1-CTRL, 2-FALS and 6-SALS]. The green data points represent Tukey identified outliers that have a percentage presence call above the user defined threshold of 50.0%. Assessment of Affymetrix® QC metrics performed using Expression Console™ software version 1.3.0.187.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, C - control, CTRL - control, F - familial, LCL - lymphoblastoid cell line, QC - quality control, S - sporadic and ST - sense target.

64.0±3.6% (n=183, 891±10,344), 62.9±4.7% (n=180,730±13,505) and 62.8±4.5% (n=180, 443±12,930) for controls, FALS and SALS, respectively.

Outliers were determined by performing a Tukey multiple comparisons test (Figure 4.18). Samples with %P calls below the applied threshold of 50.0% were considered to be of poorer quality. These included one female control [C076-(SNc0106)], two F ALS patients (1-M, 1-F) [F042-(SP3303) and F095-(SMa0008)] and 6 SALS patients (2-M, 4-F) [S044-(SP3329), S090-(SP3304), S112-(SP3363), S123-(BP6021), S130-(SNc0010) and S180-(BP6025)].

4.3.2.2.3 Area Under the Receiver Operating Characteristic Curve

The Receiver Operating Characteristic (ROC) curve plots the detection rate of true positive (+ve) controls, a measurement of sensitivity, against the false detection rate of negative (-ve) controls; which is a function of specificity. AUC values for the area under the curve lied between 0.8 and 0.9 for 432 (96.0%) of 450 GeneChips® in the final microarray cohort. Consistency was observed across sample types with means and standard deviations of 0.845±0.02, 0.849±0.02 and 0.854±0.03 for controls, FA LS and SALS, respectively. Samples falling outside this range included four controls (3-M, 1-F) [C038-(LSh0022), C076-(SNc0106), C087-(BC6166) and C091-(SC3741)], four FALS patients (2-M, 2-F) [F042-(SP3303), F080-(SP3508), F085-(LP0013) and F095-(SMa0008)] and ten SALS patients (6-M, 4-F) [S108-(SP3384), S119-(SP3073), S123-(BP6021), S130-(SNc0010), S145-(SP3065), S162-(SP3326), S215-(SP3187), S220-(SP3105), S244-(BP6052) and S352-(SP3484)].

4.3.2.3 Signal Comparability

4.3.2.3.1 All Probeset Mean Signal Intensities

Average signal intensities across all probesets included at the level of the transcript (n=22,011) (Figure 4.19a) were found to be marginally lower than those observed at the level of the individual exon (n=287,329) (Figure 4.19b). Means and standard deviations were comparable between different sample types [GENE LEVEL 6.94±0.12, 6.95±0.10 and 6.98±0.11 for controls, FALS and SALS versus EXON LEVEL 7.05±0.14, 7.06±0.13 and 7.09±0.15 for controls, FALS and SALS].

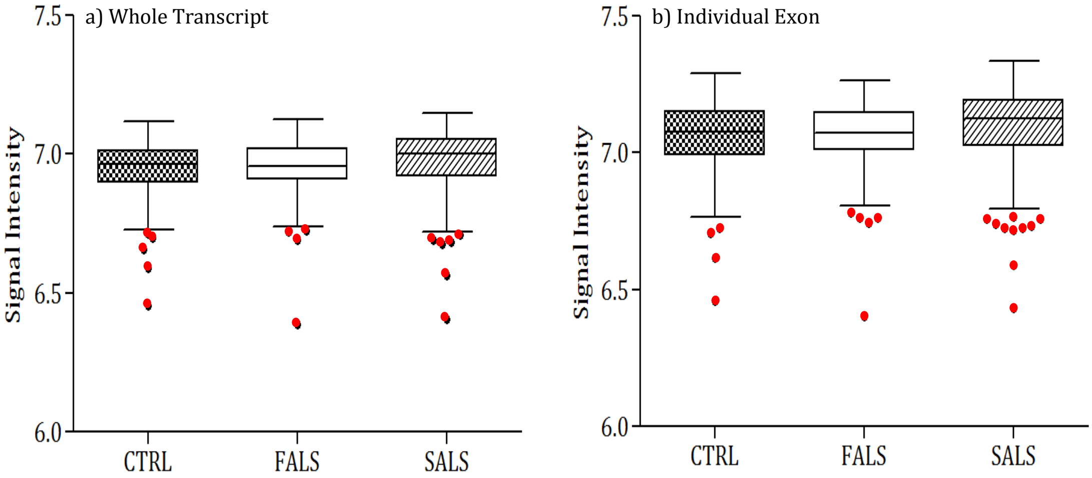


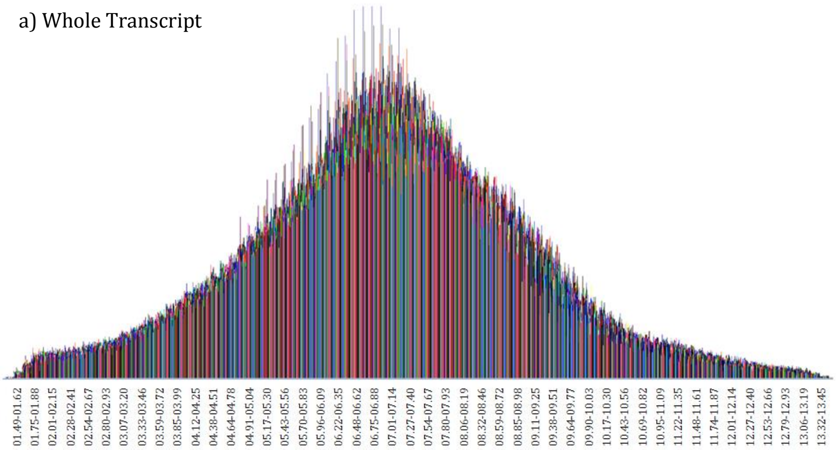
Figure 4.19 Mean Probeset Signal Intensities Across LCL Sample Types Summary box and whisker plots at a) whole transcript or b) individual exon level were produced using GraphPad Prism® software version 5.04 copyright © 1992 to 2014 (GraphPad® Software Inc., CA USA) with a Tukey multiple comparison test applied. Outliers are represented in red. Assessment of Affymetrix® QC metrics were performed in Expression Console™ software version 1.3.0.187.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, CTRL - control, F - familial, LCL - lymphoblastoid cell lines, QC - quality control and S - sporadic.

Tukey defined outliers which were detected at both levels of analyses included four controls (2-M, 2-F) [C079-(SC3279), C087-(BC6166), C090-(BOx0073) and C091-(SC3741)], for FALS patients (2-M, 2-F) [F014-(LCa0111), F042-(SP3303), F085-(LP0013) and F095-(SMa0008)] and six SALS patients (3-M, 3-F) [S06-(SP3062), S162-(SP3326), S186-(SP3090), S215-(SP3187), S220-(SP3105) and S352-(SP3484)].

4.3.2.3.2 Signal Histogram

Density histograms pertaining to log2 transformed average GC-RMA normalised signal intensity values were plotted at a) whole transcript and b) individual exon level in Expression Console™ software version 1.3.0.187. In general distributions appear highly correlated across all 450 arrays (Figure 4.20) in the final ECACC LCL micro-


a) Whole Transcript

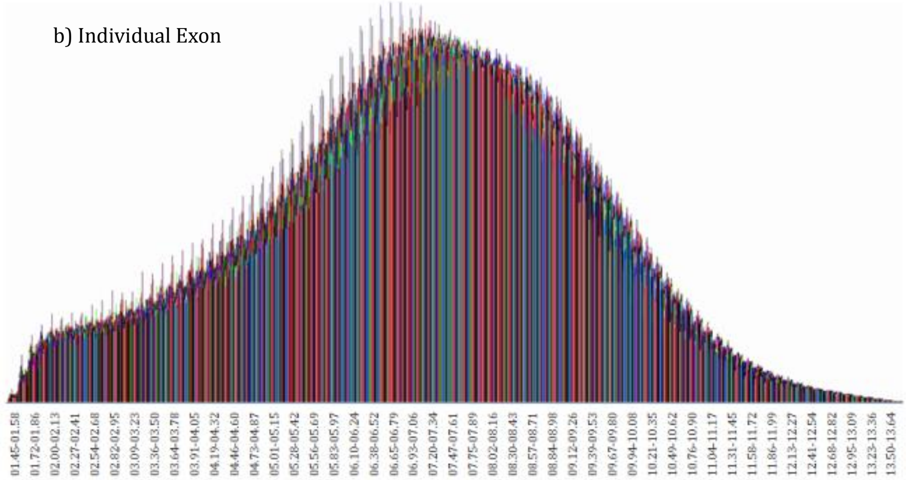

b) Individual Exon

Figure 4.20 Signal Histogram Plots Each series of coloured bars represents the distribution of log2 transformed, average GC-RMA normalised signal intensity values for a single array at a) whole transcript and b) individual exon level. Assessment of QC metrics was performed in Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK).

Abbreviations: QC - quality control and RMA - Robust Multi-array Average.

array cohort with a good degree of concordance between the two different levels of analyses.

4.3.2.3.3 Relative Log Expression Signal

Mean absolute relative log expression (RLE) is used as a measure of how the signal intensities on each individual chip compare with those across the rest of the experiment. A cohort which exhibits relative homogeneity should have scores close to zero with a small spread of values around the mean. Samples in the ECACC microarray study that deviated significantly from this scenario (Section 3.3.2.6), with means or standard deviations above the 0.500 threshold, included six controls (3-M, 3-F) [C0 38-(LSh0002), C076-(SNc0106), C079-(SC3279), C087-(BC6166), C090-(BOx0073) and C091-(SC3741)], three FALS (1-M, 2-F) [F042-(SP3303), F080-(SP3508) and F0 95-(SMa0008)] and eleven SALS (8-M, 3-F) [S108-(SP3384), S112-(SP3363), S119-(SP3073), S123-(BP6021), S130-(SNc0010), S145-(SP3065), S162-(SP3326), S189-(SP3090), S215-(SP3187), S220-(SP3105) and S352-(SP3484)] patients (Figure 4.2 1).

4.3.2.4 Pearson's Correlation Coefficient

For each pair of arrays, Expression Console™ software version 1.3.0.187 determines the Pearson's product-moment correlation coefficient (r) (Section 3.3.2.6) from the covariance divided by the product of the standard deviations. This is computed on a scale of -1 to 1 where zero equals no correlation (i.e. the data points are randomly distributed) and a value to close to plus (positive) or minus (negative) one indicates that there is a strong linear relationship between the X and Y variables (Figure 3.10). The data can be illustrated qualitatively on a coloured matrix as depicted in Figure 4.22. In the ECACC microarray experiment r exceed 0.725 for all pair-wise comparisons made across the three sample types with those hybridizations producing the weakest relationships represented in blue ($r<0.800$) or white ($0.800<r<0.850$). These included one male control [C091-(SC3741)], two FALS patients (1-M, 1-F) [F04-2-(SP3303) and F095-(SMa0008)] and three SALS patients (2-M, 1-F) [S189-(SP30 90), S215-(SP3187) and S352-(SP3484)] (Figure 4.22).

4.3.2.5 Affymetrix® Expression Console™ Summary

In total, 7.8% (n=35/450) LCL's in the final ECACC microarray cohort [7/95-CTRL, 10/116-FALS and 18/239-SALS (Table 4.6)] failed one or more post-hybridization QC parameters assessed in Expression Console™ software version 1.3.0.187. Signal intensity files (CEL files) generated for three controls (2-M, 1-F) [C076-(SNc0106), C087-(BC6166) and C091-(SC3741)], two FALS patients (1-M, 1-F) [F042-(SP3303) and F095-(SMa000 8)] and seven SALS patients (4-M, 3-F) [S123-(BP6021), S130-(SNc0010), S162-(SP3326), S189-(SP3090), S215-(SP3187), S220-(SP3105) and S3

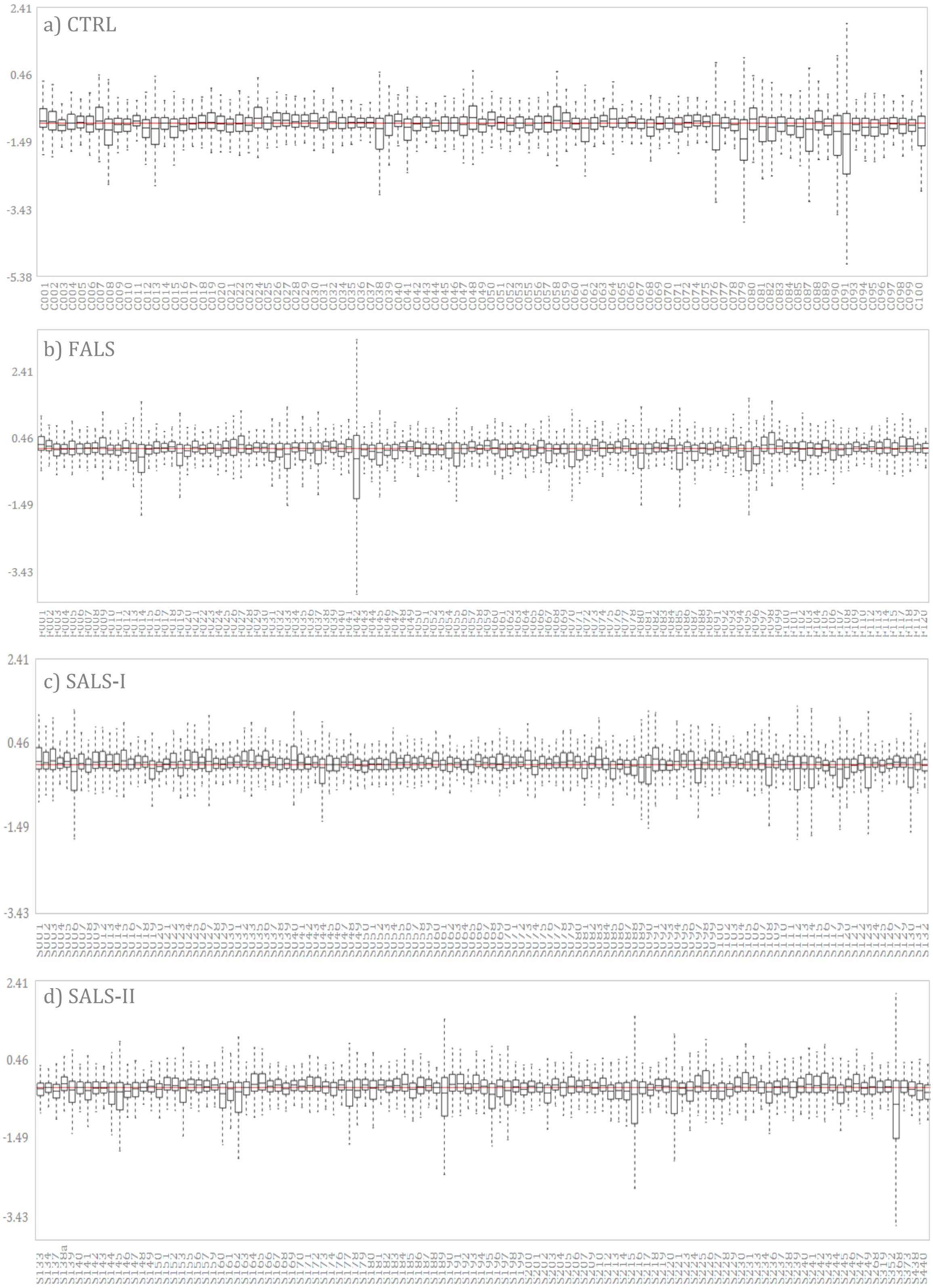


Figure 4.21 Mean Absolute RLE Boxplots Absolute Relative Log Expression (RLE) means and standard deviations for a) control (CTRL) samples, C1-100, b) familial (FALS) samples, F1-120, c) sporadic (SALS) samples, S1-132 and d) sporadic (SALS) samples, S133-440 in the ECACC microarray experiment. Whiskers represent minimum and maximum average probeset signal intensities at the level of the whole transcript. Assessment of Affymetrix® quality control (QC) metrics was performed using Expression Console™ software version 1.3.0.187.

Abbreviations: C - control, F - familial and S - sporadic.

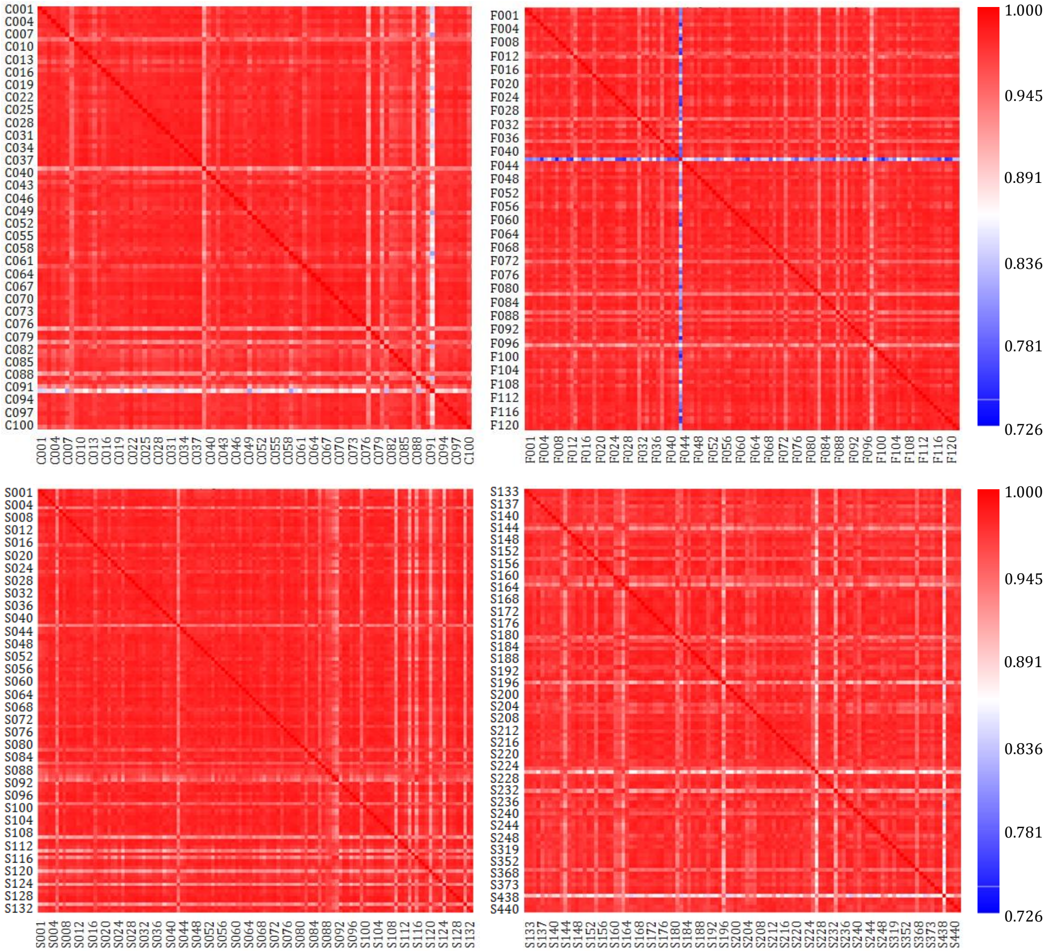


Figure 4.22 Pearson's Correlation Coefficient Each pair-wise comparison in the coloured matrix is assigned a value for r on a scale of 0.726 (blue) to 1.000 (red) where the higher the score is indicative of a stronger linear relationship between the X and Y variables. Assessment of Affymetrix® QC metrics performed in Expression Console™ software version 1.3.0.187.

Abbreviations: C - control, F - familial, QC - quality control and S - sporadic.

	Control	FALS	SALS
National DNA Bank	100	120	257
ECACC	-0	-0	-1
RNA	-0	-0	-0
ss-cDNA	-4	-4	-17
Hybridization	-1	-0	-0
Final Total	**95**	**116**	**239**

Table 4.6 Summary of Control, FALS and SALS LCL Samples in Final ECACC Microarray Cohort The initial cohort was comprised of 100 controls, 120 FALS and 257 SALS to include all of the LCLs in the ECACC discovery cohort plus an additional seven *C9ORF72+* cases from the ECACC replication cohort which met the criteria for the long (>4yrs) versus short (<2yrs) survival study. A breakdown of the number of samples passing each of the handling and processing steps is provided with the final totals highlighted in bold.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, ECACC - European Collection of Cell Cultures, F - familial, LCL - lymphoblastoid cell lines and S - sporadic.

52-(SP3484)] were of particularly poor quality having failed three or more of the QC metrics summarised in Table 4.7.

	Affymetrix® Expression Console™ QC Metric						
	bac_spike	bgrd_mean	%P	AUC	all_probeset_mean	RLE	PPMCC
C076	🟩	🟩	🟥	🟥	🟩	🟥	🟩
C087	🟩	🟩	🟩	🟥	🟥	🟥	🟩
C091	🟩	🟩	🟩	🟥	🟥	🟥	🟥
F042	🟥	🟩	🟥	🟥	🟥	🟥	🟥
F095	🟩	🟩	🟥	🟥	🟥	🟥	🟥
S123	🟩	🟩	🟥	🟥	🟩	🟥	🟩
S130	🟩	🟩	🟥	🟥	🟩	🟥	🟩
S162	🟩	🟩	🟩	🟥	🟥	🟥	🟩
S189	🟩	🟩	🟩	🟩	🟥	🟥	🟥
S215	🟩	🟩	🟩	🟥	🟥	🟥	🟥
S220	🟩	🟩	🟩	🟥	🟥	🟥	🟩
S352	🟩	🟩	🟩	🟥	🟥	🟥	🟥

Table 4.7 Affymetrix® Expression Console™ Summary of Failed LCL Samples in the ECACC Discovery and Replication Cohorts

Key: 🟩 Passed 🟥 Failed

Abbreviations: AUC - area under receiver operating curve (ROC), bac-spike - bacterial spike in control, bgrd - background, C - control, F - familial, LCL - lymphoblastoid cell line, P - present calls, PPMCC - Pearson's product moment correlation coefficient, QC - quality control, RLE - relative log expression and S - sporadic.

4.4 DISCUSSION

Participants (n=820) [120-FALS, 500-SALS and 200-CTRL] attending clinics (Section 2.1.2) in the Birmingham, London or Sheffield districts (Figure 2.1) between November 2003 and June 2011, who were subsequently recruited to the ECACC microarray cohort, were Caucasian and of North European descent. Patient partners or their unrelated carers were selected as neurologically normal, healthy control subjects. These were matched for age and gender across the SALS group, with a slightly higher than previously reported M:F ratio of approximately 1.75:1. Typically, ratios range between 1.20 and 1.50:1 (Section 1.1.2); which is comparable to the FALS group at 1.45:1 (McCombe & Henderson 2010). All patients were diagnosed according to the World Federation of Neurology's amended EEC of 1998 (Figure 1.1) (Section 1.1.3) with the majority having either definite 39.4% (n=244/620) or probable ALS 55.3% (n=343/620). There were four incidences of ALS with concomitant FTLD (Section 1.

1.5.5) [1-FALS and 3-SALS] and two further incidences of ALS with concomitant PD (Section 1.2.1) [1-FALS and 1-SALS]. In the remaining 4.4% (n=27/620) of cases it is likely that a revision has been made to the original diagnosis of ALS after the samples were accepted into the National MNDA DNA Bank. These comprised several rarer variants of MND including: PBP (Section 1.2.2.1) (n=23/27) [6-FALS and 17-SALS] in which the bulbar muscles are primarily affected (Gregoriou et al 1969, Karam et al 2010, Talacko & Reade 1990); PLS (Section 1.2.2.2) (n=3/27) [1-FALS and 2-SALS] of pure UMN involvement (Gotkine & Argov 2007, Praline et al 2010, Pringle et al 1992, Tartaglia et al 2007) and PMA (Section 1.2.2.3) (n=1/27) [1-SALS] of pure LMN involvement (de Carvalho et al 2007, Visser et al 2008, Visser et al 2007).

FALS cases exhibited a moderately younger mean age of symptom onset (defined as the point at which the patient first presented with significant weakness) than SALS cases that peaked in the mid-fifties compared to early sixties [FALS 55±11.9 (range 23-82) years and SALS 60±11.4 (range 22-87) years (student's t-test p<0.001***)]. This was consistent with the reports of Calvo et al (2014b) and Kinsley & Siddique (2001). The proportion of patients with limb onset (50%), bulbar onset (~30%), a mixed presentation (10-15%) or onset in the respiratory muscles (~2%) were also comparable to the figures published in the literature (Gautier et al 2010, Korner et al 2011, Ravits et al 2007, Sekiguchi et al 2014). In addition, survival was observed to be similar between FALS and SALS groups [FALS 2.9±2.28 (range 0.5-18.7) years and SALS 3.2±1.74 (range 0.39-10.3) years]; although differences were reported to occur between SALS of the ECACC discovery (Section 4.1.1) and replication (Section 4.1.2) cohorts with respective means and standard deviations of 2.8±1.34 years or 4.0±2.30 years and a student's t-test derived probability value of 7.26E-12 (Cluskey & Ramsden 2001, McDermott & Shaw 2007). One possible explanation for this skew in survival data stems from the fact that samples with complete clinical information immediately available to hand were prioritised to the discovery cohort at the start of the project, to prevent delays in commencing the study. Another unintentional consequence of how the LCL's were consigned to a cohort (ranking of SALS and controls in ascending order of age and arbitrarily assigning them number one or two alternately down the list) was the considerably higher M:F ratio for SALS in the replication (2.17:1) (Section 4.1.2) versus discovery cohorts (1.43:1) (Section 4.1.1) (Table 4.1).

This can be rectified, however, using the Partek® Genomics Suite™ analysis pipeline outlined in Section 2.3.2.5.2 which includes age and gender as covariates (Figure 2. 4) in order to control for any potential bias that may be introduced by such factors.

Mutations were detected in the FALS patients at a frequency of 40.8% for *C9ORF72* (n=49/120) (Section 1.2.5.4), 4.4% for *SOD1* (n=5/115) (Section 1.2.5.1.1), 3.8% for *FUS* (n=4/106) (Section 1.2.5.2.2) and 2.9% for *TARDBP* (n=3/103) (Section 1.2.5.2. 1) (Table 4.2) and in the SALS patients at a frequency of 8.0% for *C9ORF72* (n=40/ 500), 0.6% for *TARDBP* (n=3/500), 0.4% for *CHMP2B* (n=2/500) (Section 1.2.5.2.8) and 0.2% for *ANG* (n=1/500) (Section 1.2.5. 2.3) (Table 4.3). With the exception of familial *SOD1* (Rosen et al 1993) and *TARDBP* (Sreedharan et al 2008), which were recorded at a lower than anticipated frequency, the majority were found to be consistent with the previously published reports of Cooper-Knock et al (2012b), DeJesus-Hernandez et al (2011), Greenway et al (2006), Kwiatkowski et al (2009), Parkinson et al (2006), Renton et al (2011) and Vance et al (2009). Among the *C9ORF72* cases were two examples of oligogenic inheritance, including one FALS patient [F05 6-(SP3462)] with an *OPTN* mutation (Bury et al 2015) (Section 5.3.2.1) and a second SALS patients [S352-(SP3484)] with a *TARDBP* mutation (Kirby et al 2010) (Section 5.3.2.2). In this latter instance, although the patient was entered into the database as a sporadic case, it is likely, especially in light of the above, that the individual does in fact represent a familial case which has arisen as a consequence of incomplete penetrance or may have been misclassified due to a lack of information regarding family history. Since ALS is typically an adult onset disorder of relatively short life expectancy there is a chance that affected relatives of some seemingly SALS cases have died (Al-Chalabi & Lewis 2011, Conforti et al 2011) either before clinical manifestations of disease or prior to a formal diagnosis of MND having been made.

Across the ECACC discovery (Section 4.1.1) and replication (Section 4.1.2) cohorts four LCL samples [3-SALS and 1-CTRL] failed the EBV-transformation process and, following two unsuccessful attempts, were rejected from the final study design. On the NanoDrop™ 1000 Spectrophotometer (Section 2.3.1.3) high yields [APPENDIX TABLE B7] and purity ($A_{260/280}$ 2.0±0.2, 99.3%) was achieved for the remaining 816 [120-FALS, 497-SALS and 199-CTRL] samples with little or no evidence of protein/ DNA contamination following QIAGEN extraction of total RNA (Section 2.3.2.2) from the frozen cell pellets (Figure 4.6-8). The quality of the isolated material, as assessed using the Agilent 2100 Bioanalyzer, was found to be consistent across different sample types, within in each of the cohorts [Mean RIN: discovery cohort 8.3 versus replication cohort 7.4 (student's t-test $p<0.001$***)], but had steadily declined over time. All of the QIAGEN RNeasy® Mini Kits were purchased in a single batch and lot # at the beginning of the project. To test whether the storage of the kits was having an impact, some repeat extractions (Table 4.5) were performed using a new kit and freshly prepared 70% ethanol solution. This, however, proved ineffective and in some instances the RNA quality and yield had actually deteriorated rather than showing an improvement; suggesting freeze thawing of the LCL's may have caused some degradation to occur *ex vivo* (Caliskan et al 2014). Also, in simply taking a fixed volume of the suspension, different densities of cells could have been present in each round of the extractions. Another factor worth considering is the quality of the original sample used for EBV-transformation, since the extractions were performed in the order in which they were received from ECACC and it is a likely proposition that the LCL's proving most difficult to process would have been dispatched in the later batches.

For the ECACC microarray study in the subsequent two results chapters (Chapter 5: '*C9ORF72* GEP Study' and Chapter 6: '*C9ORF72* Survival Study') the Ambion® Whole Transcriptome (WT) Expression Kit was used to generate linearly amplified material for all samples received in the discovery cohort (Section 4.1.1), plus an additional seven *C9ORF72+* cases in the replication cohort (Section 4.1.2) [120-FALS, 256-S ALS and 100-CTRL] which met the criteria for inclusion into the analysis of Long (≥ 4yrs) versus Short (<2yrs) survival. Sufficient quantities of ss-cDNA were achieved in 94.7% of cases (n=451/476) [116-FALS, 239-SALS and 96-CTRL] [APPENDIX TA BLE B7]. Post-fragmentation and labelling, targets of ~40-70nt were hybridized on to Affymetrix® Human Exon 1.0ST GeneChip® Arrays. For one control, namely [C07 3-(BC6091)], the GeneChip® failed to scan and a signal intensity or (CEL) file could not be created. The remaining samples were processed using Expression Console™ software version 1.3.0.187 (Section 2.3.2.5.1) [116-FALS, 239-SALS and 95-CTRL]. Following assessment of a series of quality control (QC) parameters summarized in Table 4.7, 2.7% (n=12/450) [2-FALS, 7-SALS and 3-CTRL] were identified as having failed at least three of these measures and were removed from any subsequent downstream comparative analyses. Later it was established that 10 of the 12 LCL's (83.3%) had a RIN score of below 5.0 which suggests that the original samples were of poor quality. Therefore, given the size of the cohort, it did not warrant the expense of repeating these individual amplifications.

CHAPTER 5: *C9ORF72* GEP STUDY

The discovery by Renton et al and DeJesus-Hernandez et al, in 2011, of a pathogenic G_4C_2 repeat expansion in the previously uncharacterised *C9ORF72* gene represented a unique opportunity in which to study a specific genetic subtype that accounts for a greater proportion of cases than *SOD1* (Section 1.2.5.1.1), *TARDBP* (Section 1.2.5.2. 1) or *FUS* (Section 1.2.5.2.2) mutations combined. In this chapter global GEP's from patient derived, EBV-transformed B-lymphocytes carrying the *C9ORF72* expansion, were compared on Affymetrix® Human Exon 1.0ST GeneChip® Arrays to a subset of ECACC SALS patients and controls. Subsequent, downstream functional annotation clustering analysis conducted in DAVID bioinformatics resource version 6.7 enabled us to elucidate further the mechanisms of C9ORF72 toxicity. In addition, it was also anticipated that this approach would aid in distinguishing between the mechanisms linked, specifically, to C9ORF72-related disease from those which contribute to MN degeneration more widely in ALS.

5.1 *C9ORF72* and non*C9ORF72*-Related_SALS Cohort

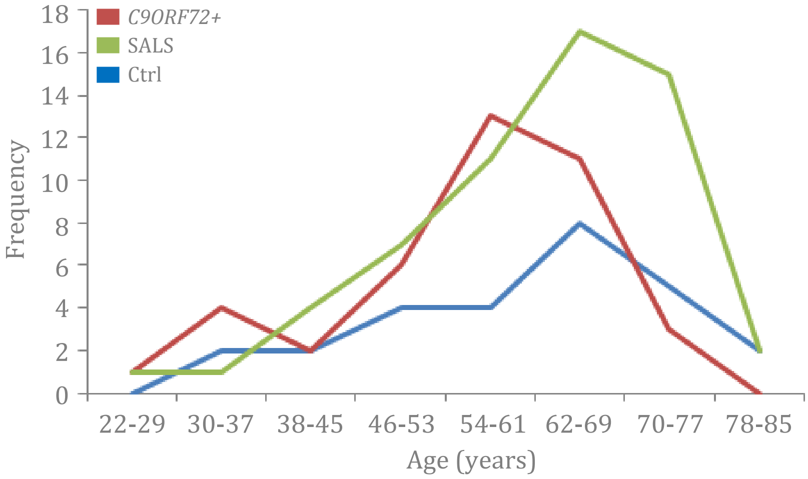
5.1.1 ECACC EBV-Transformed B-Lymphocytes

5.1.1.1 Clinical Characteristics

5.1.1.1.1 Control Cases

Neurologically normal, healthy control LCL's (n=27/100) [15-M, 12-F] selected from the ECACC discovery cohort were largely recruited from patient partners or their un-related carers (Section 4.1.1). These were comprised of 8 Birmingham (29.6%) cases including two from Liverpool [C039-(BLi0169) and C097-(BLi0083)] and one from Belfast City Hospital [C020-(BBe0006)]; 4 London (14.8%) cases including one from Cambridge [C021-LCa0076)] and one from Poole General Hospital [C05-(LPo0033)] and 15 Sheffield (55.6%) cases including three from Newcastle [C04-(SNc0091), C07 -(SNc0038) and C044-(SNc0041)], one from Preston [C08-(SPr0050)] and one from

Manchester [C036-(SMa0156)]. Age at consultation ranged between 36 and 84 years with a mean of 60.7±13yrs. The M:F ratio was 1.25:1 (Figure 5.1).



	C9ORF72+	SALS	Control
M:F	0.91:1	1.42:1	1.25:1
Age	55.7±11yrs	61.3±12yrs	60.7±13yrs
Total	**40**	**58**	**27**

Figure 5.1 Age Frequency Distribution of Patient and Control LCL's in the ECACC *C9ORF72* and Non*C9ORF72*-Related_SALS Study

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, Ctrl - control, ECACC - European Collection of Cell Cultures, F - female, LCL - lymphoblastoid cell lines, M - male and S - sporadic.

5.1.1.1.2 C9ORF72+ Cases

Patient derived LCL's carrying the G_4C_2 repeat expansion in *C9ORF72* (n=40/620) [19-M, 21-F] consisted of 18 FALS and 22 SALS selected from the ECACC discovery (Section 4.1.1) and replication (Section 4.1.2) cohorts. These were comprised of 7 Birmingham (17.5%) cases including one from Oxford [F078-(BOx0029)]; 9 London (22.5%) cases and 24 Sheffield (60.0%) cases including one from Newcastle [S203-(SNc0059)] and two from Manchester [F081-(SMa0006) and F117-(SMa0166)]. The combined M:F ratio was 0.91:1. However, differences were observed between the two sample types [*C9ORF72+* FALS 0.80:1 and *C9ORF72+* SALS 1.00:1] (Figure 5.1).

The majority of *C9ORF72+* cases, 95.0% (n=38/40) were diagnosed according to the World Federation of Neurology's amended EEC of 1998 (Figure 1.1) (Section 1.1.3) with either definite (n=22/38) [9-familial, 13-sporadic] or probable (n=16/38) [8-

familial, 8-sporadic] ALS including one incidence of concomitant FTLD [F115-(SP31 18)] and another of concomitant PD (Section 1.2.1) [F114-(SP3560)]. The remaining 5.0% (n=2/40) of the cohort were diagnosed with PBP (Section 1.2.2.1) [F100-(SP3 070) and S165-(SP3222)]. Age at symptom onset (i.e. when the patient first experienced significant weakness) ranged between 28 and 70 years with a mean of 55.7± 11yrs for *C9ORF72+* FALS or 36 and 71 years with a mean of 55.6±11yrs for *C9ORF 72+* SALS. Disease duration ranged from 7 to 107 months or 11 to 73 months with a mean of 2.93±2.3yrs for *C9ORF72+* FALS and 2.54±1.4yrs for *C9ORF72+* SALS, respectively (Table 5.1). Limb onset accounted for 50.0% of cases (n=20/40) [6-FALS, 1-FASL+PD and 13-SALS], bulbar onset and a further 32.5% (n=13/40) [6-FALS, 1-FALS+FTLD, 6-SALS and 1-PBP (sporadic)] and a mixed presentation 15.0% (n=6/40) [3-FALS, 2-SALS and 1-PBP (sporadic)]. Information regarding site of onset was not available for the remaining 2.5% of the cohort (n=1/40) [1-FALS]. ALSFRS-R scores ranged between 0 (severe disability) and 46 (near normal function) with an average of 30.1±12 for 100% of *C9ORF72+* FALS and 30.2±14 for 86.4% of *C9ORF72+* SALS (n=19/22).

For the Sheffield cases some additional clinical information could be extracted from the local database. Approximately a fifth, 20.8% (n=5/24) [1-FALS and 4-SALS] were prone to EL, another 20.8% (n=5/24) [1-FALS, 1-FALS+FTLD and 3-SALS] displayed symptoms of dyspnoea and 8.3% (n=2/24) [1-FALS and 1-SALS] had suffered from hypersialorrhea. Dysarthria and dysphagia were apparent in 45.8% (n=11/24) [2-FALS, 1-FALS+PD, 1-FALS+FTLD, 5-SALS and 2-PBP (1-familial, 1-sporadic)] of the cohort with PEG feeding (Section 1.1.4) becoming a necessary intervention in 36.4% (n=4/11) [1-FALS, 1-FALS+PD and 2-SALS] of these latter cases. There was also one sporadic individual who presented with the rare and more benign FA variant of the disease [S042-(SP3122)] (Section 1.2.1). Three patients, 12.5% [1-FALS, 1-FALS+PD and 1-SALS] were non-ambulant with a further 8.3% (n=2/24) [1-FALS and 1-SALS] unable to walk without needing assistance. Current smokers comprised 4.2% of the cohort (n=1/24) [1-PBP (familial)], ex-smokers a further 8.3% (n=2/24) [2-SALS] and non-smokers 66.7% (n=16/24) [5-FALS, 1-FALS+PD, 9-SALS and 1-PBP (sporadic)]. For the remaining 20.8% of the cohort (n=5/24) [2-FALS and 3-SALS] this information was not disclosed.

	$C9ORF72_{neg}$	----------------------------------- $C9ORF72_{pos}$ -----------------------------------			-------- Control --------
	SALS	**SALS**	**FALS**	**ALL**	**CTRL**
M:F	1.42:1	1.00:1	0.80:1	0.91:1	1.25:1
Age					
range	22-82yrs	36-71yrs	28-70yrs	28-71yrs	36-84yrs
mean	61yrs	56yrs	56yrs	56yrs	61yrs
Onset					
Limb	28 (48.2%)	13 (59.1%)	7 (38.9%)	20 (50.0%)	n/a
Bulbar	24 (41.4%)	7 (31.8%)	6 (33.3%)	13 (32.5%)	n/a
Mixed	4 (6.9%)	2 (9.1%)	4 (22.2%)	6 (15.0%)	n/a
Respiratory	2 (3.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a
unknown	0 (0.0%)	0 (0.0%)	1 (5.6%)	1 (2.5%)	n/a
Diagnosis					
ALS	51 (87.9%)	21 (95.5%)	15 (83.3%)	36 (90.0%)	n/a
ALS+FTLD	2 (3.5%)	0 (0.0%)	1 (5.6%)	1 (2.5%)	n/a
ALS+PD	0 (0.0%)	0 (0.0%)	1 (5.6%)	1 (2.5%)	n/a
PBP	5 (8.6%)	1 (4.5%)	1 (5.6%)	2 (5.0%)	n/a
PLS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a
PMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a
ALSFRS-R					
range	0-46	0-45	0-46	0-46	n/a
mean	31	30	30	30	n/a
Survival					
range	0.4-7.7yrs	0.9-6.1yrs	0.5-9.0yrs	0.5-9.0yrs	n/a
mean	2.8yrs	2.5yrs	2.9yrs	2.7yrs	n/a
Total	**58 (56)**	**22 (20)**	**18 (18)**	**40 (38)**	**27 (26)**

Table 5.1 Clinical Summary of Patient and Control LCL's in the ECACC *C9ORF72* and Non*C9ORF72*-Related_SALS Study Highlighted in red are the final sample numbers obtained following assessment of QC metrics using Expression Console™ software version 1.3.0.187 (Affymetrix® Ltd., UK).

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, CTRL - control, ECACC - European Collection of Cell Cultures, F - familial, F - female, FRS-R - Functional Rating Scale Revised, FTLD - frontotemporal lobar degeneration, LCL - lymphoblastoid cell lines, M - male, PD - Parkinson's disease, PBP - Progressive Bulbar Palsy, PLS - Primary Lateral Sclerosis, PMA - Progressive Muscular Atrophy, QC - quality control and S - sporadic.

A strong family history of ALZ [F089-(SP3331) and S121-(SP3420)], PD [F144-(SP 3560)] or dementia [F115-(SP3118) and S042-(SP3122)] was associated with up to 16.7% of *C9ORF72+* FALS (n=3/18) and 9.1% of *C9ORF72+* SALS (n=2/22). In the case of sporadic sample [S186-(SP3431)] at least one incidence of colon cancer in a first degree relative had also been reported.

5.1.1.1.3 NonC9ORF72-Related_SALS Cases

The non-expansion carrying LCL's consisted of 58 SALS [34-M, 24-F] selected from the ECACC discovery cohort (Section 4.1.1). These were comprised of 7 Birmingham (12.1%) cases including two from Belfast City Hospital [S05-(BBe0007) and S052-(BBe0016)]; 7 London (12.1%) cases including one from Poole General Hospital [S0 35-(LPo0010)] and 44 Sheffield (75.8%) cases including two from Newcastle [S012-(SNc0022) and S089-(SNc0053)] and four from Nottingham [S036-(SNt0031), S129 -(SNt0024), S198-(SNt0016) and S219-(SNt0036)]. The M:F ratio was 1.42:1 (Figure 5.1).

The majority of non*C9ORF72*-related_SALS cases, 91.4% (n=53/58) were diagnosed with either definite (n=34/53) or probable (n=19/53) ALS including two incidences of concomitant FTLD [S093-(SP3049) and S178-(SP3145)]. The remaining 8.6% of the cohort (n=5/58) were diagnosed with PBP [S040-(SP3271), S044-(SP3329), S1 29-(SNt0024), S198-(SNt 0016) and S230-(SP3159)]. Age at symptom onset ranged between 22 and 82 years with a mean of 61.3±12yrs. Disease duration ranged from 4½ to 92 months with a mean of 2.76±1.5yrs (Table 5.1). Limb onset accounted for 48.3% of cases (n=28/58) [28-SALS], bulbar onset a further 41.4% (n=24/58) [17-SALS, 2-SALS+FTLD and 5-PBP (sporadic)], mixed presentation 6.9% (n=4/58) [4-SALS] and onset in the respiratory muscles the remaining 3.4% (n=2/58) [2-SALS]. ALSFRS-R scores ranged between 0 (severe disability) and 46 (near normal function) with an average of 30.8±10 for 87.9% of non*C9ORF72*-related_SALS (n=51/58) [44-SALS, 2-SALS+FTLD and 5-PBP (sporadic)].

For the Sheffield cases some additional clinical information could be extracted from the local database. Of these, 20.5% (n=9/44) [7-SALS and 2-PBP (sporadic)] were prone to EL, a further 2.3% (n=1/44) [1-SALS] presented with a clinical history of depression and approximately one third, 34.1% (n=15/44) [12-SALS, 1-SALS+FTLD and 2-PBP (sporadic)] displayed symptoms of dyspnoea with six patients [6-SALS] requiring NIPPV support (Section 1.1.4). Dysarthria and dysphagia were apparent in 50.0% of the cohort (n=22/44) [18-SALS, 2-SALS+FTLD and 2-PBP (sporadic)] with PEG feeding becoming a necessary intervention in seven of these latter cases [6-SALS and 1-PBP (sporadic)]. Two patients, 4.6% [2-SALS] were non-ambulant with 22.7% (n=10/44) [10-SALS] unable to walk without needing assistance. Current smokers comprised 2.3% of the cohort (n=1/44) [1-SALS], ex-smokers who had not smoked a cigarette for a minimum of 20 years (mean 21.7±2.9yrs) a further 6.8% (n=3/44) [2-SALS and 1-SALS+FTLD] and non-smokers 63.6% (n=28/44) [24-SALS, 1-SALS+ FTLD and 3-PBP (sporadic)]. For the remaining 27.3% of the cohort (n=12/44) [10-SALS and 2-PBP (sporadic)] this information was not disclosed.

A strong family history of dementia was associated with up to 6.9% of non*C9ORF72*-related_SALS (n=4/58) [S08-(SP3111), S078-(SP3140), S116-(SP3351) and S172-SP 3067)]. An additional sporadic individual [S236-(SP3286)] was also known to have a maternal cousin who was diagnosed with MS and in a further 8.6% of cases (n=5/ 58) at least one incidence of colon [S044-(SP3329)], bowel/stomach [S032-(SP339 7), S062-(SP3301) and S078-(SP3140)] or throat [S076-(SP3396)] cancer had been reported in a first degree relative.

5.1.1.2 Therapeutics Used to Treat the Cohort

5.1.1.2.1 C9ORF72+ Cases

Riluzole, administered at a dose of 50mg twice daily, was being used to treat 77.8% of *C9ORF72+* FALS (n=14/18) [13-FALS, 1-FALS+FTLD and 1-FALS+PD] and 95.5% of *C9ORF72+* SALS (n=21/22) [20-SALS and 1-PBP (sporadic)]. One Sheffield patient, sporadic case [S440-(BP6297)], experienced adverse side effects and the medication was withdrawn. Vitamin C and/or E (n=12/40) [3-FALS and 9-SALS] or multivitamin supplements (n=3/40) [1-FALS and 2-SALS] were collectively being taken by 37.5% (n=15/40) of the cohort (Section 1.1.4). In addition to Riluzole, several individuals were also participants of the BDNF [F091-(SP3534)], minocycline [F073-(BP6165) and S121-(SP3420)] or ONO-2506 (Arundic acid) [S132-(SP3413) and S203-(SNc00

59)] drug trials [APPENDIX TABLE B4]. Conversely, 16.7% of *C9ORF72+* FALS (n=3 /18) [2-FALS and 1-PBP (familial)] and 4.5% of *C9ORF72+* SALS (n=1/22) [1-SALS] chose not to receive any disease modifying therapy and for the remaining 2.5% of the cohort (n= 1/40) [1-FALS] this information was not available.

5.1.1.2.2 NonC9ORF72-Related_SALS Cases

Riluzole was also being used to treat 96.6% of the non*C9ORF72*-related_SALS cases (n=56/58) [49-SALS, 2-SALS+FTLD and 5-PBP (sporadic)]. One Birmingham patient, sporadic case [S210-(BP6041)], experienced adverse side effects and the medication was withdrawn. Vitamin C and/or E (n=28/58) [23-SALS, 1-SALS+FTLD and 4-PBP (sporadic)] or multivitamin supplements (n=1/58) [1-SALS] were collectively being taken by 51.8% (n=29/58) of the cohort. In addition to Riluzole, several individuals were also participants of the Copaxone® (glatiramer acetate) [S176-(SP3385)], ONO-2506 (Arundic acid) [S149-(SP3391)] or minocycline [S050-(SP3023) and S157-(LP 0015)] drug trials. Conversely, the remaining 3.4% of the cohort (n=2/58) [2-SALS] chose not receive any kind of disease modifying therapy.

5.1.1.3 Genetic Status of the Cohort

5.1.1.3.1 C9ORF72+ Cases

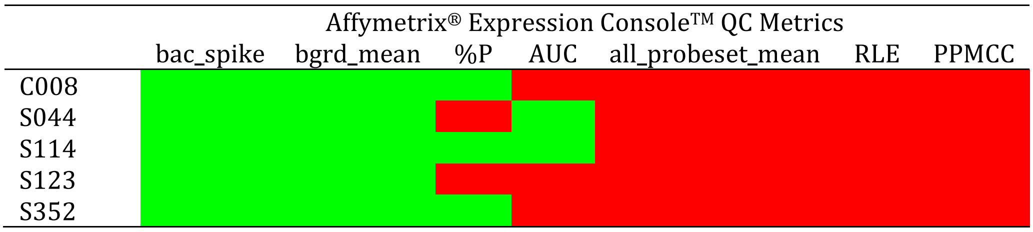
All *C9ORF72+* FALS (n=18) [8-M, 10-F] and SALS (n=22) [11-M, 11-F] patients carry more than 30 copies of the non-coding G_4C_2 hexanucleotide repeat expansion that has recently been identified in intron 1 of the previously uncharacterised *C9ORF72* gene (Cooper-Knock et al 2012b) (Section 1.2.5.4). There was also one example of oligogenic inheritance involving an apparently sporadic Sheffield sample [S352-(SP 3484)] with a deleterious heterozygous c.962C>T (p.A321V) missense mutation in exon 6 of the *TARDBP* gene (Section 4.1.2.3) (Kirby et al 2010).

5.1.1.3.2 NonC9ORF72-Related_SALS Cases

One non*C9ORF72*-related_SALS patient was reported to carry a non-synonymous c.323A>G (p.K54E) missense substitution [S062-(SP3301)] in exon 2 of the *ANG* gene (Kirby et al 2013) (Section 4.1.1.2.2). Besides the aforementioned change no further mutations which affect this cohort have been described.

5.1.2 Affymetrix® Expression Console™ QC Metrics

In vitro transcribed biotinylated ss-cDNA targets of ~40-70nt were hybridized onto Human Exon 1.0ST GeneChip® Arrays (Section 2.3.2.3 and 2.3.2.4). Affymetrix® QC metrics were assessed in Expression Console™ software version 1.3.0.187 (Section 4.3.2). One male control (n=1/27) [C08-(SPr0050)] and a further four SALS patients including two female cases from the *C9ORF72+* group (n=2/40) [S123-(BP6021) and S352-(SP3484)] and one male [S044-(SP3329)] and a third female [S114-(SP3356)] from the non*C9ORF72*-related_SALS group (n=2/58) scored poorly against three or more of the parameters summarised in Table 5.2. These samples were removed from the final ECACC LCL microarray cohort and were consequently not included in any of the subsequent downstream comparative analyses (Figure 5.2, 5.3 and 5.4).



	Affymetrix® Expression Console™ QC Metrics						
	bac_spike	bgrd_mean	%P	AUC	all_probeset_mean	RLE	PPMCC
C008	🟩	🟩	🟩	🟥	🟥	🟥	🟥
S044	🟩	🟩	🟥	🟩	🟥	🟥	🟥
S114	🟩	🟩	🟩	🟩	🟥	🟥	🟥
S123	🟩	🟩	🟥	🟥	🟥	🟥	🟥
S352	🟩	🟩	🟩	🟥	🟥	🟥	🟥

Table 5.2 Affymetrix® Expression Console™ Summary of Failed LCL Samples in the *C9ORF72* and Non*C9ORF72*-Related_SALS Study

Key: 🟩 Passed 🟥 Failed

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, AUC - area under receiver operating curve (ROC), bac-spike - bacterial spike in control, bgrd - background, C - control, *C9ORF72* - chromosome 9 open reading frame 72, LCL - lymphoblastoid cell line, PPMCC - Pearson's product moment correlation coefficient, P - present calls, RLE - relative log expression, QC - quality control and S - sporadic.

5.2 Human Exon 1.0ST GeneChip® Array Profiling

5.2.1 Differential Gene Expression Analysis

5.2.1.1 Partek® Genomics Suite™

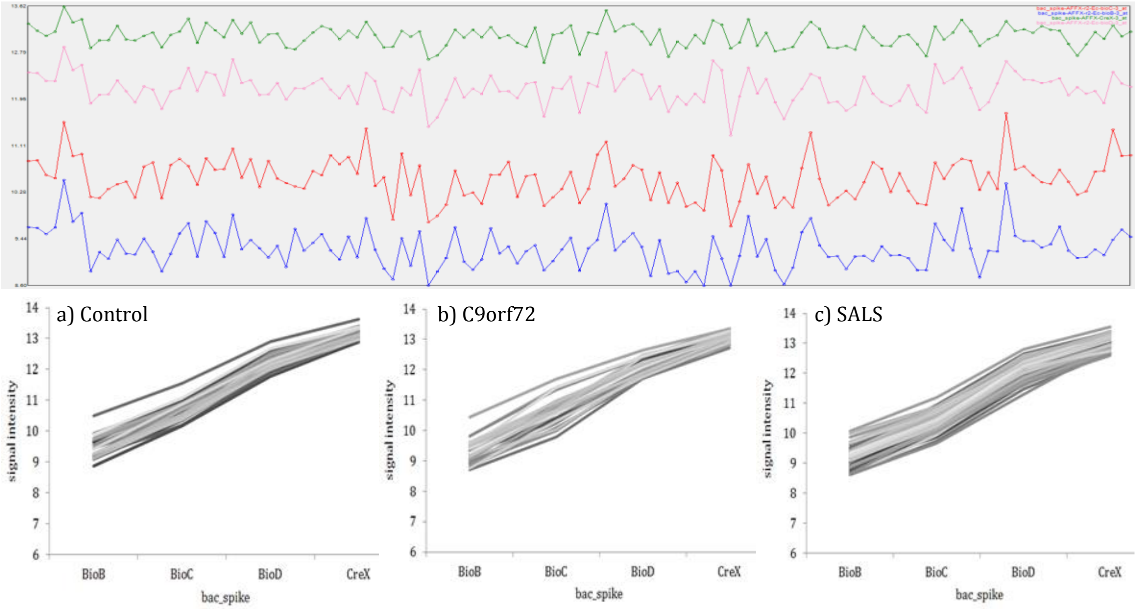


Figure 5.2 Eukaryotic Hybridization Controls for LCL Samples in the ECACC *C9ORF72* and Non *C9ORF72*-Related_SALS Study Bacterial derived genes of the *E. coli* biotin synthesis pathway [BioB (blue), BioC (red) and BioD (pink)] and the recombinase gene CreX (green) from the P1 bacteriophage were spiked in at increasing concentrations (top panel) [1.5pM (limit of detection), 5pM, 25pM and 100pM respectively] immediately prior to labelling to monitor the efficiency of the hybridization reaction. In the bottom panel mean signal intensities for each of the probesets spotted onto the Affymetrix® Human Exon 1.0ST GeneChip® Arrays are provided for a) controls (n=27), b) *C9ORF72+* FALS and SALS (n=40) and c) non*C9ORF72*-related_SALS (n=58) patients. Assessment of Affymetrix® QC metrics was performed using Expression Console™ software version 1.3.0.187.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, ECACC - European Collection of Cell Cultures, F - familial, LCL - lymphoblastoid cell lines, QC - quality control and S - sporadic.

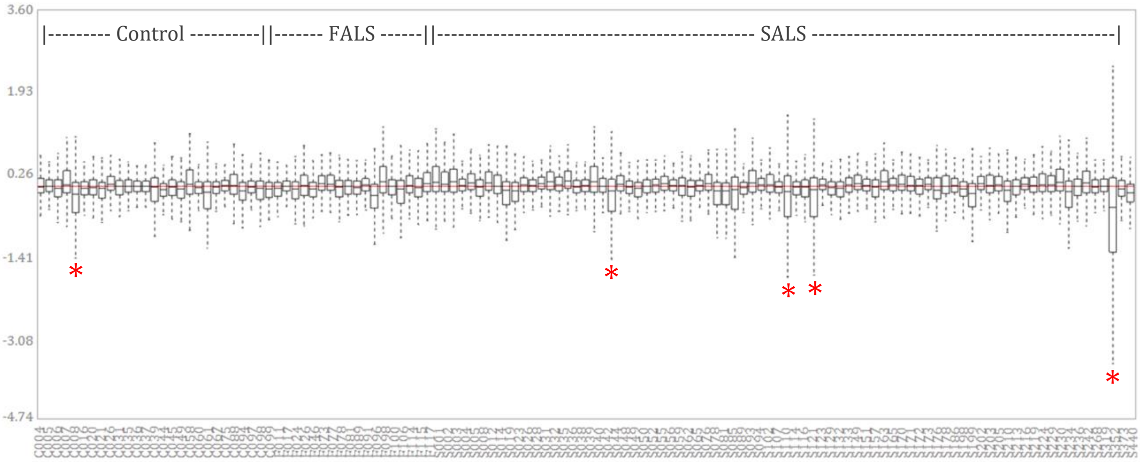


Figure 5.3 Mean Absolute RLE Boxplots for LCL Samples in the ECACC *C9ORF72* and Non*C9ORF72*-Related_SALS Study Relative log expression (RLE) means and standard deviations for a) control (n=27), b) *C9ORF72+* FALS (n=18) and c) expansion/non-expansion carrying SALS (n=80). Whiskers represent minimum and maximum average probeset signal intensities for each array at the level of the whole transcript. Asterisks (red) highlight significant outliers. Assessment of the Affymetrix® QC metrics was performed using Expression Console™ software version 1.3.0.187.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, C - control, ECACC - European Collection of Cell Cultures, F - familial, LCL - lymphoblastoid cell lines, QC - quality control and S - sporadic.

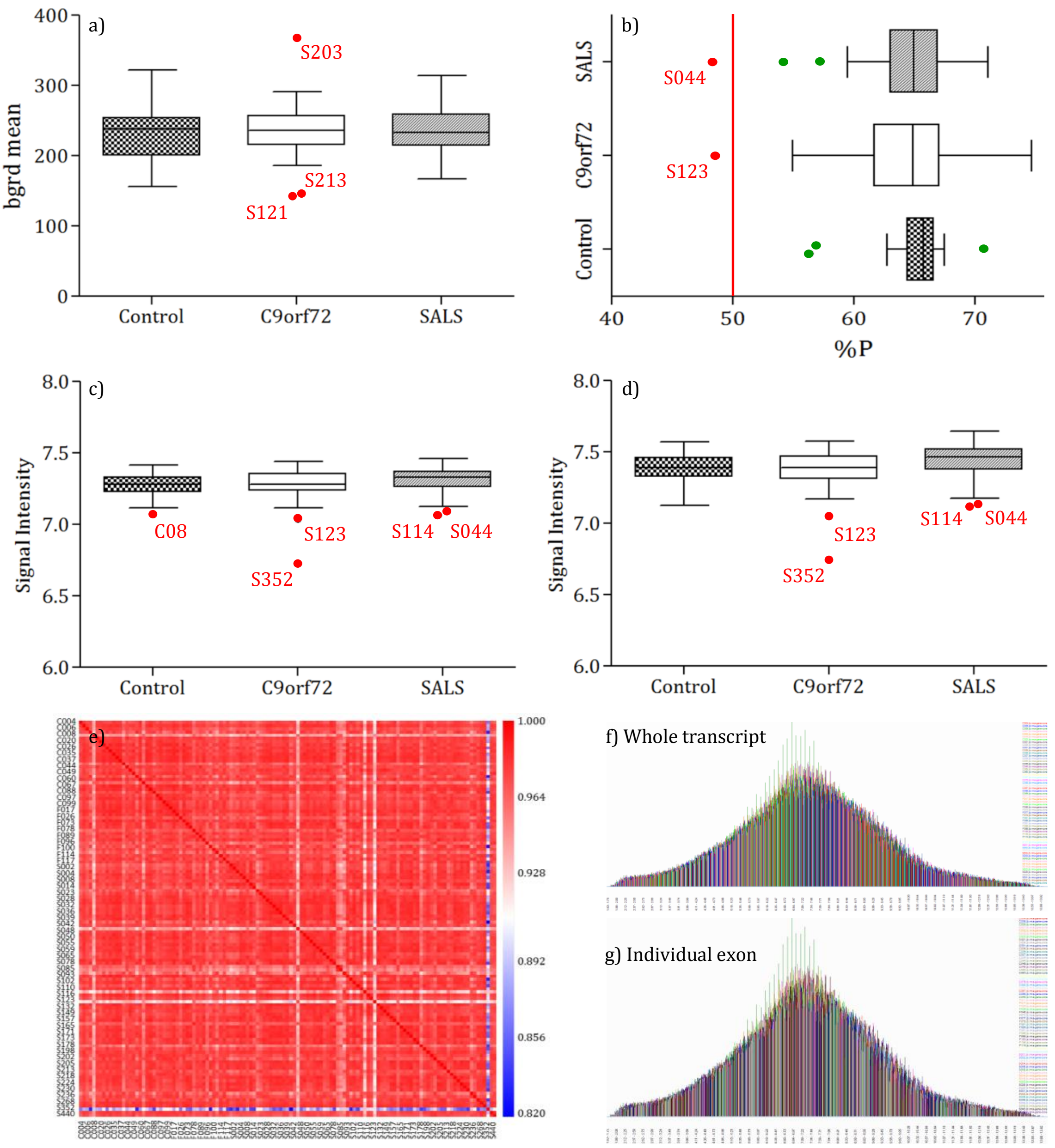


Figure 5.4 Expression Console™ Summary of Quality Control (QC) Metrics Assessed for LCL Samples in the *C9ORF72* and Non*C9ORF72*-Related_SALS Study. In the top four panels box and whisker plots were generated for the controls (checkerboard), *C9ORF72+* (unfilled) or non*C9ORF72*-related_SALS (filled) using GraphPad Prism® software version 5.04 and applying a Tukey multiple comparison test: a) average background (bgrd) signal, b) percentage presence (%P) calls, c) mean probeset signal intensities at transcript level and d) mean probeset signal intensities at individual exon level. Samples flagged as outliers are highlighted in red. Note that for %P statistically outlying cases with at least fifty percent of probesets called as present were still included in the downstream comparative analyses; these are represented in green. The coloured matrix in the bottom left hand panel e) represents the Pearson's product moment correlation coefficient (r) in which each pair-wise comparison is assigned a value on a scale of 0.820 (blue) to 1.000 (red) with a high score indicative of a strong linear relationship between the X and Y variables. Signal histogram plots are provided at f) transcript and g) individual exon level in the bottom right hand panel. Each series of coloured bars represents the distribution of log2 transformed, average GC-RMA normalised signal intensities for a single array in the experiment. Assessment of Affymetrix® QC metrics was performed in Expression Console™ software version 1.3.0.187.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, C - control, F - familial, LCL - lymphoblastoid cell line, RMA - Robust Multi-array Average and S - sporadic.

Affymetrix® CEL files (n=120/125) [*C9ORF72+* (n=38), SALS (n=56) and Ctrl (n=26)] were imported into Partek® Genomics Suite™ software version 6.6. Raw expression values were log2 transformed and a GC-RMA background normalisation procedure applied using core metaprobesets (n=287,329) (Section 2.3.2.5.2) that relate to over twenty-two thousand unique clusters pertaining to full length protein coding mRNA sequences in the RefSeq or GenBank® database. DE transcripts identified between ECACC *C9ORF72+* or non*C9ORF72*-related_SALS LCL cases and neurologically normal healthy controls were detected at the 5% significance level (unadjusted p<0.05) by performing a 2-way ANCOVA statistical test controlling for the effects of gender and age. Lists were filtered to remove unannotated transcripts (n=4,377/22,011) and a FC threshold of ≥ ±1.20 applied. In instances where there were multiple Affymetrix® transcript cluster ID's for a single gene the identification number producing the most significant outcome with the greatest level of coverage (i.e. highest number of probe-sets and/or exon clusters) was retained (Section 2.3.2.5.2). However, if the direction of change was opposing then both transcripts were removed.

*5.2.1.1.1 C9ORF72*vCtrl

An analysis of *C9ORF72+* FALS and SALS (n=40) patients in comparison to controls (n=26) identified 1,096 DE transcripts [Partek® unadjusted p<0.05, FC ≥ ±1.20] that included 650 genes (59.3%) which were significantly up-regulated (⇧) and a further 446 genes (40.7%) which were significantly down-regulated (⇩).

5.2.1.1.2 Non*C9ORF72*-Related_SALSvCtrl

A similar analysis of non-expansion carrying SALS (n=56) patients in comparison to identical controls identified 1,796 DE transcripts [Partek® unadjusted p<0.05, FC ≥ ±1.20] that included 1,148 genes (63.9%) which were significantly up-regulated (⇧) and a further 648 genes (36.1%) which were significantly down-regulated (⇩).

*5.2.1.1.3 C9ORF72*vCtrl and Non*C9ORF72*-Related_SALSvCtrl Comparison

A GeneVenn diagram of the two analyses described above in Sections 5.2.1.1.1 and 5. 2.1.1.2 highlighted 501 (45.7%) of 1,096 DE transcripts (Yellow) [294 genes ⇧ and

207 genes ⇩] as being specifically dysregulated in *C9ORF72+* FALS and SALS patients (i.e. absent from non*C9ORF72*-related_SALS patients and controls) and an additional 1,201 (66.9%) of 1,796 DE transcripts (Green) [792 genes ⇧ and 409 genes ⇩] which were specifically dysregulated in non*C9ORF72*-related_SALS patients. The remaining 54.3% (n=595/1,096) or 33.1% (n=595/1,796) of DE transcripts [356 genes ⇧ and 239 genes ⇩] represented by the intersection of the GeneVenn diagram depicted in Figure 5.5 [Partek® unadjusted p<0.05, FC ≥ ±1.20] are shared in common between the *C9ORF72*vctrl and non*C9ORF72*-related_SALSvctrl analyses. It is likely, therefore that these reflect disease relevant changes associated with the broader ALS phenotype rather than being specific to individual genetic subtypes [APPENDIX TABLE B8, B9 and B10].

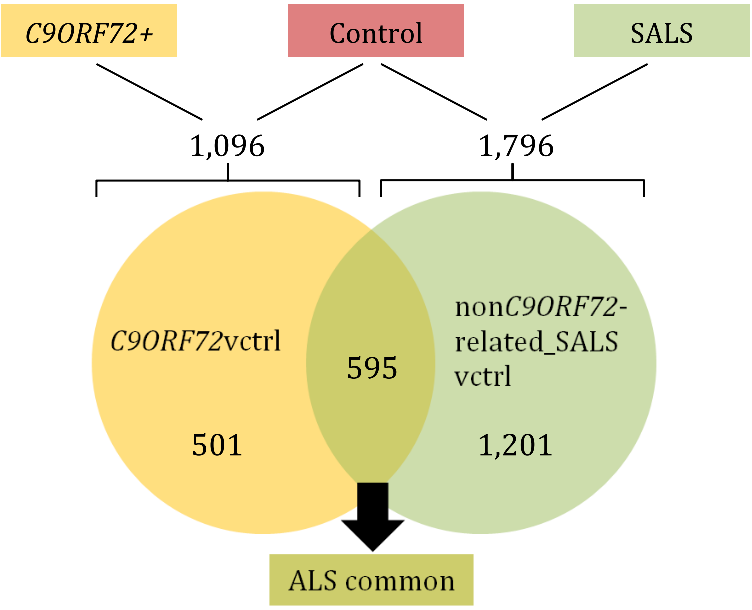


Figure 5.5 GeneVenn *C9ORF72*vCtrl and Non*C9ORF72*-Related_SALSvctrl [Partek® unadjusted p<0.05, FC≥ ±1.20] Lists of DE transcripts generated in Partek® Genomics Suite™ software version 6.6 copyright © 2013 (Partek® Inc., St Louis, MO, USA). The GeneVenn application was freely available online at genevenn.sourceforge.net (Pirooznia et al 2007) (University of Southern Mississippi, USA).

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control, DE - differentially expressed, FC - fold-change and S - sporadic.

5.2.1.2 DAVID Functional Enrichment Analysis

Partek® generated lists of Affymetrix® transcript cluster ID's [Partek® unadjusted p<0.05, FC ≥ ±1.20] were imported into DAVID bioinformatics resource version 6.7. Functional annotation clustering analysis was performed on GOTERM_BP_FAT and GOTERM_MF_FAT gene ontology (GO) terms applying a *Homo sapiens* background and filtering using 'Medium' classification stringency (Section 2.3.2.5.4). Categories with an EASE score above 1.30 and Benjamini-Hochberg FDR corrected p<0.05 were considered as statistically significant. Transcripts identified as being significantly up (⇧) or down (⇩)-regulated under different experimental conditions were analysed independently. The software mapped 1,088 (99.3%) of 1,096 [644 genes ⇧ and 444 genes ⇩] and 1,778 (99.0%) of 1,796 [1,137 genes ⇧ and 641 genes ⇩] DE transcripts identified in the analysis of *C9ORF72*vctrl (Section 5.2.1.1.1) or non*C9ORF72*-related _SALSvctrl (Section 5.2.1.1.2), respectively. DAVID ID's could not be returned for the remaining 26 transcript clusters which were subsequently removed.

*5.2.1.2.1 C9ORF72*vCtrl

In *C9ORF72+* patient derived LCL's the single most significant biologically enriched GO term associated with the G_4C_2 hexanucleotide repeat expansion from the Partek® generated list of up-regulated gene expression changes (n=644/650) was related to RNA processing [Partek® unadjusted p<0.05, FC ≥ ±1.20]. RNP complex biogenesis and endoribonuclease activity, producing 5'-phosphomonoesters were also ranked highly. Other categories included translation and translation factor activity, nucleic acid binding, in addition to, several processes involved in DNA metabolism, the cell cycle and respiratory electron transport chain (Table 5.3a). From the list of down-regulated gene expression changes (n=444/446) ion binding and transport were among those most significantly featured along with cell adhesion, lipid biosynthesis and sterol metabolism [Partek® unadjusted p<0.05, FC ≥ ±1.20]. Other categories included the regulation of cell migration, glycoprotein binding & metabolism as well as ATPase activity, coupled to the transmembrane movement of substances (Table 5.3b).

5.2.1.2.2 Non*C9ORF72*-Related_SALSvCtrl

Conversely, some of the most significant biologically enriched GO terms associated with non-expansion carrying SALS derived LCL's from the Partek® generated list of

a) *C9ORF72*vctrl ⇧$_{\text{reg}}$ [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

#	GO term	Functional category	EASE	Count	Benjamini
1	GO:0006396	RNA processing	8.62	55	1.30E-08
2	GO:0006412	translation	7.52	41	9.30E-09
3	GO:0006259	DNA metabolic process	5.45	43	6.20E-05
4	GO:0022613	ribonucleoprotein complex biogenesis	3.92	23	8.90E-05
5	GO:0016891	endoribonuclease activity, producing 5’-phosphomonoesters	3.24	8	5.40E-03
6	GO:0007049	cell cycle	3.18	61	2.60E-06
7	GO:0044265	cellular macromolecule catabolism	3.10	50	1.50E-03
8	GO:0043933	macromolecular complex organisation	2.74	50	1.00E-03
9	GO:0022904	respiratory electron transport chain	2.72	11	6.40E-03
10	GO:0008135	translation factor activity, nucleic acid binding	2.61	13	0.020
11	GO:0051340	regulation of ligase activity	2.61	13	3.10E-03
12	GO:0051656	establishment of organelle localisation	2.19	10	0.034
13	GO:0000166	nucleotide binding	1.46	105	0.036

b) *C9ORF72*vctrl ⇩$_{\text{reg}}$ [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

#	GO term	Functional category	EASE	Count	Benjamini
1	GO:0006811	ion transport	5.83	48	6.60E-06
2	GO:0007155	cell adhesion	4.56	39	8.20E-04
3	GO:0016125	sterol metabolic process	3.89	14	3.40E-04
4	GO:0043167	ion binding	3.68	137	5.40E-04
5	GO:0008610	lipid biosynthetic process	3.29	33	3.90E-08
6	GO:0031418	L-ascorbic acid binding	3.11	7	5.30E-04
7	GO:0030334	regulation of cell migration	3.10	14	0.028
8	GO:0042626	ATPase activity, coupled to transmembrane movement of substances	3.05	14	5.20E-04
9	GO:0016717	oxidoreductase activity, acting on paired donors, with oxidation of a pair of donors resulting in the reduction of molecular oxygen to two molecules of water	2.86	5	4.70E-04
10	GO:0009100	glycoprotein metabolic process	2.70	19	6.00E-04
11	GO:0015295	solute:hydrogen symporter activity	2.48	6	9.60E-03
12	GO:0001666	response to hypoxia	2.42	12	0.039
13	GO:0015294	solute:cation symporter activity	2.30	12	8.10E-04
14	GO:0000041	transition metal ion transport	2.24	10	6.80E-03
15	GO:0001948	glycoprotein binding	1.94	6	0.043
16	GO:0030246	carbohydrate binding	1.41	20	0.023

Table 5.3 DAVID Partek® *C9ORF72*vCtrl Functional Annotation Clustering Analysis

Abbreviations: # - rank, ⇧$_{\text{reg}}$ - up-regulated, ⇩$_{\text{reg}}$ - down-regulated, *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control, EASE - enrichment score, FC - fold-change, DAVID - Database for Annotation, Visualisation and Integrated Discovery and GO - gene ontology.

up-regulated gene expression changes (n=1,137/1,148) were relating to aspects of the cell cycle including cell cycle checkpoint control, chromosome localisation, DNA packaging, spindle organisation, regulation of the cell cycle, mitotic sister chromatid segregation and interphase of the mitotic cell cycle [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]. Those involved in DNA replication/recombination or damage response &

repair pathways also featured prominently. Other categories included several which are important for RNA processing and RNP biogenesis as well as DNA metabolism & protein degradation (Table 5.4a). From the list of down-regulated gene expression changes (n=641/648) ion transport & homeostasis [Partek® unadjusted $p<0.05$, FC ≥ ±1.20] were among those most significantly enriched along with regulation of cell migration, carbohydrate binding, phospholipid biosynthesis and signal transduction (Table 5.4b). Other categories included solute: hydrogen symporter activity, positive regulation of transferase activity and response to wounding.

*5.2.1.2.3 C9ORF72*vctrl and *NonC9ORF72*-Related_SALSvctrl Comparison

The results of a direct comparison between DAVID *C9ORF72*vctrl (Section 5.2.1.2.1) and non*C9ORF72*-related_SALSvctrl (Section 5.2.1.2.2) analyses could be displayed in the form of a stacked column graph that is represented in Figure 5.6. Biologically significant GO terms which were found to be specific to the *C9ORF72+* FALS and SALS patient derived LCL's were highlighted in yellow. In descending order of enrichment these included: translation as well as translation factor activity, nucleic acid binding relating to protein synthesis; endoribonuclease activity, producing 5'-phosphomono -esters and the respiratory electron transport chain (Figure 5.6a) from the list of up-regulated gene expression changes, in addition to, cell adhesion, sterol metabolism, ion binding, lipid biosynthesis and ATPase activity, coupled to the transmembrane movement of substances (Figure 5.6b) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20] from the list of down-regulated gene expression changes. In contrast, GO terms specific to non-expansion carrying SALS patient derived LCL's were highlighted in green. These included multiple categories involved in regulating the cell cycle, as well as, protein degradation, DNA replication/recombination and mechanisms relating to the DNA damage response & repair pathways (Figure 5.6a) from the list of up-regulated gene expression changes, in addition to, signal transduction, phospholipid metabolism and homeostasis (Figure 5.6b) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20] from the list of down-regulated gene expression changes. Shared categories (ALS common) which were significantly up-regulated included RNP complex biogenesis, RNA processing and DNA metabolism (Figure 5.6a) whereas those reported to be significantly down-regulated included regulation of cell migration and ion transport (Figure 5.6b).

a) non*C9ORF72*-related_SALSvctrl ⇧$_{\text{reg}}$ [Partek® unadjusted $p<0.05$, FC ±1.20]

#	GO term	Functional category	EASE	Count	Benjamini
1	GO:0007049	cell cycle	34.27	169	2.10E-44
2	GO:0006259	DNA metabolic process	23.00	110	5.00E-28
3	GO:0022613	ribonucleoprotein complex biogenesis	7.98	42	1.10E-10
4	GO:0051276	chromosome organisation	7.81	89	3.30E-17
5	GO:0000070	mitotic sister chromatid segregation	7.68	18	1.80E-09
6	GO:0051329	interphase of mitotic cell cycle	7.33	27	1.10E-07
7	GO:0051726	regulation of cell cycle	7.21	57	2.70E-09
8	GO:0006323	DNA packaging	7.09	32	9.90E-10
9	GO:0000166	nucleotide binding	6.82	200	3.00E-06
10	GO:0043933	macromolecular complex organisation	6.53	91	3.30E-08
11	GO:0006310	DNA recombination	6.52	25	3.10E-06
12	GO:0006302	double-strand break repair	6.25	22	1.30E-08
13	GO:0006396	RNA processing	6.23	77	1.30E-08
14	GO:0007051	spindle organisation	5.50	17	7.20E-07
15	GO:0000072	cell cycle checkpoint	4.49	27	6.50E-09
16	GO:0031396	regulation of protein ubiquitination	4.31	23	2.00E-05
17	GO:0009314	response to radiation	3.47	31	5.10E-04
18	GO:0006297	nucleotide-excision repair, DNA gap filling	3.37	9	2.00E-04
19	GO:0050000	chromosome localization	2.85	7	6.40E-03
20	GO:0051186	cofactor metabolic process	2.82	29	1.90E-03
21	GO:0044265	cellular macromolecular catabolism	2.53	71	0.012
22	GO:0051052	regulation of DNA metabolic process	2.43	19	0.010
23	GO:0009451	RNA modification	2.37	11	0.020
24	GO:0010605	negative regulation of macromolecule metabolic process	2.25	80	1.90E-04
25	GO:0003677	DNA binding	2.16	200	3.10E-05
26	GO:0051259	protein oligomerization	2.07	23	0.042
27	GO:0032259	methylation	1.61	15	9.10E-03
28	GO:0006282	regulation of DNA repair	1.31	7	0.047

b) non*C9ORF72*-related_SALSvctrl ⇩$_{\text{reg}}$ [Partek® unadjusted $p<0.05$, FC ±1.20]

#	GO term	Functional category	EASE	Count	Benjamini
1	GO:0006811	ion transport	4.73	52	3.80E-03
2	GO:0015295	solute:hydrogen symporter activity	3.75	10	2.70E-05
3	GO:0042592	homeostatic process	3.57	51	1.50E-03
4	GO:0030334	regulation of cell migration	3.33	18	4.90E-03
5	GO:0009967	positive regulation of signal transduction	2.66	28	2.20E-03
6	GO:0008654	phospholipid biosynthetic process	2.51	15	1.60E-03
7	GO:0000041	transition metal ion transport	2.46	13	1.10E-03
8	GO:0006826	iron ion transport	2.45	8	4.00E-03
9	GO:0006643	membrane lipid metabolic process	2.32	12	6.00E-03
10	GO:0009611	response to wounding	2.25	33	0.043
11	GO:0051347	positive regulation of transferase activity	1.99	22	5.10E-03
12	GO:0030246	carbohydrate binding	1.99	27	0.010
13	GO:0031418	L-ascorbic acid binding	1.68	6	0.042
14	GO:0050850	positive regulation of calcium-mediated signalling	1.52	6	0.013

Table 5.4 DAVID Partek® Non*C9ORF72*-Related_SALSvCtrl Functional Annotation Clustering Analysis

Abbreviations: # - rank, ⇧$_{\text{reg}}$ - up-regulated, ⇩$_{\text{reg}}$ - down-regulated, *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control, ALS - Amyotrophic Lateral Sclerosis, EASE - enrichment score, GO - gene ontology, DAVID - Database for Annotation, Visualisation and Integrated Discovery, FC - fold-change and S - sporadic.

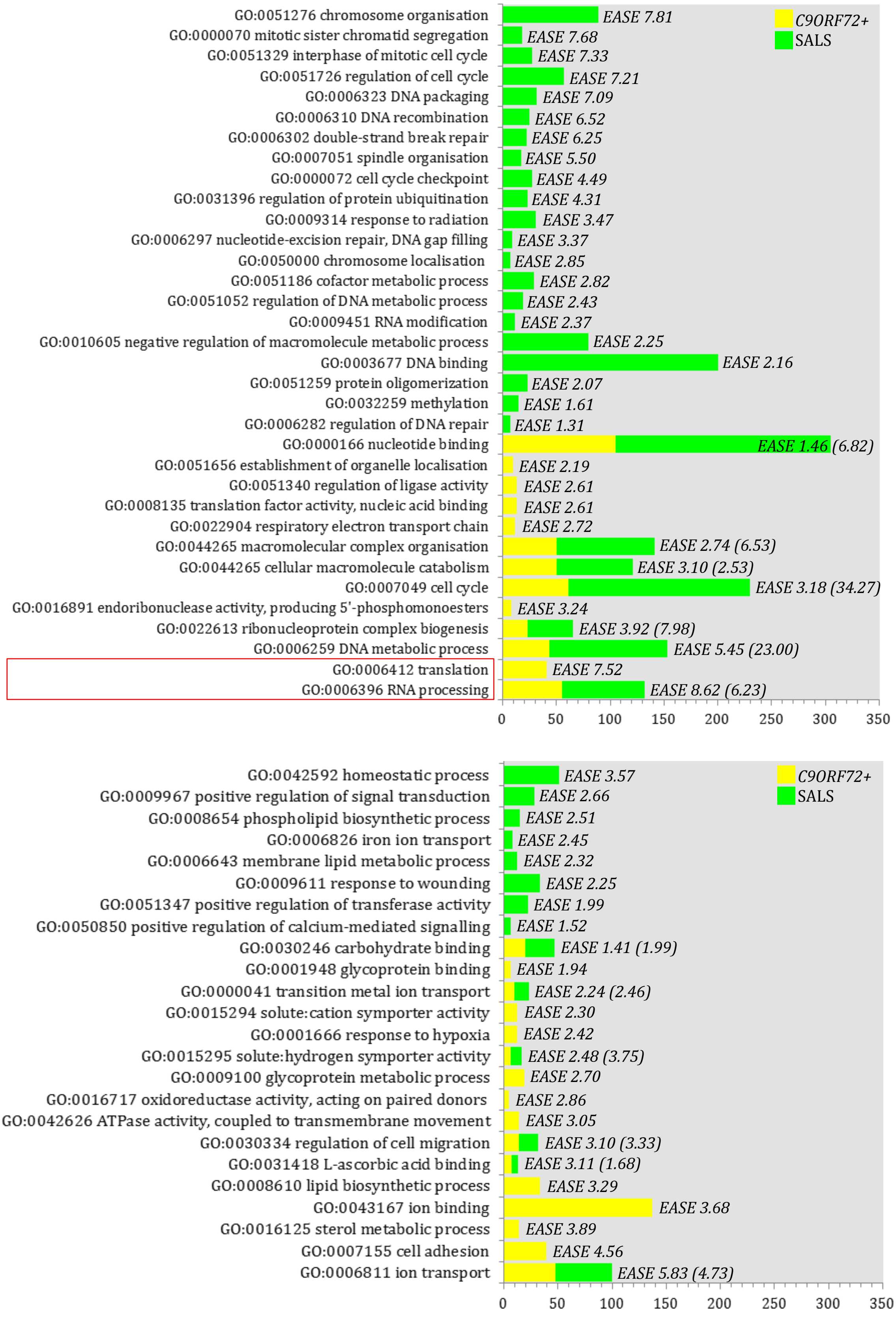


Figure 5.6 DAVID Comparison GO Terms *C9ORF72*vCtrl and Non*C9ORF72*-Related_SALSvCtrl

Abbreviations: ⇧$_{reg}$ - up-regulated, ⇩$_{reg}$ - down-regulated, ALS - Amyotrophic Lateral Sclerosis, ctrl - control, *C9ORF72* - chromosome 9 open reading frame 72, GO - gene ontology, DAVID - Database for Annotation, Visualisation and Integrated Discovery, EASE - enrichment score and S - sporadic.

In order to elucidate further the molecular signatures underpinning mechanisms of neurotoxicity associated with the hexanucleotide G_4C_2 repeat expansion in *C9ORF72* the top two most highly enriched GO terms [GO: 0006396 RNA processing (Section 5.2.1.3) and GO: 0006412 translation (Section 5.2.1.4) (Table 5.3)] were selected for a more in depth comparative analysis and the subsequent identification of potential candidate genes that could be taken forward for qRT-PCR validation.

5.2.1.3 RNA Processing

Over the past few years aberrant RNA metabolism has emerged as one of the major players in the pathogenesis of a number of neurodegenerative diseases that include ALS and FTLD (Section 1.2.4.9) (Baumer et al 2010, Droppelmann et al 2014, Lee et al 2013b, Ling et al 2013, Polymenidou et al 2012, van Blitterswijk & Landers 2010). It encompasses a diverse array of biological processes, from the regulation of RNA transcription (Section 5.2.1.3.1) and small nuclear RNP (snRNP) biogenesis (Figure 5.7) (Section 5.2.1.3.2) to pre-mRNA splicing & editing (Section 5.2.1.3.3) in addition to stabilization, transportation and post-translational degradation of mature mRNA species (Al-Chalabi et al 2013). Table 5.5 lists the DAVID output of RNA processing related genes identified in the *C9ORF72*vctrl analysis [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]. DE transcripts specific to the G_4C_2 repeat expansion are denoted by the three asterisks inserted immediately after the gene symbol in the first column. Key validation targets selected for qRT-PCR are shaded in grey.

5.2.1.3.1 Regulation of RNA Transcription

A GeneVenn diagram comparing DAVID outputs of RNA processing related genes for the Partek® generated lists of up-regulated gene expression changes in the analysis of *C9ORF72*vctrl (n=56/644) (Section 5.2.1.2.1) and non*C9ORF72*-related_SALSvctrl (n=77/1,137) (Section 5.2.1.2.2) identified DNA-directed RNA polymerase activity as a GO term which was specific to LCL cases carrying the G_4C_2 repeat (Figure 5.8). The category contained three transcripts encoding the 4th, 6th and 7th subunit of the large 550kDa complex that constitutes RNA polymerase II (Pol II). Collectively, they comprise components of the Rpb4/7 sub-complex; a heterodimeric association of

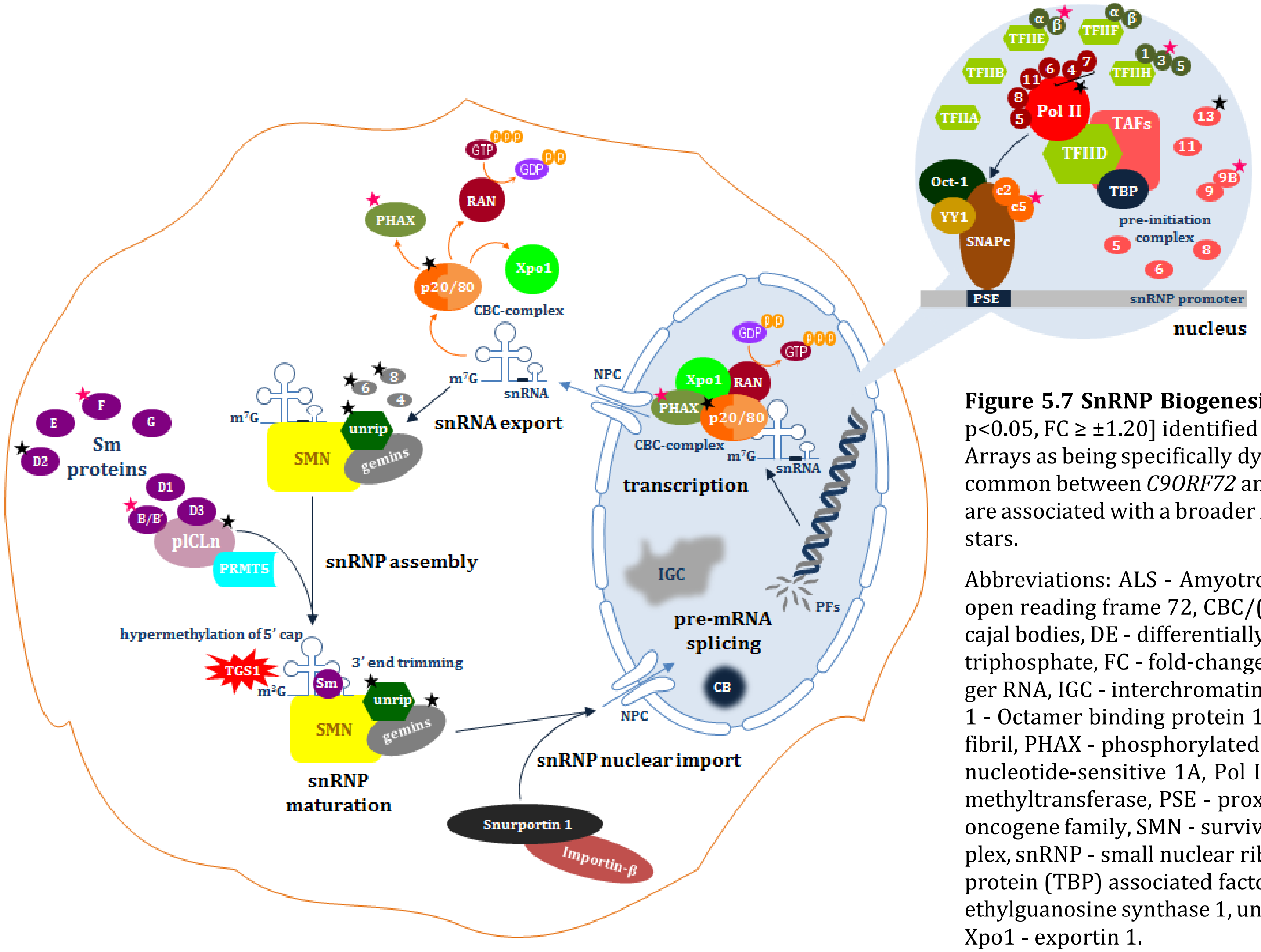


Figure 5.7 SnRNP Biogenesis Schematic DE transcripts [Partek® unadjusted $p<0.05$, FC ≥ ±1.20] identified on the Affymetrix® Human Exon 1.0ST GeneChip® Arrays as being specifically dysregulated in relation to *C9ORF72* (★) or shared in common between *C9ORF72* and non*C9ORF72*-related_SALS (★) (i.e. changes that are associated with a broader ALS phenotype) are denoted by different coloured stars.

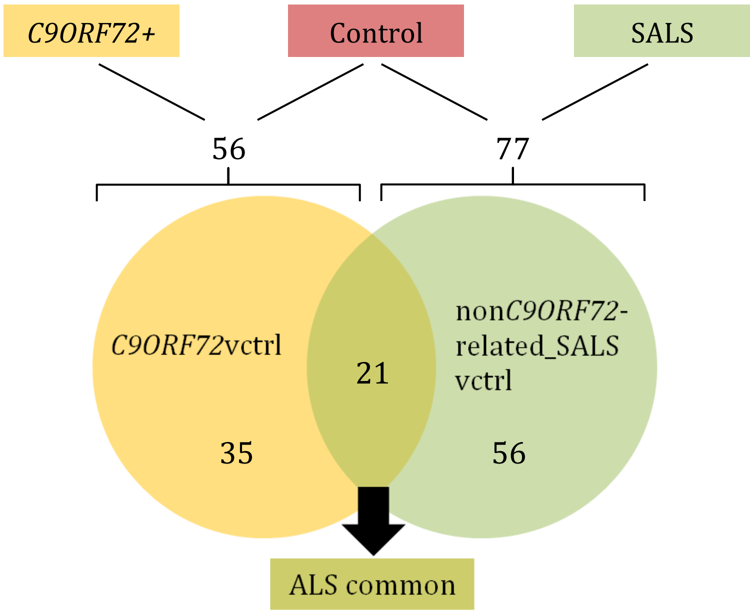
Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, CBC/(CBP) - nuclear cap binding complex/protein, CB - cajal bodies, DE - differentially expressed, GDP/(GTP) - guanosine diphosphate/triphosphate, FC - fold-change, m7G - seven methyl guanosine, mRNA - messenger RNA, IGC - interchromatin granule cluster, NPC - nuclear pore complex, Oct-1 - Octamer binding protein 1, p20/80 - CBP20/80 subunit, PF - perichromatin fibril, PHAX - phosphorylated adaptor for RNA export, plCLn - chloride channel nucleotide-sensitive 1A, Pol II - RNA polymerase II, PRMT5 - protein arginine methyltransferase, PSE - proximal sequence element, RAN - RAN, member RAS oncogene family, SMN - survival motor neurone, SNAPc - snRNA activating complex, snRNP - small nuclear ribonucleoprotein, S - sporadic, TAF - TATA-binding protein (TBP) associated factor, TF - transcription initiation factor, TGS1 - trimethylguanosine synthase 1, unrip - Unr-interacting protein, YY1 - Yin Yang-1 and Xpo1 - exportin 1.

Symbol	RefSeq	Transcript	Gene		Fold	p-value
*ARFGAP3****	NM_014570	3962587	ADP-ribosylation factor GTPase activating protein 3	⇧	1.24	1.28E-03
*ARL6IP4****	NM_001002252	3435681	ADP-ribosylation-like factor 6 interacting protein 4	⇧	1.26	8.01E-05
CD2BP2	NM_006110	3687698	CD2 (cytoplasmic tail) binding protein 2	⇧	1.21	0.015
CDKN2A	NM_001195132	3201437	cyclin-dependent kinase inhibitor 2A (melanoma, p16, inhibits CDK4)	⇧	1.24	5.29E-03
*CLNS1A****	NM_001293	3382948	chloride channel, nucleotide-sensitive, 1°	⇧	1.20	7.29E-03
*ELAC1****	NM_018696	3788270	elaC homolog 1 (E. coli)	⇧	1.24	1.30E-03
*EXOSC4****	NM_019037	3120008	exosome component 4	⇧	1.27	2.04E-04
FTSJ2	NM_013393	3035682	FtsJ homolog 2 (E. coli)	⇧	1.30	1.86E-04
FUS	NM_004960	3656904	fused in sarcoma	⇧	1.23	7.50E-04
*GAR1****	NM_018983	2739242	GAR1 ribonucleoprotein homolog (yeast)	⇧	1.31	6.95E-05
*GEMIN6****	NM_024775	2477980	gem (nuclear organelle) associated protein 6	⇧	1.29	1.16E-04
*GEMIN8P4****	NR_002830	2422227	gem (nuclear organelle) associated protein 8 pseudogene 4	⇧	1.25	0.014
HNRNPA0	NM_006805	2877141	heterogeneous nuclear ribonucleoprotein A0	⇧	1.23	2.35E-07
*HNRNPF****	NM_004966	3286286	heterogeneous nuclear ribonucleoprotein F	⇧	1.22	6.15E-04
HNRNPH2	NM_019597	3984779	heterogeneous nuclear ribonucleoprotein H2 (H’)	⇧	1.28	0.024
HNRNPM	NM_005968	3819543	heterogeneous nuclear ribonucleoprotein M	⇧	1.21	8.06E-03
*LAP7****	NM_016648	2740005	La ribonucleoprotein domain family, member 7	⇧	1.20	0.022
LSM4	NM_012321	3854892	LSM4 homolog, U6 small nuclear RNA associated (S. cerevisiae)	⇧	1.24	7.86E-03
*NCBP2****	NM_007362	2713074	nuclear cap binding protein subunit 2, 20kDa	⇧	1.20	0.010
NOP10	NM_018648	3617403	NOP10 ribonucleoprotein homolog (yeast)	⇧	1.32	0.013
*NUDT21****	NM_007006	3692895	nudix (nucleoside diphosphate linked moiety X)-type motif 21	⇧	1.20	6.68E-05
PHAX	NM_032177	2827156	phosphorylated adaptor for RNA export	⇧	1.27	1.79E-04
*PHF5A****	NM_0327528	3961955	PHD finger protein 5A	⇧	1.21	0.020
*POLR2D****	NM_004805	2575134	polymerase (RNA) II (DNA directed) polypeptide D	⇧	1.22	0.010
*POLR2F****	NM_021974	3945133	polymerase (RNA) II (DNA directed) polypeptide F	⇧	1.22	0.020
*POLR2G****	NM_002696	3333622	polymerase (RNA) II (DNA directed) polypeptide G	⇧	1.24	3.80E-04
*POP4****	NM_006627	3828032	processing of precursor 4, ribonuclease P/MRP subunit (S. cerevisiae)	⇧	1.20	0.022
POP7	NM_005837	3015769	processing of precursor 7, ribonuclease P/MRP subunit (S. cerevisiae)	⇧	1.23	9.28E-03
*PPIL1****	NM_016059	2952065	peptidylprolyl isomerase (cyclophilin)-like 1	⇧	1.22	0.017
*PRPF19****	NM_014502	3375049	PRP19/PSO4 pre-mRNA processing factor 19 homolog (S. cerevisiae)	⇧	1.21	2.24E-04
PRPF4	NM_004697	3185558	PRP4 pre-mRNA processing factor 4 homolog (yeast)	⇧	1.24	7.62E-05
*RBM3****	NM_017495	3976519	RNA binding motif (RNP1, RRM) protein 3	⇧	1.22	9.22E-05
*RPL11****	NM_170739	2325192	ribosomal protein L11	⇧	1.25	0.035
*RPP14****	NM_001098783	2626141	ribonuclease P/MRP 14kDa subunit	⇧	1.37	1.18E-03

*RPP21****	NM_024839	2901552	ribonuclease P/MRP 21kDa subunit	⇧	1.23	5.12E-03
*RPP38****	NM_183005	3236538	ribonuclease P/MRP 38kDa subunit	⇧	1.34	0.011
*RRAGC****	NM_022157	2407729	Ras-related GTP binding C	⇧	1.25	6.98E-04
*SF3B14****	NM_016047	2544179	splicing factor 3B, 14kDa subunit	⇧	1.21	1.84E-03
*SF3B4****	NM_005850	2434159	splicing factor 3B, subunit 4, 49kDa	⇧	1.20	0.019
SNRNP40	NM_004814	2404377	small nuclear ribonucleoprotein 40kDa (U5)	⇧	1.30	0.027
SNRPB2	NM_003092	3877776	small nuclear ribonucleoprotein polypeptide B	⇧	1.24	0.040
*SNRPD2****	NM_177542	3865568	small nuclear ribonucleoprotein D2 polypeptide 16.5kDa	⇧	1.23	0.012
SNRPF	NM_003095	3427014	small nuclear ribonucleoprotein polypeptide F	⇧	1.27	7.15E-03
SRSF3	NR_036610	2905118	serine/arginine-rich splicing factor 3	⇧	1.20	0.015
*SSU72****	NM_014188	2391647	SSU72 RNA polymerase II CTD phosphatase homolog (S. cerevisiae)	⇧	1.25	0.034
*STRAP****	NM_007178	3406421	serine/threonine kinase receptor associated protein	⇧	1.20	1.27E-03
*TAF13****	NM_005645	4054117	TAF13 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 18kDa	⇧	1.37	3.39E-04
TRMT6	NM_015939	3896524	tRNA methyltransferase 6 homolog (S. cerevisiae)	⇧	1.27	1.11E-05
TRUB2	NM_015679	3226493	TruB pseudouridine (psi) synthase homolog 2 (E. coli)	⇧	1.21	2.04E-03
TSEN15	NR_023349	2371474	tRNA splicing endonuclease 15 homolog (S. cerevisiae)	⇧	1.28	6.40E-03
*TYW3****	NR_027962	2342391	tRNA-yW synthesizing protein 3 homolog (S. cerevisiae)	⇧	1.24	9.91E-03
UTP15	NM_032175	2815455	UTP15, U3 small nucleolar ribonucleoprotein, homolog (S. cerevisiae)	⇧	1.28	5.25E-04
UTP23	NM_032334	3112543	UTP23, small subunit (SSU) processome component, homolog (yeast)	⇧	1.25	1.38E-03
*WBP4****	NM_007187	3486807	WW domain binding protein 4 (formin binding protein 21)	⇧	1.20	2.28E-03
*ZCRB1****	NM_033114	3451318	zinc finger CCHC-type and RNA binding motif 1	⇧	1.26	7.15E-05
*ZMAT5****	NM_019103	3956984	zinc finger, matrin-type 5	⇧	1.26	2.98E-04

Table 5.5 DAVID *C9ORF72*vCtrl List of RNA Processing Related Genes (n=56) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

Abbreviations: *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control, DAVID - Database for Annotation, Visualisation and Integrated Discovery and FC - fold-change.



a) *C9ORF72+* specific

#	GO term	Functional category	EASE	Count	Benjamini
1	GO:0008380	RNA splicing	15.42	21	5.40E-24
2	GO:0034470	ncRNA processing	6.24	10	1.10E-08
3	GO:0022613	ribonucleoprotein complex biogenesis	4.34	10	9.00E-09
4	GO:0003899	DNA-directed RNA polymerase activity	1.32	3	0.022

b) ALS common

#	GO term	Functional category	EASE	Count	Benjamini
1	GO:0006397	mRNA processing	11.65	13	2.70E-13
2	GO:0034470	ncRNA processing	6.74	9	4.10E-09

c) non*C9ORF72*-related_SALS specific

#	GO term	Functional category	EASE	Count	Benjamini
1	GO:0022613	ribonucleoprotein complex biogenesis	27.44	29	1.40E-36
2	GO:0006397	mRNA processing	16.44	27	2.30E-26
3	GO:0008033	tRNA processing	5.57	8	4.00E-07
4	GO:0009451	RNA modification	4.00	7	6.40E-07
5	GO:0010608	posttranscriptional regulation of gene expression	2.53	8	2.90E-04
6	GO:0004540	ribonuclease activity	2.49	4	0.033

Figure 5.8 GeneVenn of DAVID *C9ORF72*vCtrl and Non*C9ORF72*-Related_SALSvCtrl RNA Processing Related Genes Lists of DE transcripts generated using Partek® Genomics Suite™ software version 6.6 copyright © 2013 (Partek® Inc., St Louis, MO, USA). GeneVenn application freely available online at genevenn.sourceforge.net (University of Southern Mississippi, USA) (Pirooznia et al 2007). Functional annotation clustering analysis of up (⇧)/down (⇩) regulated Affymetrix® transcript cluster ID's was performed independently using DAVID bioinformatics resource version 6.7 (david.abccc.ncifcrf.gov) (Huang da et al 2009a, Huang da et al 2009b).

Abbreviations: # - rank, ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control, DAVID - Database for Annotation, Visualisation and Integrated Discovery, DE - differentially expressed, EASE - enrichment score, GO - gene ontology, mRNA - messenger RNA, ncRNA - non-coding RNA, S - sporadic and tRNA - transfer RNA.

POLR2D (subunit 4) [*POLR2D* (polymerase (RNA) II (DNA directed) polypeptide D) ⇧1.22-fold, p=0.01], with POLR2G (subunit 7) [*POLR2G* (polymerase (RNA) II (DNA directed) polypeptide G) ⇧1.24-fold, p<0.001] and POLR2F (subunit 6) (Figure 5.8) [*POLR2F* (polymerase (RNA) II (DNA directed) polypeptide F ⇧1.22-fold, p<0.05]. An IDT PrimeTime® Mini qPCR assay, conducted using a larger validation cohort of pooled RNA samples from the microarray plus additional *C9ORF72+* case (n=75) and control (n=35) LCL's from the ECACC discovery and replication cohorts (Section 2.3. 2.6.3), confirmed a disease related increase in the expression of *POLR2G* (subunit 7) (p<0.05*) (Figure 5.9).

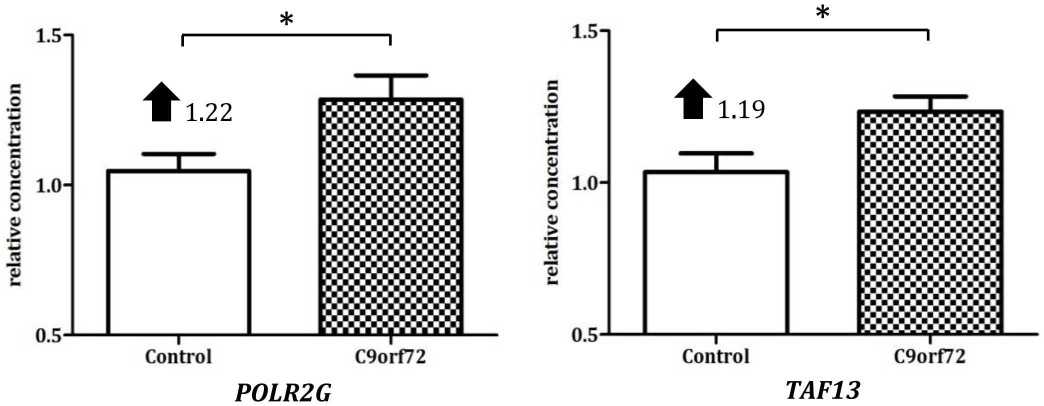


Figure 5.9 Regulation of RNA Transcription qRT-PCR Validation Relative concentrations measured against the standard housekeeping gene *18SrRNA*. Means and SEM were plotted in GraphPad® Prism software version 5.04. Probability values calculated in Microsoft Excel 2010 (Microsoft Corporation UK) using a one tailed student's t-test. Gene expression changes were confirmed if the direction of change (arrow) was the same as the microarray with p<0.05*

Abbreviations: *18SrRNA* - 18S ribosomal RNA, *C9ORF72* - chromosome 9 open reading frame 72, *POLR2G* - polymerase (RNA) II (DNA directed) polypeptide G, qRT-PCR - quantitative real-time PCR, SEM - standard error of the mean and TAF13 - RNA polymerase II, TATA box binding protein (TBP)-associated protein, 18kDa.

RNA polymerase II is found in all eukaryotic cells. It functions as an enzyme which is essential for the synthesis of mRNA precursors during transcription and to a lesser extent the synthesis of spliceosomal small nuclear RNA's (snRNA's) (Egloff & Murphy 2008) including: U1, U2, U4 (U4atac) and U5 [*SNRNP40* (small nuclear ribonucleoprotein, 40kDa (U5)) ⇧1.30-fold, p<0.05 *C9ORF72*vctrl and ⇧1.50-fold, p<0.001 non-*C9ORF72*-related_SALSvctrl], which are all components of the major spliceosome, in addition to, the U7 and U11/12 [*SNRNP25* (small nuclear ribonucleoprotein, 25kDa (U11/12)) ⇧1.32-fold, p<0.0001 non*C9ORF72*-related_SALSvctrl] components of the minor spliceosome. SnRNA's produce transcripts which are intronless and typically shorter (~150nt), than those derived from protein-coding mRNA's, and rather than being under the direction of a poly(A) signal their 3'-end formation is controlled by a unique *cis*-acting 3' box element (Cuello et al 1999, Zaborowska et al 2012).

The five subunit snRNA activating complex (SNAPc) [*SNAPC5* (small nuclear RNA activating complex, polypeptide 5, 19kDa) ⇧1.27-fold, p<0.05 *C9ORF72*vctrl; ⇧1.44-fold, p<0.0001 non*C9ORF72*-related_SALSvctrl] is triggered by the Yin Yang-1 (YY1) transcription factor and Octamer-binding protein 1 (Oct-1) in order to initiate Pol II mediated transcription (Emran et al 2006). SNAPc recognises the proximal sequence element (PSE) contained within the upstream promoter region which promotes the subsequent assembly of the pre-initiation complex (PIC) at this site (Figure 5.8). The PIC comprises Pol II and a set of general transcription factors (GTF's) (Hanzlowsky et al 2006, Kim et al 2010) which include TFIIA/B (GTF2A1-2/B), TFIID (GTF2D), TFIIEαβ (GTF2E1-2) [*GTF2E2* (general transcription factor IIE, polypeptide 2, beta 34kDa) ⇧1.23-fold, p<0.01 *C9ORF72*vctrl], TFIIFαβ (GTF2F1-2) and TFIIH (GTF2H3) [*GTF2H3* (general transcription factor IIH, polypeptide 3, 34kDa) ⇧1.20-fold, p<0.01 *C9ORF72*vctrl]. TFIID (GTF2D) is itself a multiprotein complex containing the TATA-binding protein (TBP) and various TBP associated factors (TAF's), including TAF9B (TFIID subunit 9-like) [*TAF9B* (TAF9B RNA polymerase II, TBP associated factor, 31 kDa) ⇧1.34-fold, p<0.05 *C9ORF72*vctrl and ⇧1.42-fold, p<0.01 non*C9ORF72*-related_ SALSvctrl (Zaborowska et al 2012)], TAF12 (TFIID subunit 12) [*TAF12* (TAF12 RNA polymerase II, TBP associated factor, 20kDa) ⇧1.30-fold, p<0.001 *C9ORF72*vctrl and ⇧1.27-fold, p<0.001 non*C9ORF72*-related_SALSvctrl] and TAF13 (TFIID subunit 13) [*TAF13* (TAF13 RNA polymerase II, TBP associated factor, 18kDa) ⇧1.38-fold, p<0.01 *C9ORF72*vctrl and ⇧1.27-fold, p<0.01 non*C9ORF72*-related_SALSvctrl]. The increase in *TAF13* expression in *C9ORF72+* cases compared to controls was later confirmed in a SYBR® Green qRT-PCR Assay (p<0.05*) (Figure 5.9).

5.2.1.3.2 SnRNP Biogenesis

Precursor snRNA's are bound by the nuclear cap binding (CBC)-complex composed of CBP20/80 subunits [*NCBP2* (nuclear cap binding protein subunit 2, 2kDa) ⇧1.20-fold, p=0.01 *C9ORF72*vctrl] and, in association with PHAX, [*PHAX* (phosphorylated adaptor for RNA export) ⇧1.27-fold, p<0.001 *C9ORF72*vctrl and ⇧1.22-fold, p<0.001 non*C9ORF72*-related_SALSvctrl] transported into the cytoplasm under the direction of exportin 1 (Xpo1) and Ran-GTPase (RAN) (Massenet et al 2002, Pabis et al 2013) (Figure 5.7).

Within the cytoplasm, snRNP's are assembled by the survival motor neurone (SMN) complex comprising SMN protein (Battle et al 2006); reduced levels of which are a cause of AR inherited juvenile-onset Spinal Muscular Atrophy (SMA) (Lefebvre et al 1995, Rodrigues et al 1995), gemins 2 through to 8 (Carissimi et al 2006a, Carissimi et al 2006b) [*GEMIN6* (gem (nuclear organelle) associated protein 6) ⇧1.29-fold, p< 0.001 *C9ORF72*vctrl; *GEMIN8* (gem (nuclear organelle) associated protein 8) ⇧1.25-fold, p<0.05 *C9ORF72*vctrl] and the Unr interacting protein, unrip (alternative name STRAP) (Carissimi et al 2005) [*STRAP* (serine/threonine kinase receptor associated protein) ⇧1.20-fold, p<0.01 *C9ORF72*vctrl]. The SMN complex associates with seven members of the Sm protein family that include B/B" (snRNP-B/B") [*SNRPB2* (small nuclear ribonucleoprotein polypeptide B) ⇧1.24-fold, p<0.05 *C9ORF72*vctrl and ⇧1. 38-fold, p<0.01 non*C9ORF72*-related_SALSvctrl], D1, D2 (snRNP-D2) [*SNRPD2* (small nuclear ribonucleoprotein polypeptide D2) ⇧1.23-fold, p<0.05 *C9ORF72*vctrl], D3, E, F (snRNP-F) [*SNRPF* (small nuclear ribonucleoprotein polypeptide F) ⇧1.27-fold, p <0.01 *C9ORF72*vctrl and ⇧1.27-fold, p<0.01 non*C9ORF72*-related_SALSvctrl] and G. The affinity for SMN binding is further regulated in a subset of these, namely snRNP -B/B'', D1 and D3, by plCLn [*CLNS1A* (chloride channel, nucleotide-sensitive, 1a) ⇧1. 20-fold, p<0.01 *C9ORF72*vctrl] (Figure 5.7) and PRMT5 (protein methyltransferase 5), which serves as a catalyst for the symmetrical dimethylation of specific arginine residues. The subsequent interaction between the SMN complex, bound Sm proteins and precursor snRNA's (Matera et al 2007, Meister et al 2001, Pesiridis et al 2009) drives the ATP-dependent formation of an evolutionarily conserved heptameric ring structure that constitutes the Sm core of the mature snRNP. Following hypermethylation, by TGS1 (trimethylguanosine synthase 1), of the 5' cap, and truncation of the 3' end, snRNP specific nuclear import receptor, Snurportin 1, binds and the importin sub-complex, containing alpha and beta subunits (alternative name karyopherins) [*KPNA4* (karyopherin alpha 4 (importin alpha 3)) ⇧1.27-fold, p<0.001 *C9ORF72*vctrl and ⇧1.20-fold, p<0.001 non*C9ORF72*-related_SALSvctrl], is recruited to the nuclear localisation signal (NLS) (Massenet et al 2002), which facilitates snRNP import into the nucleus. Transportation occurs through nuclear pore complexes (NPC's) [*NUP43* (nucleoporin 43kDa) ⇧1.21-fold, p<0.0001 *C9ORF72*vctrl] which are embedded in the nuclear envelope (Figure 5.7).

The SMN complex may also function in ribosome biogenesis and multiple aspects of pre-ribosomal RNA (pre-rRNA) processing through its association with Cajal bodies (CB's) and small nucleolar RNP's (snoRNP's) including FBL (fibrillarin), GAR1 [*GAR1* (GAR1 ribonucleoprotein homolog (yeast)) ⇧1.31-fold, p<0.0001 *C9ORF72*vctrl] and UTP15 [*UTP15* (U3 small nucleolar ribonucleoprotein homolog (*S. cerevisiae*)) ⇧1.28-fold, p<0.001 *C9ORF72*vctrl and ⇧1.20-fold, p<0.01 non*C9ORF72*-related_SALSvctrl] (Pellizzoni et al 2001, Sato et al 2013, Whitehead et al 2002).

From the snRNP biogenesis pathway six genes were selected as candidates for qRT-PCR. Of the six, only two (33.3%) validated: *CLNS1A* which was confirmed in an IDT PrimeTime® Mini qPCR Assay (p<0.05*) and *UTP15* which was confirmed using the traditional SYBR® Green technology (p<0.001***) (Figure 5.10). *GEMIN6, NCBP2* and *PHAX* were not significant and for *STRAP* (unrip) a small trend (⇧1.14-fold, p=0.068) in the same direction as the microarray was observed (Table 5.5).

5.2.1.3.3 Regulation of the Spliceosome

With an enrichment score of 15.42 (count 21, 61.8%) RNA splicing was identified as the highest ranking RNA processing related GO term in DAVID (Figure 5.8) which is specific to the *C9ORF72* expansion. Transcripts of interest included: those encoding nudix (nucleoside diphosphate linked moiety X)-type motif 21 (NUDT21) [*NUDT21* ⇧1.20-fold, p<0.0001 *C9ORF72*vctrl], a component of the cleavage factor Im (CFIm)-complex that is strongly associated with nuclear paraspeckles and has been shown to be responsible for regulating alternative polyadenylation as well as 3' end poly(A) site cleavage of nascent lncRNA's (Naganuma et al 2012); serine/arginine-rich (SR) splicing factor 3 (SRp20) [*SRSF3* ⇧1.20-fold, p<0.05 *C9ORF72*vctrl and ⇧1.33-fold, p< 0.0001 non*C9ORF72*-related_SALSvctrl]; pre-mRNA processing factors 4 (hRprp4p) [*PRPF4* ⇧1.24-fold, p<0.0001 *C9ORF72*vctrl and ⇧1.24-fold, p<0.0001 non*C9ORF72*-related_SALSvctrl] and 19 (hPrp19) [*PRPF19* ⇧1.21-fold, p<0.001 *C9ORF72*vctrl]; a

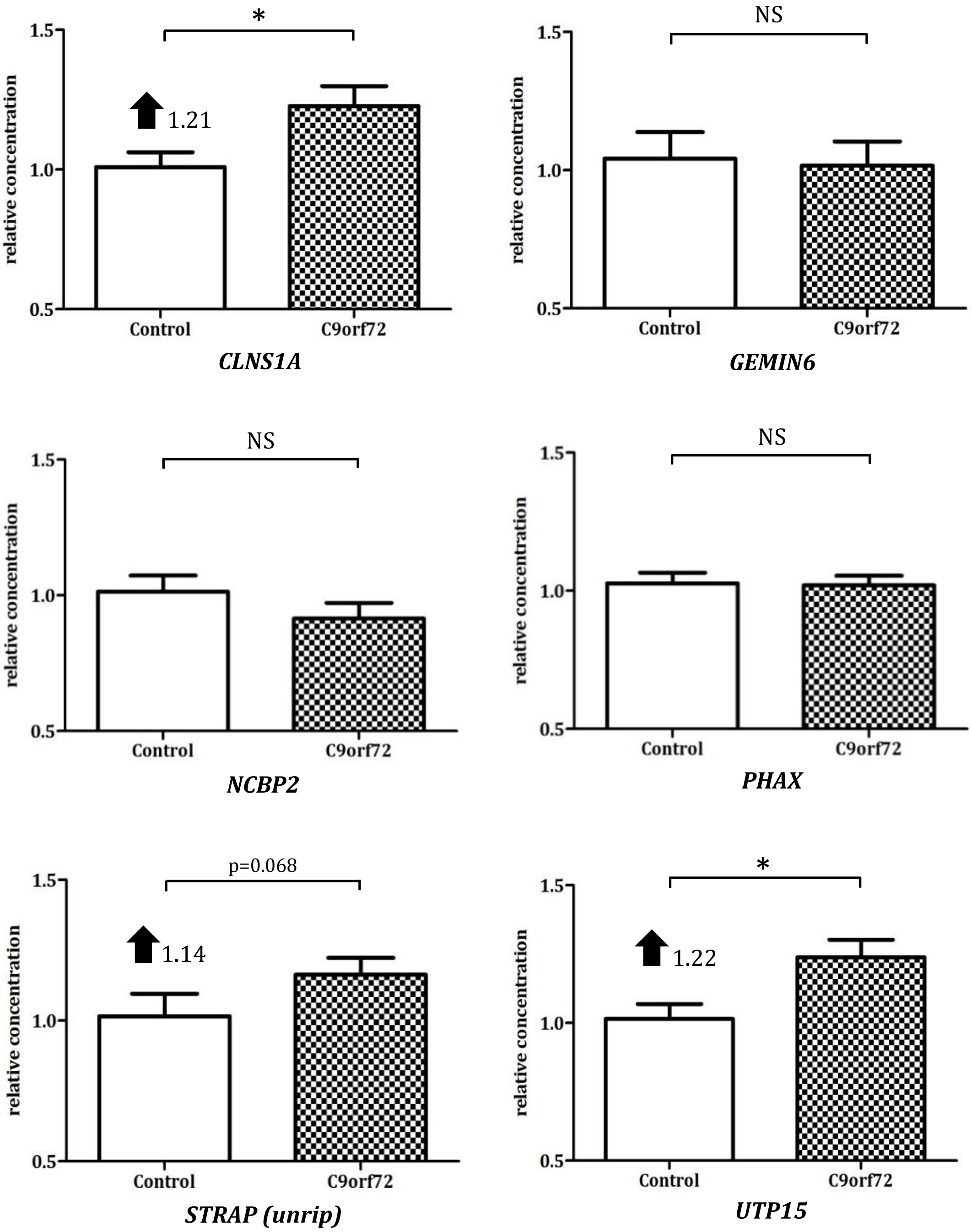


Figure 5.10 SnRNP Biogenesis qRT-PCR Validation Relative concentrations measured against the standard housekeeping gene *18SrRNA*. Means and SEM were plotted using GraphPad® Prism software version 5.04. Probability values calculated in Microsoft Excel 2010 (Microsoft Corporation UK) using a one tailed student's t-test. Gene expression changes were confirmed if the direction of change was the same as the microarray with $p<0.05$* (arrow).

Abbreviations: *18SrRNA* - 18S ribosomal RNA, *C9ORF72* - chromosome 9 open reading frame 72, *CLNS1A* - chloride channel, nucleotide-sensitive, 1A, *GEMIN6* - gem (nuclear organelle) associated protein 6, NS - not significant, *NCBP2* - nuclear cap binding protein subunit 2, 20kDa, *PHAX* - phosphorylated adaptor for RNA export, qRT-PCR - quantitative real-time PCR, RNP - ribonucleoprotein, SEM - standard error of the mean, snRNP - small nuclear RNP, *STRAP* - serine/threonine kinase receptor associated protein and *UTP15* - U3 small nucleolar ribonucleoprotein, homolog (*S. cerevisiae*).

developmentally controlled, cold inducible apoptotic regulator; RNA binding motif (RNP1, RRM) protein 3 (RBM3) [*RBM3* ⇧ 1.22-fold, p<0.0001 *C9ORF72*vctrl] that is of fundamental importance in miRNA biogenesis and has been shown, under both normal physiological conditions, as well as, mild hypoxia to be capable of enhancing the basal rate of protein synthesis, particularly in the dendritic branches of cortical and hippocampal MN's (Dresios et al 2005, Pilotte et al 2011, Smart et al 2007) and the minor U11/12 spliceosomal component, zinc finger CCHC-type and RNA binding motif 1 (ZCRB1) [*ZCRB1* ⇧1.26-fold, p<0.0001 *C9ORF72*vctrl] (Figure 5.11). Several members of the ubiquitously expressed heterogeneous nuclear RNP (hnRNP) class of RNA binding proteins that regulate aspects of the spliceosomal machinery, essential for pre-mRNA splicing & editing [*HNRNPA0* ⇧1.23-fold, p<0.0001 *C9ORF72*vctrl and ⇧1.23-fold, p<0.0001 non*C9ORF72*-related_SALSvctrl; *HNRNPH2* ⇧1.28-fold, p<0.05 and ⇧1.32-fold, p<0.01 non*C9ORF72*-related_SALSvctrl and *HNRNPF* ⇧1.22-fold, p< 0.001 *C9ORF72*vctrl] and their associated partners including the ALS causative gene *FUS* [*FUS* ⇧1.23-fold, p<0.001 *C9ORF72*vctrl and ⇧1.33-fold, p<0.0001 non*C9ORF72*-related_SALSvctrl (Section 1.2.5.2.2)] had also exhibited altered levels of expression between hexanucleotide G_4C_2 repeat, expansion carrying and control LCL's (Baralle et al 2013, Baumer et al 2010, Bekenstein & Soreq 2013, Romano & Buratti 2013).

Eight of the aforementioned genes were taken forward as candidates for qRT-PCR including five (62.5%) which validated: *HNRNPA0* (p<0.01**), *HNRNPF* (p<0.01**), *NUDT21* (p<0.01**) and *ZCRB1* (p<0.05*) were confirmed using traditional SYBR® Green technology whilst *FUS* (p<0.01**) was confirmed in an IDT PrimeTime® Mini qPCR Assay. *HNRNPH2* was not significant (Figure 5.13) and for *PRPF19* (⇧1.14-fold, p=0.071) and *RBM3* (⇧1.14-fold, p=0.069) a small trend in the same direction as the microarray was observed (Figure 5.12).

5.2.1.4 Translation

Translation and translation factor activity, nucleic acid binding with EASE scores of 7.52 or 2.61, respectively (Table 5.3a) were ranked as the 2nd (count 41, 6.4%) and 10th (count 13, 2.0%) most highly enriched GO terms (Section 5.2.1.2.1) in a DAVID functional annotation clustering analysis of *C9ORF72*vctrl (n=644/1,088) [Partek®

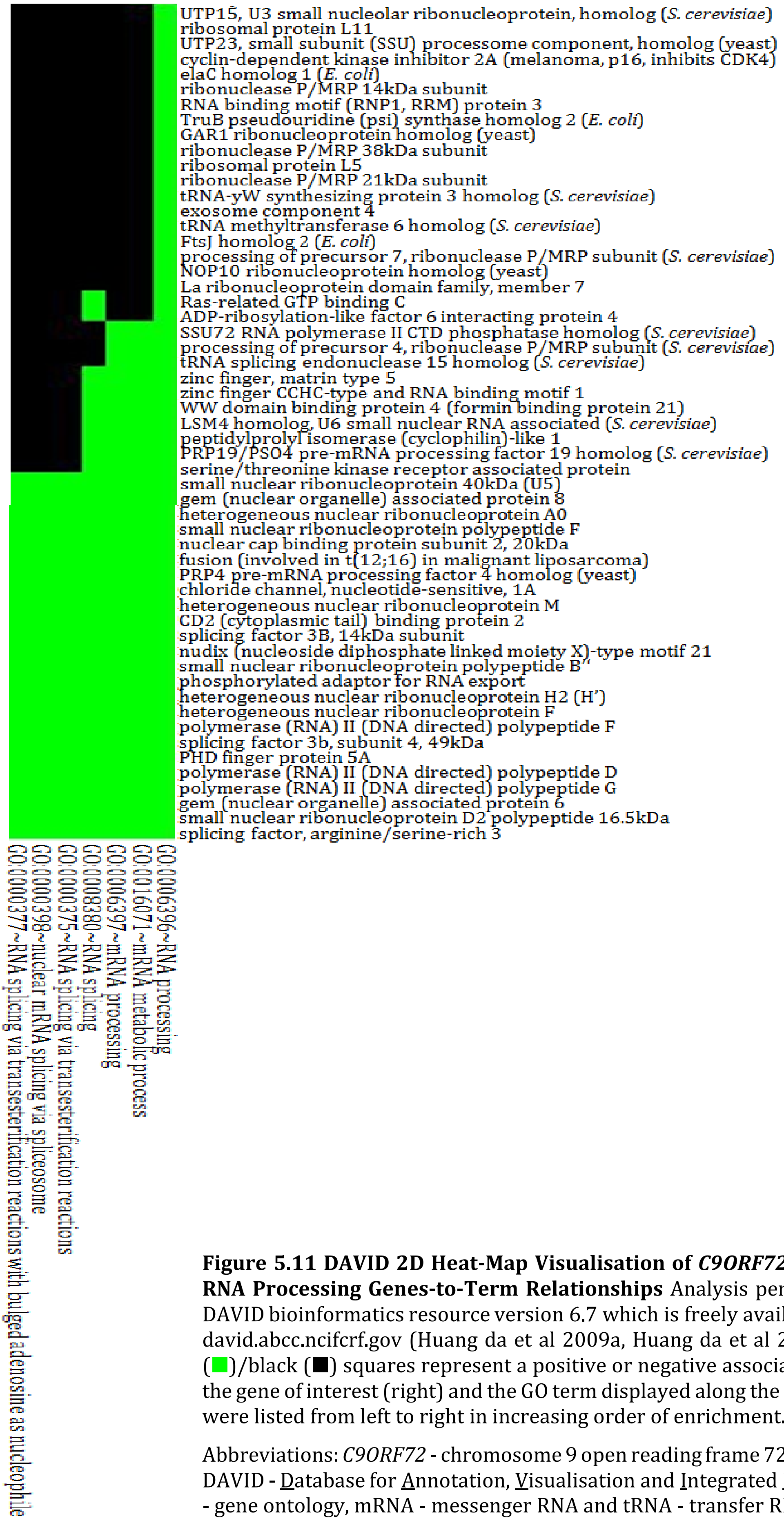
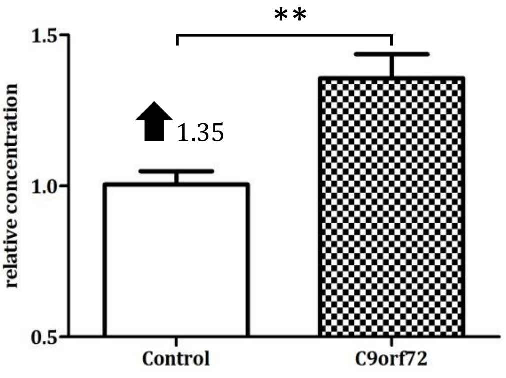
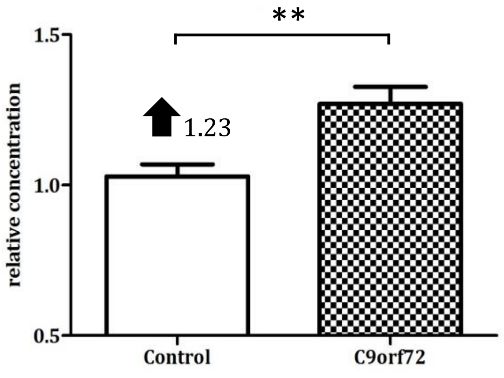


Figure 5.11 DAVID 2D Heat-Map Visualisation of *C9ORF72*vCtrl (n=56) RNA Processing Genes-to-Term Relationships Analysis performed using DAVID bioinformatics resource version 6.7 which is freely available online at david.abcc.ncifcrf.gov (Huang da et al 2009a, Huang da et al 2009b). Green (🟩)/black (■) squares represent a positive or negative association between the gene of interest (right) and the GO term displayed along the bottom; these were listed from left to right in increasing order of enrichment.

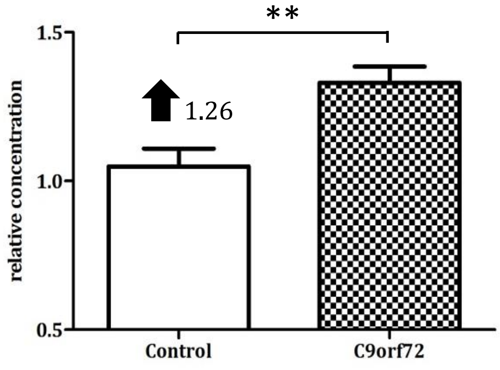
Abbreviations: *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control, DAVID - Database for Annotation, Visualisation and Integrated Discovery, GO - gene ontology, mRNA - messenger RNA and tRNA - transfer RNA.



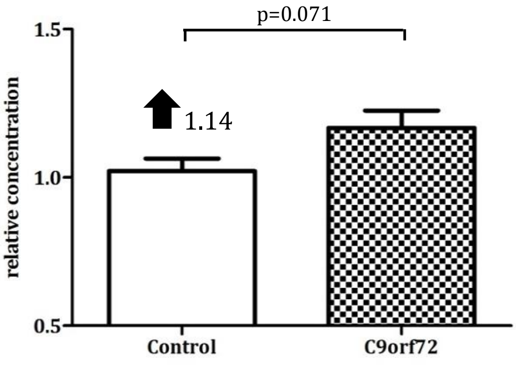
FUS



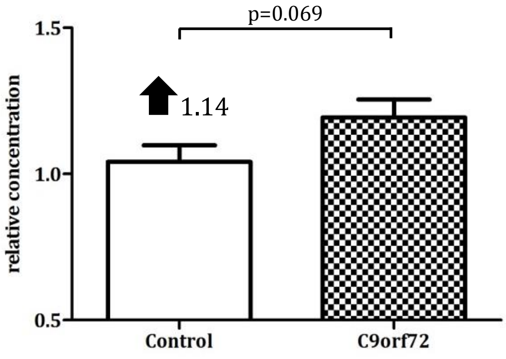
HNRNPA0



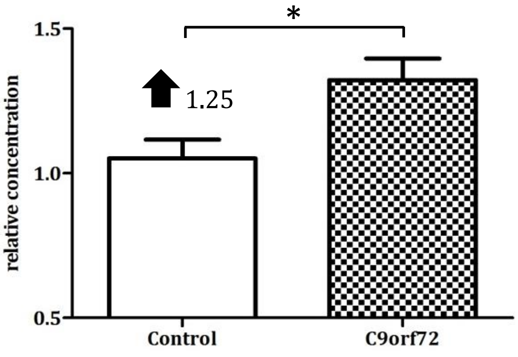
NUDT21



PRPF19



RBM3



ZCRB1

Figure 5.12 Regulation of the Spliceosome qRT-PCR Validation I Relative concentrations measured against the standard housekeeping gene *18SrRNA*. Means and SEM were plotted in GraphPad® Prism software version 5.04. Probability values calculated in Microsoft Excel 2010 (Microsoft Corporation UK) using a one tailed student's t-test. Gene expression changes were confirmed if the direction of change (arrow) was the same as the microarray with p<0.05* (p<0.01**).

Abbreviations: *18SrRNA* - 18S ribosomal RNA, *C9ORF72* - chromosome 9 open reading frame 72, *FUS* - fused in sarcoma, *HNRNPA0* - heterogeneous nuclear ribonucleoprotein A0, *NUDT21* - nudix (nucleoside diphosphate linked moiety X)-type motif 21, pre-mRNA - precursor mRNA, *PRPF19* - PRP19/PSO4 pre-mRNA processing factor 19 homolog (*S. cerevisiae*), qRT-PCR - quantitative real-time PCR, *RBM3* - RNA binding motif (RNP1, RRM) protein 3, SEM - standard error of the mean and *ZCRB1* - zinc finger CCHC-type and RNA binding motif 1.

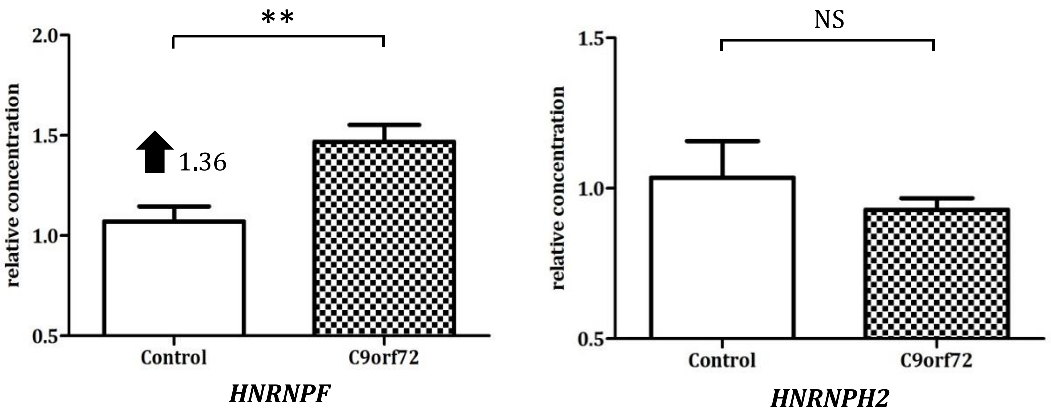


Figure 5.13 Regulation of the Spliceosome qRT-PCR Validation II Relative concentrations measured against the standard housekeeping gene *18SrRNA*. Means and SEM were plotted in GraphPad® Prism software version 5.04. Probability values calculated in Microsoft Excel 2010 (Microsoft Corporation UK) using a one tailed student's t-test. Gene expression changes were confirmed if the direction of change (arrow) was the same as the microarray with p<0.01**

Abbreviations: *18SrRNA* - 18S ribosomal RNA, *C9ORF72* - chromosome 9 open reading frame 72, *HNRNPF* - heterogeneous nuclear ribonucleoprotein F, *HNRNPH2* - heterogeneous nuclear ribonucleo protein H2, NS - not significant, qRT-PCR - quantitative real-time PCR and SEM - standard error of the mean.

unadjusted p<0.05, FC ≥ ±1.20] up-regulated gene expression changes. A list of the DAVID output of genes relating to translation is provided in Table 5.6. DE transcripts specific to the G_4C_2 repeat are denoted by three asterisks inserted immediately after the gene symbol in the first column. Key validation targets which were selected for qRT-PCR are shaded in grey.

Translation describes the processes by which mRNA targets that are transcribed in the nucleus are decoded by the ribosomal machinery in the cytoplasm. In eukaryotes protein synthesis is an ongoing, cyclical event that is defined by an initiation phase (Section 5.2.1.4.1) followed by an elongation (Section 5.2.1.4.2), termination (Section 5.2.1.4.3) and ribosome recycling step (Section 5.2.1.4.4).

5.2.1.4.1 Translation Initiation

Translation initiation begins with the assembly of the 43S PIC (Figure 5.14) (Jackson et al 2010, Mayer et al 2001, RajBhandary 1994) comprising components of the 40S ribosomal subunit [*RPS15A* (ribosomal protein S15a) ⇧1.27-fold, p<0.05 *C9ORF72*v ctrl; *RPS2* (ribosomal protein S2) ⇧1.49-fold, p<0.01 *C9ORF72*vctrl], a ternary sub-complex of the initiator methionine transfer RNA ($tRNA_i^{met}$) [*TRMT6* (tRNA methyl

Symbol	RefSeq	Transcript	Gene		Fold	p-value
DENR	NM_003677	3435490	density-regulated protein	⇧	1.30	1.64E-03
EIF3J	NM_003758	3591963	eukaryotic translation initiation factor 3, subunit J	⇧	1.23	0.012
*EIF3K****	NM_013234	3832616	eukaryotic translation initiation factor 3, subunit K	⇧	1.33	1.68E-04
*EIF4B****	NM_001417	3455946	eukaryotic translation initiation factor 4B	⇧	1.45	0.011
*EIF4E2****	NM_004846	2532422	eukaryotic translation initiation factor 4E, family member 2	⇧	1.23	0.011
EIF4H	NM_022170	3008144	eukaryotic translation initiation factor 4H	⇧	1.31	5.01E-03
*EIF5****	NM_183004	3553607	eukaryotic translation initiation factor 5	⇧	1.20	1.12E-03
ETF1	NM_004730	2877465	eukaryotic translation termination factor 1	⇧	1.27	6.75E-05
*GARS****	NM_002047	2995420	glycyl-tRNA synthetase	⇧	1.24	3.85E-03
HARS	NM_002109	2878474	histidyl-tRNA synthetase	⇧	1.20	4.98E-03
ICT	NM_001545	3734575	immature colon carcinoma transcript 1	⇧	1.22	4.71E-03
KARS	NM_001130089	3699757	lysyl-tRNA synthetase	⇧	1.20	2.32E-04
*MRPL10****	NM_145255	3760945	mitochondrial ribosomal protein L10	⇧	1.21	0.037
*MRPL15****	NM_014175	3098454	mitochondrial ribosomal protein L15	⇧	1.27	1.83E-04
*MRPL16****	NM_017840	3374856	mitochondrial ribosomal protein L16	⇧	1.21	0.022
MRPL18	NM_014161	2934167	mitochondrial ribosomal protein L18	⇧	1.22	5.06E-03
*MRPL19****	NM_014763	2489806	mitochondrial ribosomal protein L19	⇧	1.22	0.012
*MRPL21****	NM_181515	3379708	mitochondrial ribosomal protein L21	⇧	1.32	3.21E-03
MRPL22	NM_014180	2836886	mitochondrial ribosomal protein L22	⇧	1.22	0.014
*MRPL30****	NM_145212	2495806	mitochondrial ribosomal protein L30	⇧	1.20	0.014
*MRPL34****	NM_023937	3824197	mitochondrial ribosomal protein L34	⇧	1.33	6.39E-05
*MRPL4****	NM_146388	3820414	mitochondrial ribosomal protein L4	⇧	1.21	1.82E-03
MRPL41	NM_032477	3195344	mitochondrial ribosomal protein L41	⇧	1.43	5.85E-04
MRPL47	NM_020409	2706985	mitochondrial ribosomal protein L47	⇧	1.34	2.52E-03
MRPL51	NM_016497	3441955	mitochondrial ribosomal protein L51	⇧	1.22	1.80E-05
*MRPL9****	NM_031420	2435195	mitochondrial ribosomal protein L9	⇧	1.21	6.78E-03
*MRPS11****	NM_022839	3607183	mitochondrial ribosomal protein S11	⇧	1.33	1.60E-05
*MRPS12****	NM_021107	3832777	mitochondrial ribosomal protein S12	⇧	1.29	1.89E-05
*MRPS16****	NM_016065	3294348	mitochondrial ribosomal protein S16	⇧	1.21	1.83E-04
*MRPS2****	NM_016034	3193900	mitochondrial ribosomal protein S2	⇧	1.26	1.35E-03
*MTFMT****	NM_139242	3629378	mitochondrial methionyl-tRNA formyltransferase	⇧	1.24	7.48E-03
*RBM3****	NM_017495	3976519	RNA binding motif (RNP1, RRM) protein 3	⇧	1.22	9.22E-05

*RPL11****	NM_170739	2325192	ribosomal protein L11	⇧	1.25	0.035
*RPL22****	NM_000983	2394558	ribosomal protein L22	⇧	1.40	1.06E-04
RPL36A	NM_019597	3984779	ribosomal protein L36a	⇧	1.28	0.024
*RPL39L****	NM_052969	2709606	ribosomal protein L39L	⇧	1.35	7.08E-03
*RPL5****	NM_014570	3962587	ribosomal protein L5	⇧	1.24	1.28E-03
*RPL9****	NM_001024921	2766419	ribosomal protein L9	⇧	1.24	0.014
*RPS15A****	NM_001019	3683018	ribosomal protein S15a	⇧	1.27	0.039
*RPS2****	NM_002952	3676300	ribosomal protein S2	⇧	1.49	2.73E-03
*TRMT6****	NM_015939	3896524	tRNA methyltransferase 6 homolog (*S. cerevisiae*)	⇧	1.27	1.11E-05

Table 5.6 DAVID *C9ORF72*vCtrl List of Translation Related Genes (n=41) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

Abbreviations: *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control, DAVID - Database of Annotation, Visualisation and Integrated Discovery, FC - fold-change, RNP - ribonucleoprotein processing, RRM - RNA recognition motif and tRNA - transfer RNA.

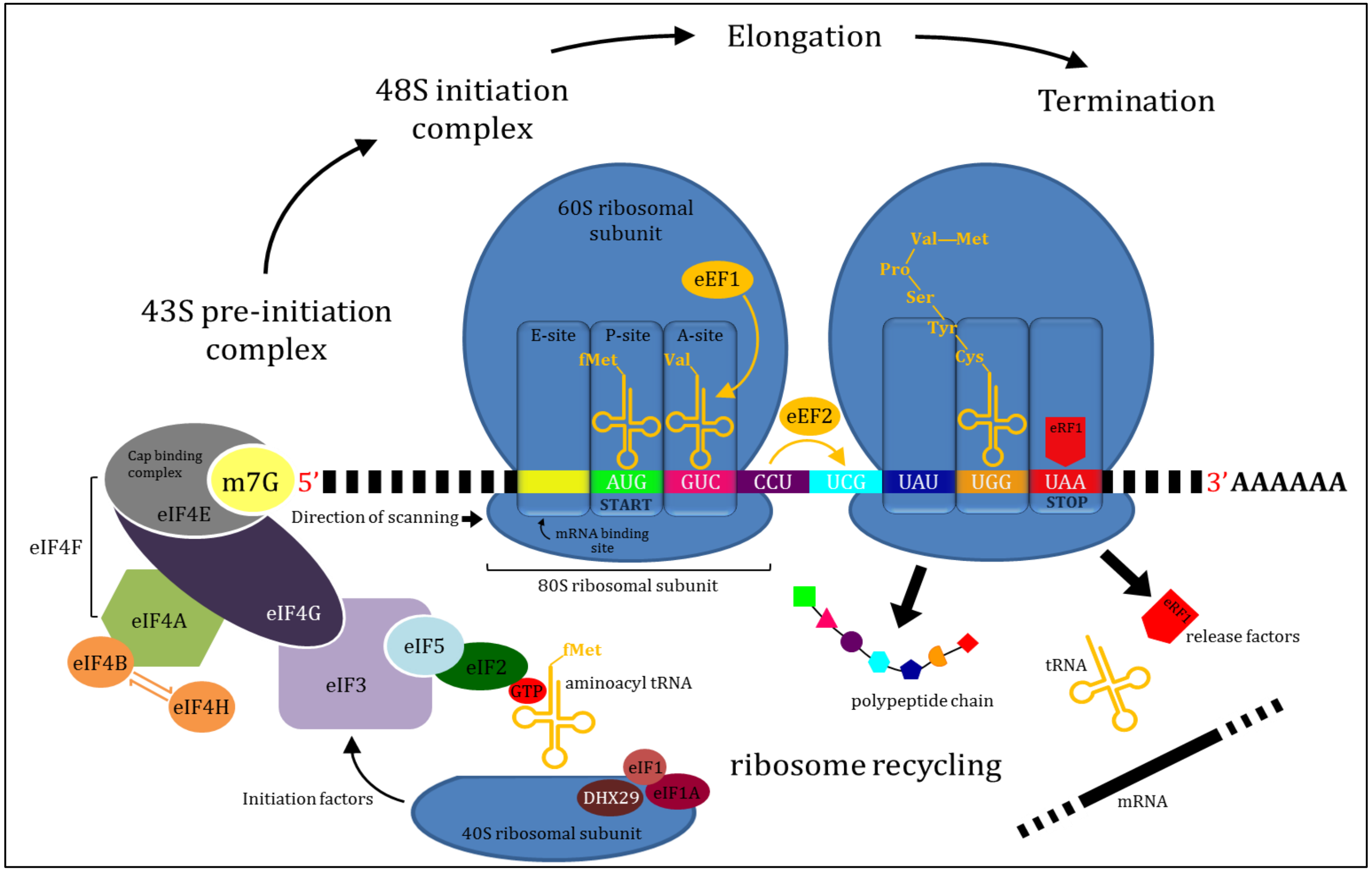


Figure 5.14 Eukaryotic Translation Initiation, Elongation, Termination and Ribosome Recycling Schematic

Abbreviations: *DHX29* - DExH box protein DEAH (Asp-Glu-Ala-His) box polypeptide 29, eEF - eukaryotic translation elongation factor, eIF - eukaryotic translation initiation factor, eRF - eukaryotic translation release factor, fMet - *N*-formylmethionine, GTP - guanosine triphosphate, m^{7}G - methylguanosine cap structure, mRNA - messenger RNA and tRNA - transfer RNA.

transferase 6 homolog (*S. cerevisiae*)) encoding the substrate binding motif, TRM6 ⇧ 1.27-fold, p<0.0001 *C9ORF72*vctrl and ⇧1.26-fold, p<0.0001 non*C9ORF72*-related_SALSvctrl] in association with guanosine triphosphate (GTP) bound eIF2 (eukaryotic translation initiation factor 2) and eukaryotic translation initiation factors eIF1/1A and eIF3 (Figure 5.14) [*EIF3J* (eukaryotic translation initiation factor 3, subunit J) ⇧ 1.23-fold, p<0.05 *C9ORF72*vctrl and ⇧1.24-fold, p<0.05 non*C9ORF72*-related_SALSvctrl; *EIF3K* (eukaryotic translation initiation factor 3, subunit K) ⇧1.33-fold, p<0.001 *C9ORF72*vctrl]. Attachment of the 43S PIC to the seven methylguanosine (m^{7}G) cap structure at the 5' end of the mRNA target is mediated by eIF4B [*EIF4B* (eukaryotic translation initiation factor 4B) ⇧1.44-fold, p<0.05 *C9ORF72*vctrl] and 4F; the latter of which is itself composed of three subunits containing a scaffolding protein eIF4G, an ATP-dependent RNA helicase eIF4A, that is under the direction of eIF4H [*EIF4H* (eukaryotic translation initiation factor 4H) ⇧1.31-fold, p<0.01 *C9ORF72*vctrl and ⇧ 1.38-fold, p<0.001 non*C9ORF72*-related_SALSvctrl], and cap binding complex eIF4E [*EIF4E2* (eukaryotic translation initiation factor 4E, family member 2) ⇧1.23-fold, p< 0.05 *C9ORF72*vctrl]. Scanning is then prompted by the DExH-box protein DEAH (Asp-Glu-Ala-His) box polypeptide 29 (DHX29) (Hashem et al 2013) (Figure 5.14). The increase in *EIF4H* expression in *C9ORF72+* cases compared to controls (p<0.001***) (Figure 5.15) was later confirmed in an IDT PrimeTime® Mini qPCR Assay.

Upon recognition of the translation initiation start codon, hydrolysis of bound GTP into guanosine diphosphate (GDP) and, release of inorganic phosphate (P_i), triggers eIF2 dissociation from the ternary sub-complex. Established base pairing between the tRNA$_i^{met}$ and the AUG trinucleotide sequence now located within the P site of the ribosomal 40S subunit results in the formation of the 48S initiation complex (Figure 5.14). The recruitment of eIF5 [*EIF5* (eukaryotic translation initiation factor 5) ⇧1.20-fold, p<0.01 *C9ORF72*vctrl] and 5B are required for docking of the large ribosomal 60S subunit [*RPL5* (ribosomal protein L5) ⇧1.24-fold, p<0.01 *C9ORF72*vctrl; *RPL9* (ribosomal protein L9) ⇧1.24-fold, p<0.05 *C9ORF72*vctrl; *RPL11* (ribosomal protein L11) ⇧1.25-fold, p<0.05 *C9ORF72*vctrl; *RPL22* (ribosomal protein L22) ⇧1.40-fold, p<0.01 *C9ORF72*vctrl; *RPL36A* (ribosomal protein L36a) ⇧1.28-fold p<0.05 *C9ORF72*vctrl and ⇧1.32-fold, p<0.01 non*C9ORF72*-related_SALSvctrl and *RPL39L* (ribosomal protein L39-like) ⇧1.35-fold, p<0.01 *C9ORF72*vctrl (Ben-Shem et al 2011, Klinge et

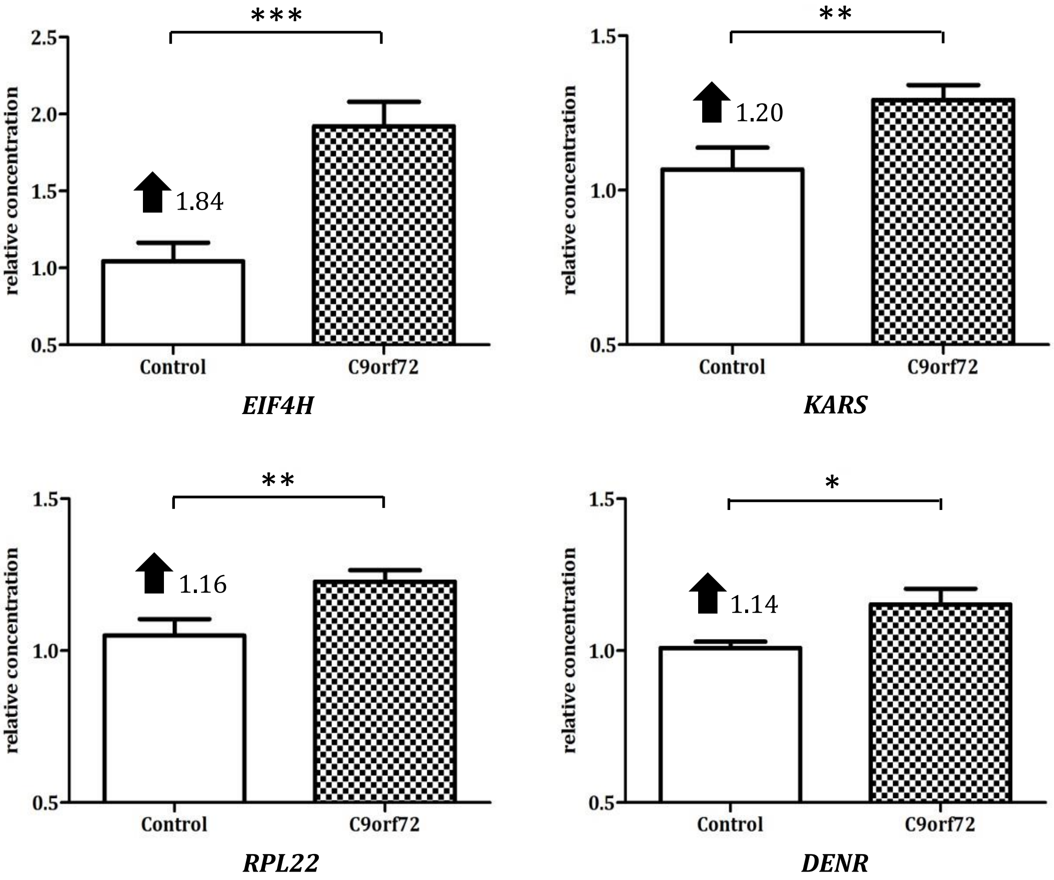


Figure 5.15 Eukaryotic Translation qRT-PCR Validation Relative concentrations were measured against the standard housekeeping gene *18SrRNA*. Means and SEM plotted in GraphPad® Prism software version 5.04. Probability values calculated in Microsoft Excel 2010 (Microsoft Corporation UK) with a one tailed student's t-test applied. Gene expression changes were confirmed if the direction of change (arrow) was the same as the microarray with p<0.05* (p<0.01**, p<0.001***).

Abbreviations: *C9ORF72* - chromosome 9 open reading frame 72, *DENR* - density-regulated protein, *EIF4H* - eukaryotic translation initiation factor 4H, *KARS* - lysyl-tRNA synthase, qRT-PCR - quantitative real-time PCR, *18SrRNA* - 18S ribosomal RNA, *RPL22* - ribosomal protein L22, SEM - standard error of the mean and tRNA - transfer RNA.

al 2011)] in order to establish an 80S ribosome that is primed for elongation (Figure 5.14) (Lomakin & Steitz 2013). An increase in *RPL22* expression in *C9ORF72+* cases compared to controls (p<0.01**) (Figure 5.15) was later confirmed in a traditional SYBR® Green qRT-PCR Assay.

It is interesting to note that whilst an overall up-regulation in the gene expression of transcripts associated with protein synthesis was observed in *C9ORF72*vctrl (Table 5.3a) [Partek® unadjusted p<0.05, FC ≥ ±1.20] the abundance of mRNA encoding the translational repressor 4E-BP2 [*EIF4EBP2* (eukaryotic translation initiation factor 4E binding protein 2) ⇧1.32-fold, p<0.0001 non*C9ORF72*-related_SALSvctrl (Ayuso et al 2013, Banko et al 2005, Paku et al 2012)] was found to be significantly elevated in the SALS patient derived LCL's which do not carry the G_4C_2 repeat. In these cases there was also a concomitant decrease in the expression of eEF1a1 [*EEF1A1* (eukaryotic translation elongation factor 1, alpha 1) ⇩1.29-fold, p<0.0001 non*C9ORF72*-related _SALSvctrl] in addition to a marked reduction in the levels of multiple components of the 60S ribosomal subunit [*RPL5* ⇩1.28-fold, p<0.0001; *RPL10* (ribosomal subunit L10) ⇩1.37-fold, p<0.001; *RPL13* (ribosomal subunit L13) ⇩1.29-fold, p<0.05; *RPL17* (ribosomal subunit L17) ⇩1.28-fold, p<0.01 non*C9ORF72*-related_SALSvctrl].

5.2.1.4.2 Translation Elongation

Elongation of the nascent polypeptide chain is driven by the eukaryotic translation elongation factor 1 (eEF-1) complex composed of five subunits that include: eEF1A-1 (alpha 1), eEF1A-2 (alpha 2), eEF1B-2 (beta 2), eEF1D (delta) and eEF1E (epsilon) responsible for delivering amino-acetylated tRNA molecules to the ribosomal A site which normally occurs at a rate of approximately two amino acids per second. EEF-2 (eukaryotic translation elongation factor 2) is then required, following sequential formation of each peptide bond (Figure 5.14), in order to shift the mRNA template along one codon at a time in relation to the positioning of the 80S ribosome (Skabkin et al 2013).

The charging of the tRNA molecules with their cognate amino acids is performed by the class I and class II aminoacyl-tRNA synthetase enzymes; several of which were found to be DE in expansion carrying LCL's (Guo et al 2010, Hausmann & Ibba 2008, Ibba & Soll 2000) [*GARS* (glycyl-tRNA synthetase) ⇧1.24-fold, p<0.01 *C9ORF72*vctrl; *HARS* (histidyl-tRNA synthetase) ⇧1.20-fold, p<0.01 *C9ORF72*vctrl and *KARS* (lysyl-tRNA synthetase) ⇧1.20-fold, p<0.001 *C9ORF72*vctrl and ⇧1.23-fold, p<0.0001 non *C9ORF72*-related_SALSvctrl (Table 5.6)]. An increase in *KARS* expression (p<0.01**) (Figure 5.15) was later confirmed in a traditional SYBR® Green qRT-PCR Assay.

5.2.1.4.3 Translation Termination

Assembly of the eukaryotic translation pre-termination (pre-TC) complex is initiated by occupation of the ribosomal A site by one of three stop codons, namely UAG, UAA or UGA which are decoded by the eukaryotic release factor eRF1 [*ETF1* (eukaryotic translation termination factor 1) ⇧1.27-fold, $p<0.0001$ *C9ORF72*vctrl and ⇧1.21-fold, $p<0.001$ non*C9ORF72*-related_SALSvctrl (Alkalaeva et al 2006)]. Recognition of any one of these specific trinucleotide sequences at this site triggers GTPase mediated inactivation of a second eukaryotic release factor (eRF3a/b) (Beznoskova et al 2013). The subsequent dissociation of GDP-bound eRF3a/b liberates eRF1 and facilitates its mobilisation of the ribosomal peptidyl transferase centre responsible for the hydrolytic breakdown of the covalently linked amide bond between the P-site deacylated tRNA and the carboxyl-terminus of the newly synthesised protein; thus, releasing it from the translational machinery (Figure 5.14) (Dever & Green 2012).

5.2.1.4.4 Ribosome Recycling

The dissolution of the eukaryotic translation post-termination (post-TC) complex is understood to be under the control of the ABCE1 protein (alternative name RNase L (2', 5'-oligoisodenylate synthetase dependent inhibitor (Rli1)) [*ABCE1* (ATP-binding cassette, sub-family E (OABP), member 1) ⇧1.29-fold, $p<0.01$ *C9ORF72*vctrl (Pisarev et al 2010, Shoemaker & Green 2011) (Figure 5.14)]. A molecular switch that results in the hydrolysis of bound ATP into adenosine diphosphate (ADP) and the release of P_i produces a conformational change which leads to the dissociation of the ribosomal 60S subunit (Barthelme et al 2011, Becker et al 2012, Dever & Green 2012). EIF1/1A and eIF3J complete the cycle; either acting alone or in concert with the solute carrier family 16 (monocarboxylate transporter), member 1 (MCT-1) and density regulated protein (DRP1) complex [*DENR* ⇧1.30-fold, $p<0.01$ *C9ORF72*vctrl and ⇧1.31-fold, $p<0.001$ non*C9ORF72*-related_SALSvctrl] to release the mRNA template and deacylated tRNA from the 40S ribosomal subunit (Figure 5.14) (Dever & Green 2012, Dmitriev et al 2010, Pisarev et al 2007, Skabkin et al 2010). An increase in *DENR* expression was later confirmed in a traditional SYBR® Green qRT-PCR Assay ($p<0.05$*) (Figure 5.15).

5.2.1.5 Qlucore Omics Explorer

The Partek® generated GC-RMA normalised pivot tables of log2 transformed signal intensities relating to Affymetrix® core meta-probesets (n=287,329) on the Human Exon 1.0ST GeneChip® Arrays for samples in the final ECACC microarray experiment (n=120/125) [*C9ORF72+* (n=38), SALS (n=56) and Ctrl (n=26) (Section 5.2.1.1)] were also interrogated visually using Qlucore Omics Explorer software version 2.3. F-test statistical outputs for the ANOVA were applied at the 5% significance level ($p<0.05$) in order to generate lists of variables or genes (transcripts) (Section 2.3.2.5.3) which are best able to separate patient and control groupings [i.e. *C9ORF72*vctrl (Section 5.2.1.5.1) and non*C9ORF72*-related_SALSvctrl (Section 5.2.1.5.2)] on the PCA plot or hierarchically clustered HeatMap. Any potentially confounding effects due to age or gender were eliminated and the lists filtered to removed unannotated clusters using the NetAffx™ Analysis Centre (n=3,356/22,011) which is freely available online at affymetrix.com/analysis/index.affx (Affymetrix® Ltd, UK) (Liu et al 2003). Finally, a FC threshold of ≥ ±1.20 was applied and functional annotation clustering analysis performed using DAVID bioinformatics resource version 6.7 (Section 2.3.2.5.4). GO categories with an EASE score above 1.30 and Benjamini-Hochberg FDR corrected $p<0.05$ were considered statistically significant. Transcripts identified as being up (⇧)/down(⇩)-regulated under different experimental conditions were analysed independently.

5.2.1.5.1 *C9ORF72*vCtrl

Qlucore Omics Explorer identified 1,173 of 18,655 variables or genes (transcripts) as being differentially regulated between LCL's carrying the G_4C_2 repeat expansion in *C9ORF72* and neurologically normal, healthy controls. These included 755 (64.4%) variables that were significantly up-regulated (⇧) and a further 418 (35.6%) variables which were significantly down-regulated (⇩). Overall there was a good degree of concordance between the Qlucore (n=1,173/18,655) [ANOVA F-test $p<0.05$, FC ≥ ± 1.20] and Partek® (n=1,097/17,635) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20 (Section 5.2.1.1.1)] generated lists with a respective 84.5% (n=991/1,173) or 90.3% (n= 991/17,635) [597 genes ⇧ and 394 genes ⇩] of DE transcripts (Figure 5.16) shared in common between to two analyses platforms.

In the functional annotation clustering analysis 1,074 DAVID ID's were returned for

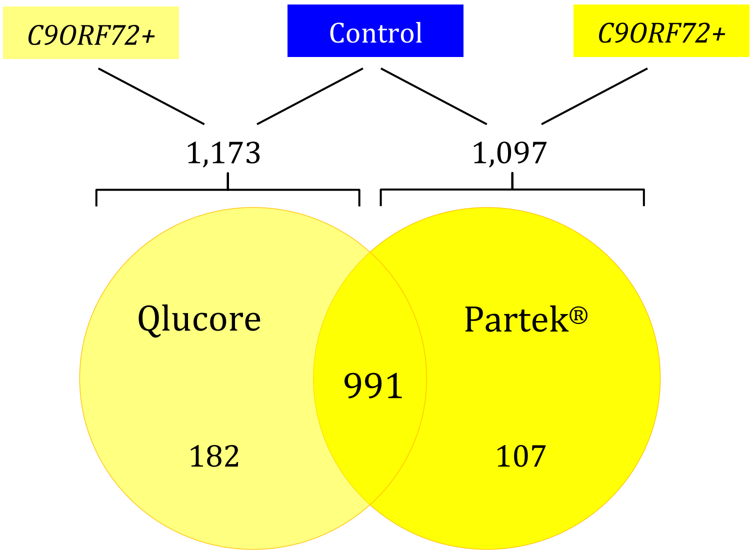


Figure 5.16 GeneVenn *C9ORF72*vctrl [ANOVA F-test p<0.05, FC ≥ ±1.20; Partek® unadjusted p<0.05, FC ≥ ±1.20] Lists of DE variables/genes were generated using Qlucore Omics Explorer software version 2.3 (Lund, Sweden) or Partek® Genomics Suite™ software version 6.6 copyright © 2013 (Partek® Inc., St Louis, MO, USA). The GeneVenn application was freely available online from genevenn.sourceforge.net (Pirooznia et al 2007) (University of Southern Mississippi, USA).

Abbreviations: ANOVA - analysis of variance, *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control, DE - differentially expressed and FC - fold-change.

91.6% of the 1,173 DE variables [644 genes ⇧ and 410 genes ⇩]. GO terms highlighted in Table 5.7 were almost identical (Yellow) to those identified in the original Partek® *C9ORF72*vctrl analysis (Table 5.3). Once again RNA processing (Section 5.2.1.3) and translation (Section 5.2.1.4) featured prominently and were, by far, the most highly enriched categories, with respective EASE scores of 8.56 (count 57, FDR p<0.0001) and 13.10 (count 56, FDR p<0.0001) (Table 5.7).

The same list of 1,173 DE variables [ANOVA F-test p<0.05, FC ≥ ±1.20] could also be applied in Qlucore Omics Explorer in order to determine whether, following a PCA, clearly defined genetic sub-groups were evident within the *C9ORF72+* LCL samples. This, however, proved not to be the case when comparing the software generated PCA plot [*C9ORF72+* (Yellow) and Ctrl (Blue)] and hierarchically clustered HeatMap [Up (⇧)-regulated (Red) and down (⇩)-regulated (Green)]. Although the separation was not entirely distinct, yellow spheres representing the G_4C_2 repeat carriers were predominantly concentrated within the upper (Figure 5.17a) or right (Figure 5.17b)

a) *C9ORF72*vctrl ⇧$_{\text{reg}}$ [ANOVA F-test p<0.05, FC ≥ ±1.20]

#	GO term	Functional category	EASE	Count	Benjamini
1	GO:0006412	translation	13.10	56	1.80E-18
2	GO:0006396	RNA processing	8.56	57	1.80E-09
3	GO:0006974	response to DNA damage stimulus	5.08	35	1.10E-04
4	GO:0007049	cell cycle	4.14	65	3.50E-07
5	GO:0022613	ribonucleoprotein complex biogenesis	3.96	26	2.70E-06
6	GO:0051340	regulation of ligase activity	3.93	16	3.10E-05
7	GO:0044265	cellular macromolecule catabolic process	3.75	53	2.30E-04
8	GO:0043933	macromolecular complex subunit organisation	3.50	52	2.50E-04
9	GO:0008135	translation factor activity, nucleic acid binding	3.44	17	6.10E-05
10	GO:0006368	RNA elongation from RNA polymerase II promoter	2.88	10	2.70E-03
11	GO:0034622	cellular macromolecular complex assembly	2.43	27	5.20E-03
12	GO:0006297	nucleotide-excision repair, DNA gap filling	2.15	6	0.012
13	GO:0022904	respiratory electron transport chain	2.04	10	0.020
14	GO:0000166	nucleotide binding	1.53	109	0.029

b) *C9ORF72*vctrl ⇩$_{\text{reg}}$ [ANOVA F-test p<0.05, FC ≥ ±1.20]

#	GO term	Functional category	EASE	Count	Benjamini
1	GO:0007155	cell adhesion	5.06	39	2.60E-04
2	GO:0016125	sterol metabolic process	4.59	14	2.50E-04
3	GO:0006811	ion transport	4.47	43	8.20E-05
4	GO:0008610	lipid biosynthetic process	3.32	31	1.30E-07
5	GO:0005506	iron ion binding	3.12	20	4.50E-03
6	GO:0015294	solute:cation symporter activity	3.11	11	3.80E-03
7	GO:0051270	regulation of cellular component movement	2.78	14	0.050
8	GO:0009100	glycoprotein metabolic process	2.56	17	2.80E-03
9	GO:0043167	ion binding	2.33	117	0.017
10	GO:0042626	ATPase activity, coupled to transmembrane movement of substances	2.29	12	0.011
11	GO:0016717	oxidoreductase activity, acting on paired donors, with oxidation of a pair of donors resulting in the reduction of molecular oxygen to two molecules of water	1.97	4	0.010
12	GO:0030246	carbohydrate binding	1.67	20	9.60E-03
13	GO:0030169	low-density lipoprotein binding	1.51	5	0.030

Table 5.7 DAVID Qlucore *C9ORF72*vCtrl Functional Annotation Clustering Analysis

Abbreviations: # - rank, ⇧$_{\text{reg}}$ - up-regulated, ⇩$_{\text{reg}}$ - down-regulated, ANOVA - analysis of variance, *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control, EASE - enrichment score, FC - fold-change and GO - gene ontology.

segment whilst blue spheres which represent the control cases were predominantly concentrated within the lower (Figure 5.17a) or left (Figure 5.17b) segment of each graph, respectively.

5.2.1.5.2 Non*C9ORF72*-Related_SALSvCtrl

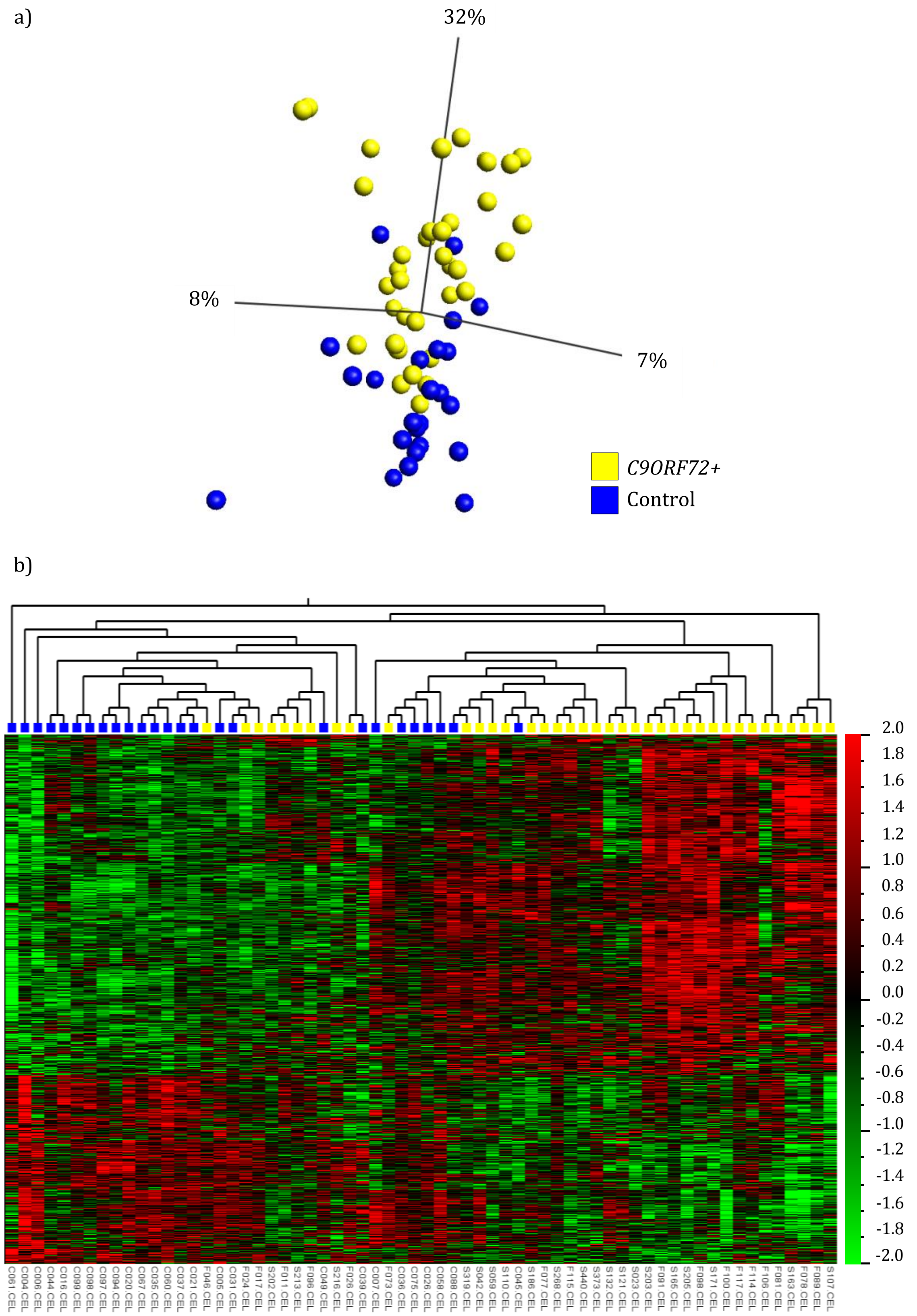


Figure 5.17 *C9ORF72*vctrl Clustering Analysis Applying the 1,173 List of Variables in Qlucore Omics Explorer [ANOVA F-test p<0.05, FC ≥ ±1.20]

Abbreviations: ANOVA - analysis of variance, *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control and FC - fold change.

Qlucore Omics Explorer also identified 1,960 of 18,655 variables or genes as being differentially regulated between non-expansion carrying SALS patient and control LCL's including 1,299 (66.3%) variables which were significantly up-regulated (⇧) and a further 661 (33.7%) variables that were significantly down-regulated (⇩). As seen before (Section 5.2.1.5.1), there was a good degree of concordance between the Qlucore (n=1,960/18,655) [ANOVA F-test p<0.05, FC ≥ ±1.20] and Partek® (n=1,802/17,635) [Partek® unadjusted p<0.05, FC ≥ ±1.20 (Section 5.2.1.1.2)] generated lists with a respective 83.3% (n=1,730/1,173) or 96.0% (n=1,730/17,635) [1,113 genes ⇧ and 617 genes ⇩] of DE transcripts shared in common between the two analyses platforms (Figure 5.18).

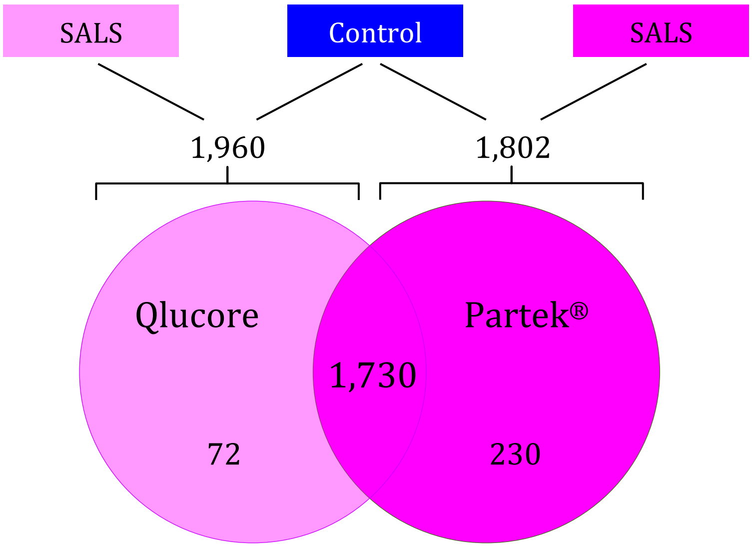


Figure 5.18 GeneVenn Non*C9ORF72*-Related_SALSvCtrl [ANOVA F-test p< 0.05, FC ≥ ±1.20; Partek® unadjusted p<0.05, FC ≥ ±1.20] Lists of DE genes /variables generated using Qlucore Omics Explorer software version 2.3 (Lund, Sweden) or Partek® Genomics Suite™ software version 6.6 copyright © 2013 (Partek® Inc., St Louis, MO, USA). The GeneVenn application is freely available online at genevenn.sourceforge.net (University of Southern Mississippi, USA) (Pirooznia et al 2007).

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, ANOVA - analysis of variance, *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control, DE - differentially expressed, FC - fold-change and S - sporadic.

In the functional annotation clustering analysis 1,768 DAVID ID's were returned for 90.2% of the 1,960 DE variables [1,299 genes ⇧ and 661 genes ⇩]. The GO categories highlighted in Table 5.8 were almost identical (yellow) to those identified from the original Partek® non*C9ORF72*-related_SALSvctrl analysis (Table 5.4) and once again

a) non*C9ORF72*-related_SALSvctrl ⇧$_{\text{reg}}$ [ANOVA F-test $p<0.05$, FC ≥ ±1.20]

#	GO term	Functional category	EASE	Count	Benjamini
1	GO:0007049	cell cycle	36.02	174	2.00E-46
2	GO:0006259	DNA metabolic process	21.34	109	1.30E-26
3	GO:0007059	chromosome segregation	9.00	33	2.30E-15
4	GO:0006396	RNA processing	8.99	86	8.90E-12
5	GO:0051276	chromosome organisation	8.35	90	4.20E-17
6	GO:0022613	ribonucleoprotein complex biogenesis	8.10	43	4.70E-11
7	GO:0051329	interphase of mitotic cell cycle	7.64	28	3.40E-08
8	GO:0006323	DNA packaging	7.06	32	1.60E-09
9	GO:0043933	macromolecular complex subunit organisation	6.66	93	2.10E-08
10	GO:0006310	DNA recombination	6.36	25	4.20E-06
11	GO:0000166	nucleotide binding	6.31	204	1.10E-06
12	GO:0006302	double-strand break repair	6.14	22	2.00E-08
13	GO:0007051	spindle organisation	5.33	17	9.60E-07
14	GO:0031396	regulation of protein ubiquitination	4.71	24	6.30E-06
15	GO:0000072	cell cycle checkpoint	3.48	27	1.10E-08
16	GO:0009314	response to radiation	3.34	31	6.60E-04
17	GO:0006297	nucleotide-excision repair, DNA gap filling	3.32	9	2.00E-04
18	GO:0006511	ubiquitin-dependent protein catabolism	2.81	33	3.80E-03
19	GO:0051186	cofactor metabolic process	2.72	29	2.50E-03
20	GO:0010605	regulation of macromolecule metabolism	2.50	84	3.70E-05
21	GO:0003677	DNA binding	2.47	202	4.20E-05
22	GO:0008134	transcription factor binding	2.46	52	0.028
23	GO:0051052	regulation of DNA metabolic process	2.37	19	0.012
24	GO:0009451	RNA modification	2.32	11	0.023
25	GO:0051259	protein oligomerization	2.17	24	0.025
26	GO:0016579	protein deubiquitination	2.04	8	0.026
27	GO:0050000	chromosome localisation	2.03	6	0.045
28	GO:0032259	methylation	1.57	15	0.011

b) non*C9ORF72*-related_SALSvctrl ⇩$_{\text{reg}}$ [ANOVA F-test $p<0.05$, FC ≥ ±1.20]

#	GO term	Functional category	EASE	Count	Benjamini
1	GO:0006811	ion transport	4.00	49	4.50E-03
2	GO:0030334	regulation of cell migration	3.83	18	5.80E-03
3	GO:0015295	solute:hydrogen symporter activity	3.80	10	2.20E-05
4	GO:0042592	homeostatic process	3.36	50	4.30E-03
5	GO:0008219	cell death	2.83	42	0.019
6	GO:0010647	positive regulation of cell communication	2.81	29	3.30E-03
7	GO:0008654	phospholipid biosynthetic process	2.44	14	6.00E-03
8	GO:0000041	transition metal ion transport	2.44	12	5.90E-03
9	GO:0006643	membrane lipid metabolic process	2.42	11	0.020
10	GO:0006826	iron ion transport	2.26	7	0.018
11	GO:0010038	response to metal ion	2.18	14	0.019
12	GO:0051347	positive regulation of transferase activity	1.95	22	5.50E-03
13	GO:0051249	regulation of lymphocyte activation	1.91	15	0.020
14	GO:0031418	L-ascorbic acid binding	1.67	6	0.037
15	GO:0050850	regulation of calcium-mediated signalling	1.49	6	0.013
16	GO:0006826	iron ion transport	1.34	7	0.018

Table 5.8 DAVID Qlucore Non*C9ORF72*-Related_SALSvCtrl Functional Annotation Clustering Analysis

Abbreviations: # - rank, ⇧$_{\text{reg}}$ - up-regulated, ⇩$_{\text{reg}}$ - down-regulated, ALS - Amyotrophic Lateral Sclerosis, ANOVA - analysis of variance, *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control, EASE - enrichment score, FC - fold-change, GO - gene ontology and S - sporadic.

cell cycle and DNA metabolism featured prominently with respective EASE scores of 36.02 (count 174, FDR $p<0.0001$) and 21.34 (count 109, FDR $p<0.0001$).

Applying the same list of 1,960 DE variables [ANOVA F-test $p<0.05$, FC ≥ ±1.20] in Qlucore Omics Explorer was unsuccessful in producing distinct clusters on the PCA plot [SALS (Pink) and Ctrl (Blue)] or hierarchically clustered HeatMap (Figure 5.19); thus, highlighting the heterogeneity that is present within the ECACC non*C9ORF72*-related_SALS patient and control LCL populations.

5.2.2 Alternative Splicing Analysis

Alternatively spliced transcripts (Section 2.3.2.5.2) were predicted at the level of the whole gene by performing an ALT-SPLICE ANOVA using Partek® Genomics Suite™ software version 6.6. In order to reduce the probability of predicting a false positive outcome, attributable to a type I error: a) probesets with a maximum value for log2 transformed signal intensities below three across all of the GeneChips® in the ECACC *C9ORF72*vctrl and non*C9ORF72*-related_SALSvctrl experiment were removed except for instances where there was a significant difference in the expression of a single exon between two groups; b) exons residing in genes whose expression at the whole transcript level was found to be significantly altered [Partek® unadjusted $p<0.05$, FC ≥ ±1.20] were excluded and c) transcript clusters were filtered which had no observable difference in the expression of individual exons (Gillett et al 2009, Rabin et al 2010, Tian et al 2011). In addition, transcripts with fewer than four or greater than forty probesets were removed (n=2,077/17,273) since the presence of such a small or large number of markers makes it prohibitively more difficult to interpret the alternative splicing events occurring within these genes (Whistler et al 2010).

At the 5% significance threshold [Partek® unadjusted p-value (fold-change) ≥0.05 and p-value (alt. splicing) <0.05] this approach identified 2,511 (14.5%) of 17,273 transcripts predicted to be alternatively spliced in the analysis of *C9ORF72*vctrl and a further 3,163 (18.3%) of 17,273 transcripts predicted to be alternatively spliced in the analysis of non*C9ORF72*-related_SALSvctrl. These included: a) 1,765 (70.3%) of 2,511 transcripts that were specifically altered in relation to the G_4C_2 repeat; b) 746 (29.7%) of 2,511 (*C9ORF72*vctrl) or 3,163 (23.6%) (non*C9ORF72*-related_SALSvctrl)

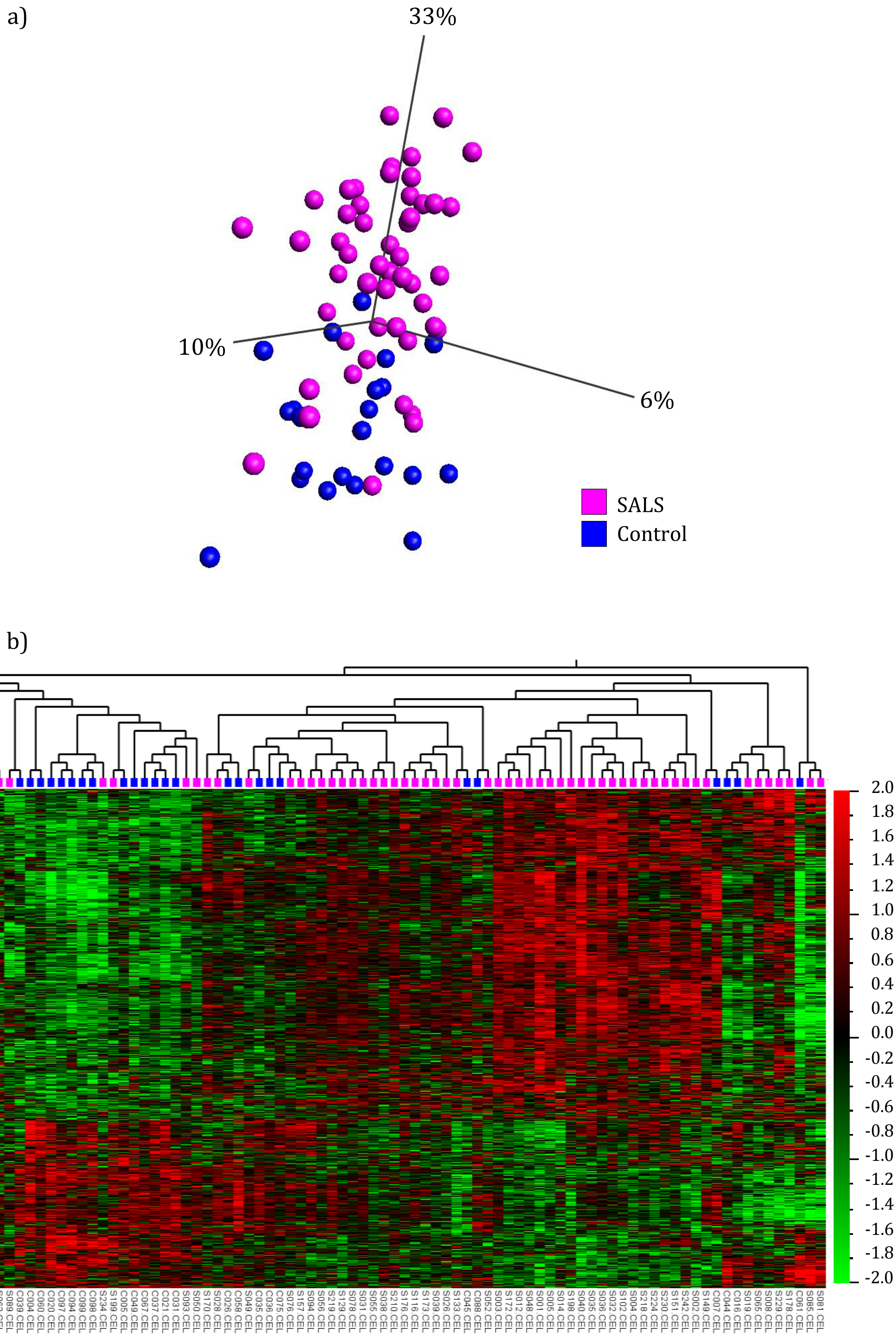
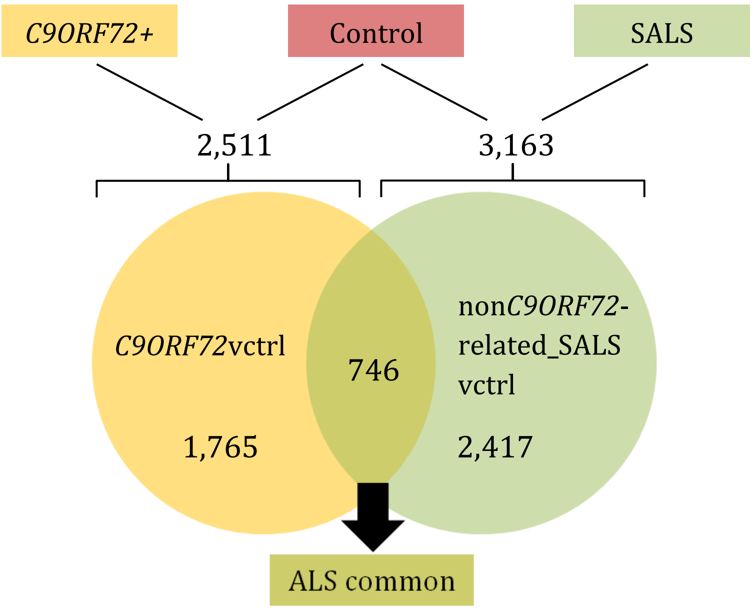


Figure 5.19 Non*C9ORF72*-Related_SALSvCtrl Clustering Analysis Applying the 1,960 List of Variables in Qlucore Omics Explorer [ANOVA F-test p<0.05, FC ≥ ±1.20]

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, ANOVA - analysis of variance, *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control, FC - fold-change and S - sporadic.

transcripts, respectively which are commonly shared and more broadly reflect those changes associated with the wider ALS disease process and c) 2,417 (76.4%) of 3,163 transcripts that are specifically altered in relation to the non-expansion carrying SALS patient derived LCL's (Figure 5.20) [APPENDIX TABLE B11 and B12].



a) *C9ORF72+* specific

#	GO term	Functional category	EASE	Count	p-value
1	GO:0030528	transcription regulator activity	2.98	190	1.30E-05
2	GO:0006357	regulation of transcription from RNA polymerase II promoter	2.94	99	3.40E-04
3	GO:0001882	nucleoside binding	2.35	187	1.30E-03
4	GO:0043167	ion binding	2.21	450	7.40E-04
5	GO:0005524	ATP binding	1.90	168	5.10E-03
6	GO:0016570	histone modification	1.81	22	6.10E-03
7	GO:0000278	mitotic cell cycle	1.66	52	5.60E-03
8	GO:0010629	negative regulation of gene expression	1.47	68	4.00E-03

b) ALS common

#	GO term	Functional category	EASE	Count	p-value
1	GO:0006915	apoptosis	2.95	49	7.70E-06
2	GO:0048871	multicellular organismal homeostasis	2.31	12	6.80E-04
3	GO:0019941	modification-dependent protein catabolic process	1.74	37	7.50E-03
4	GO:0000166	nucleotide binding	1.72	118	3.40E-03
5	GO:0030695	GTPase regulator activity	1.68	31	1.40E-03
6	GO:0008134	transcription factor binding	1.60	34	7.80E-03
7	GO:0043167	ion binding	1.40	200	0.014
8	GO:0048870	cell motility	1.40	21	0.028

c) non*C9ORF72*-related_SALS specific

#	GO term	Functional category	EASE	Count	p-value
1	GO:0016310	phosphorylation	3.04	137	8.70E-05

2	GO:0030182	neuron differentiation	2.17	81	2.70E-04
3	GO:0043169	cation binding	1.86	579	3.70E-03
4	GO:0010828	positive regulation of glucose transport	1.57	8	0.015
5	GO:0043010	camera-type eye development	1.48	24	6.10E-03
6	GO:0009991	response to extracellular stimulus	1.46	41	9.20E-03
7	GO:0035295	tube development	1.46	41	9.20E-03
8	GO:0032559	adenyl ribonucleotide binding	1.46	221	8.20E-03

Figure 5.20 ALT-SPLICE GeneVenn *C9ORF72*vCtrl and Non*C9ORF72*-Related_SALSvCtrl [Partek® unadjusted p-value (fold-change) ≥0.05 and p-value (alt. splicing) <0.05] The Affymetrix® transcript cluster ID's predicted to be alternatively spliced between disease and control LCL's in the ECACC microarray cohort were detected using Partek® Genomics Suite™ software version 6.6 copyright © 2013 (Partek® Inc., St Louis, MO, USA). GeneVenn application freely available online at genevenn.sourceforge.net (University of Southern Mississippi, USA) (Pirooznia et al 2007). Functional Annotation Clustering performed in DAVID bioinformatics resource version 6.7 (david.abccc.ncifcrf.gov) (Huang da et al 2009a, Huang da et al 2009b).

Abbreviations: # - rank, ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, ctrl - control, DAVID - Database for Annotation, Visualisation and Integrated Discovery, EASE - enrichment score, ECACC - European Collection of Cell Cultures, GO - gene ontology, LCL - lymphoblastoid cell line and S - sporadic.

In DAVID a fixed upper limit of 3,000 represents the maximum number of transcript cluster ID's that the software is capable of handling in each run. In view of this, it was not possible, therefore, to conduct down-stream comparative analyses in exactly the same manner as described previously for Partek® generated gene level expression data (Section 5.2.1.2). Since the non*C9ORF72*-related_SALSvctrl alt. splicing list (n= 3,163) could not be interrogated in its entirety, functional annotation clustering was performed instead by exploring the *C9ORF72+* (99.4% of 1,765 ID's mapped), ALS common (99.7% of 746 ID's mapped) or SALS specific (99.0% of 2,417 ID's mapped) lists independently (Figure 5.20). Initially, applying a *Homo sapiens* background and filtering on GOTERM_BP_FAT and GOTERM_MF_FAT gene ontology (GO) terms using 'Medium' classification stringency (Section 2.3.2.5.4), very few biologically enriched categories were returned; only two in fact across all three comparisons (highlighted in red). When the stringency was lowered to remove the Benjamini-Hochberg FDR correction, but maintaining a 5% significance threshold ($p<0.05$) (EASE score ≥1.30), this number was markedly increased (Figure 5.20). Upon re-analysis of the gene lists GO terms associated with the regulation of transcription, ATP binding and histone modification were identified in relation to the G_4C_2 repeat carrying LCL's in contrast to phosphorylation, neuron differentiation/tube development and glucose transport which were described in relation to non-expansion carrying SALS cases. Universally enriched categories included transcription factor binding and regulation of GTPase activity, in addition to protein degradation in the form of proteolysis and apoptosis (programmed cell death) (Figure 5.20).

Graphical outputs from the easyExon 1.0.4 Java-based platform copyright © 2006 to 2014 (National Yang-Ming University, Taiwan) (Chang et al 2008) for the top 5 most highly ranked *C9ORF72*vctrl aberrant splicing events are represented in Figure 5.21. These include transcripts which encode: a) tight junction protein 2 (*TJP2*) [AS-ANOVA p=4.08E-18]; b) peptidylprolyl isomerase F (*PPIF*) [AS-ANOVA p=3.77E-16]; c) nuclear factor of activated T-cells 5 (*NFAT5*) [AS-ANOVA p=1.58E-15]; d) epidermal growth factor receptor (*EGFR*) [AS-ANOVA p=1.67E-14] and e) RNA binding motif protein 5 (*RBM5*) [AS-ANOVA p=4.76E-14] (Figure 5.21). Despite probability values exceeding orders of magnitude below 10^{-14}, bars representing SEM were substantial. Moreover, changes in mean probeset signal intensities associated with the different sample types [*C9ORF72+* (Red) versus Ctrl (Blue)] appeared modest. Consequently, it was decided not to pursue selected targets for qRT-PCR validation.

5.2.3 *C9ORF72*

Following publication of *C9ORF72* haploinsufficiency (Section 1.2.5.4) as a potential mechanism of action in ALS (DeJesus-Hernandez et al 2011) an initial subset of the LCL's (n=14) [*C9ORF72+* (n=7) and Ctrl (n=7)] were assayed against the endogenous standard actin, beta (*ACTB*) in a traditional SYBR® Green based qRT-PCR (Section 2.3. 2.6.5) that used isoform A specific primers [Variant I (NM_001256054) and Variant II (NM_145005) (Figure 5.22)] designed to target the 3'UTR (Figure 5.23a) of the full length protein coding mRNA. A subsequent 1.64-fold reduction in the abundance of isoform A was confirmed in carriers of the G_4C_2 repeat relative to controls ($p<0.05^*$) (Figure 5.24) (Cooper-Knock et al 2013b).

A similar strategy was extended to include both isoform A (full length) and isoform B (truncated) [Variant III (NM_018325) (Figure 5.22)] specific transcripts with 18S ribosomal RNA (*18SrRNA*) now selected as the new internal reference control gene (Figure 5.23b). The size of the validation cohort was also increased to accommodate all *C9ORF72+* FALS and apparently SALS cases in the ECACC discovery (Section 4.1.1) and replication (Section 4.1.2) cohorts combined (n=75) [RIN score of 7.0 or above]

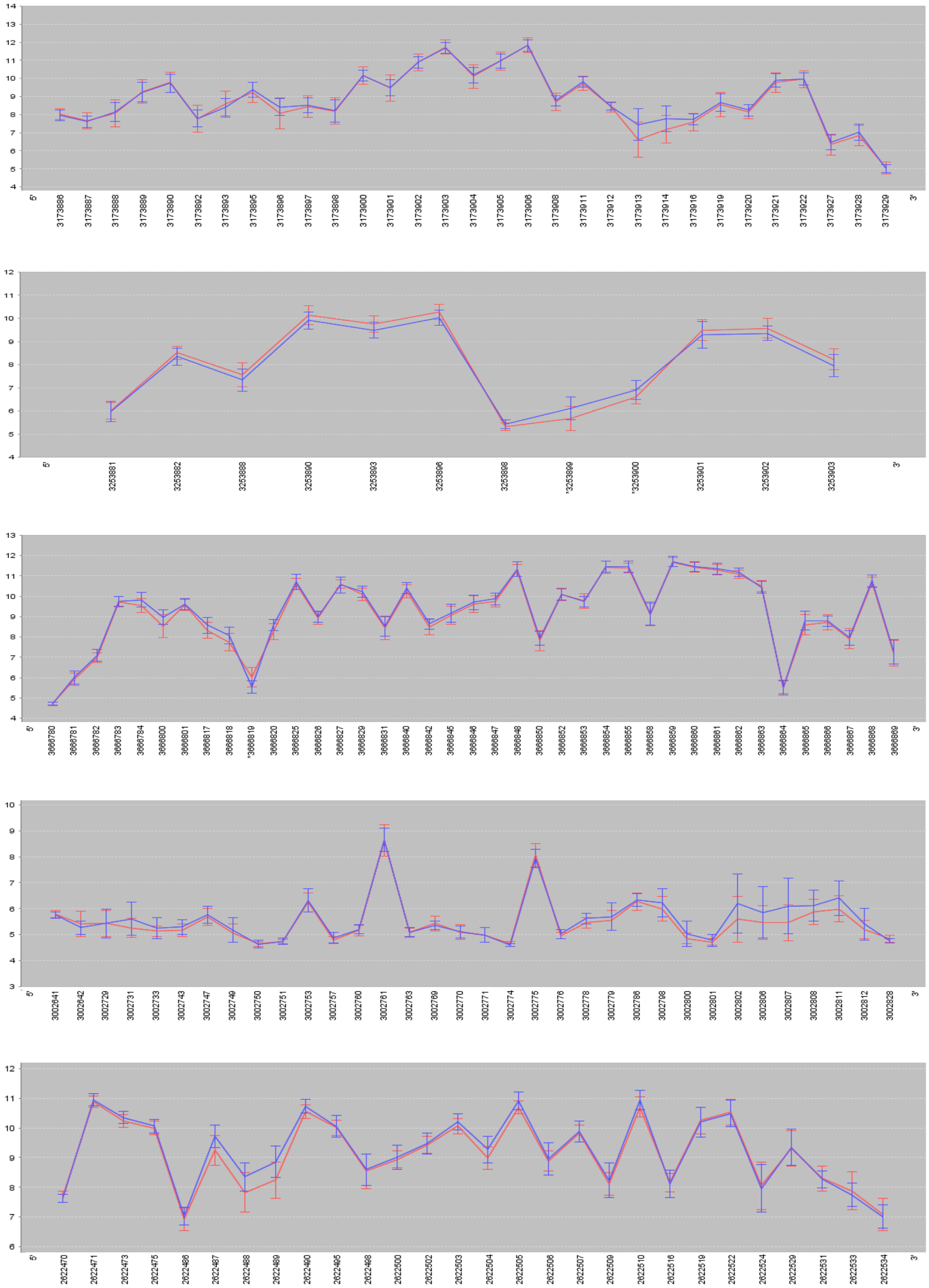


Figure 5.21 Graphical Representations of the *C9ORF72*vCtrl Top 5 Most Significant Aberrant Splicing Events [Partek® unadjusted p-value (fold-change) ≥0.05 and p-value (alt. splicing) <0.05] Lists of AS transcripts predicted in Partek® Genomics Suite™ software version 6.6 copyright © 2013 (Partek® Inc., St Louis, MO, USA). Mean probeset signal intensities and SEM plotted using the easyExon 1.0.4 Java-based platform copyright © 2006 to 2014 (microarray.ym.edu.tw/easyExon) (National Yang-Ming University, Taiwan) (Chang et al 2008).

Key: *C9ORF72+* 🟥 and Ctrl 🟦

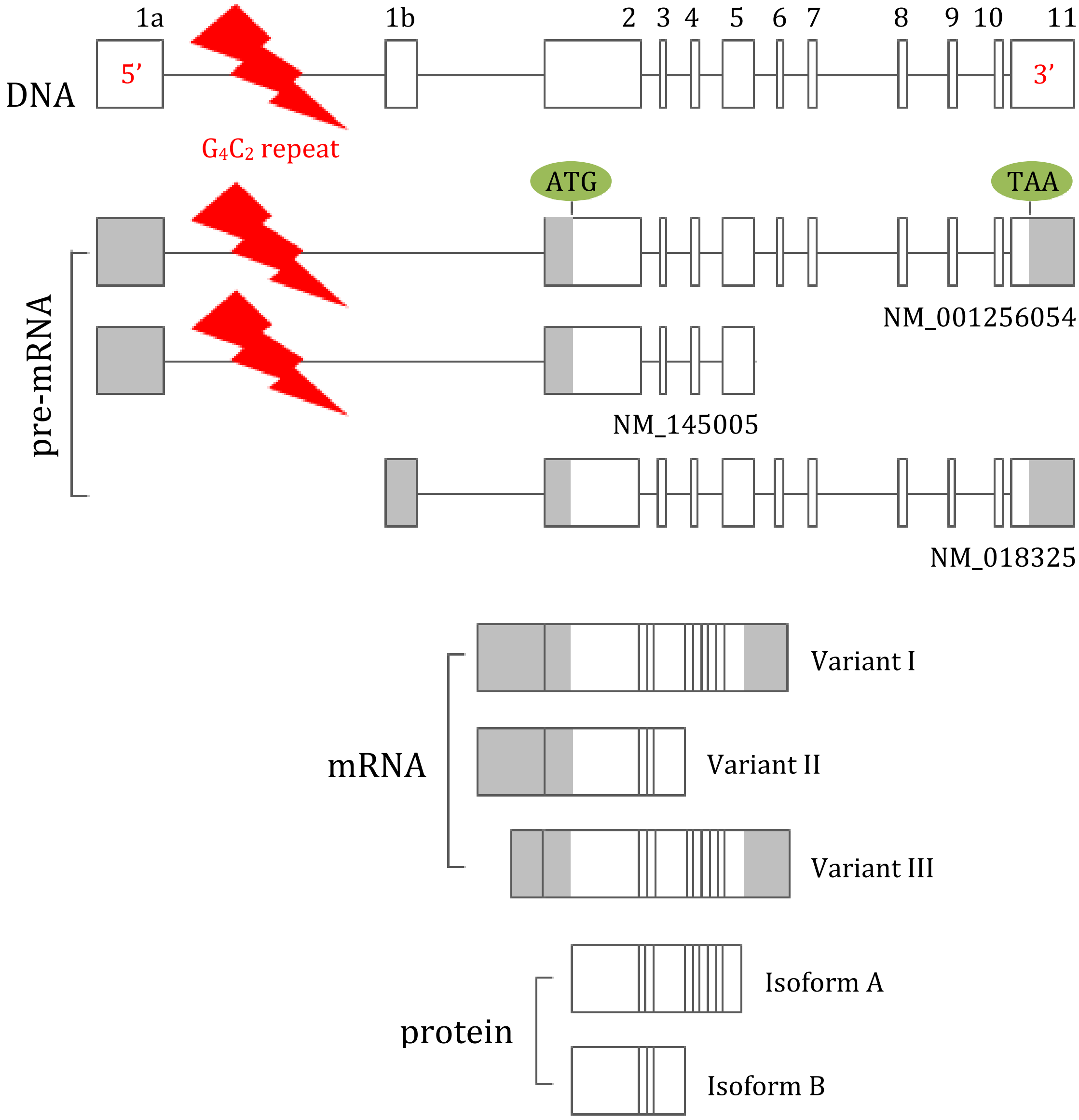
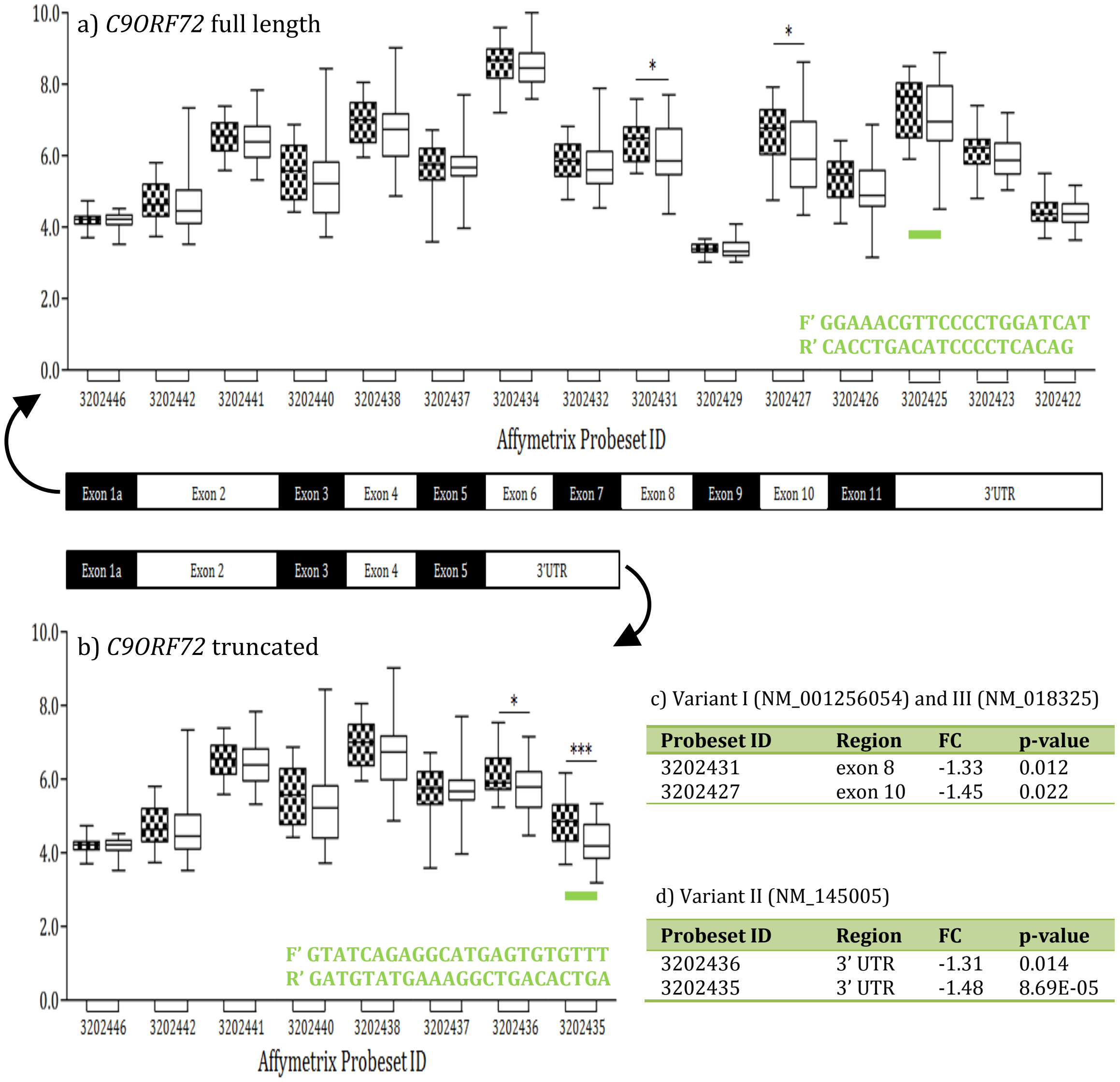


Figure 5.22 Schematic of *C9ORF72* Transcript Variants and Protein Isoforms The *C9ORF72* gene consists of 11 exons which span a 27.3Mb region of the human 9p21.2 locus. There are multiple alt. spliced transcripts in the Ensembl database (ensembl.org) (Flicek et al 2014); three of which were protein coding. These include two full length variants with alternate first exons [Variant I (NM_001256054) exon 1a, 2-11 and Variant III (NM_018325) exon 1b, 2-11] in addition to a stable truncation [Variant II (NM_145005) exon 1a, 2-5]. The translational start site (ATG/methionine codon) resides in exon 2. As a consequence only two protein isoforms are produced from the three different mRNA sequences [Isoform A (54.3kDa) 481a.a. and Isoform B (24.8kDa) 222a.a]. The hexanucleotide G_4C_2 repeat expansion identified in ALS and FTLD patients (DeJesus-Hernandez et al 2011, Renton et al 2011) is located between exons 1a and 1b in the first intronic region and is situated upstream of the translational start site (illustrated by the red lightning bolt). Pathogenicity is thought to arise when the expanded allele contains 30 or more copies of the 6bp repeat (Cooper-Knock et al 2012b). Figure adapted from Donnelly et al (2013) and Fernandes et al (2013).

Key: Grey – non-coding exons [5’ UTR upstream of ATG start codon and 3’ UTR downstream of TAA stop codon] and White – coding exons.

Abbreviations: 3’ - three prime, 5’ - five prime, ALS - Amyotrophic Lateral Sclerosis, alt. - alternative, *C9ORF72* - chromosome 9 open reading frame 72, FTLD - frontotemporal lobar degeneration, mRNA - messenger RNA, pre-mRNA - precursor mRNA and UTR - untranslated region.



c) Variant I (NM_001256054) and III (NM_018325)

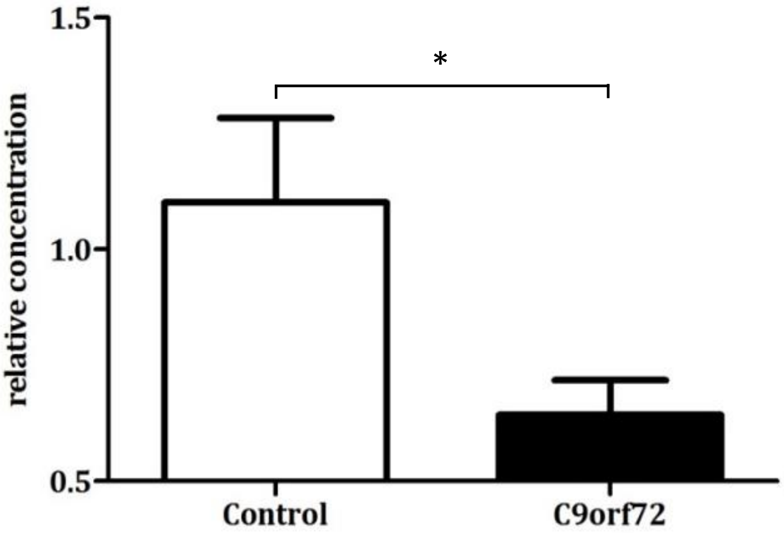
Probeset ID	**Region**	**FC**	**p-value**
3202431	exon 8	-1.33	0.012
3202427	exon 10	-1.45	0.022

d) Variant II (NM_145005)

Probeset ID	**Region**	**FC**	**p-value**
3202436	3' UTR	-1.31	0.014
3202435	3' UTR	-1.48	8.69E-05

Figure 5.23 Exon Level GC-RMA Normalised Signal Intensities for the Differentially Spliced *C9ORF72* Transcript Variants I/III (Isoform A) and II (Isoform B) Affymetrix® Human Exon 1.0ST GeneChip® Array probeset ID's for a) *C9ORF72* full length transcript variant I (NM_001256054) and III (NM_018325) and b) *C9ORF72* truncated transcript variant II (NM_145005) plotted (x-axis) against GC-RMA normalised signal intensities (y-axis) for control (n=26) [checkerboard pattern] and *C9ORF72+* (n=38) [white] LCL's in the final ECACC microarray cohort (Table 5.1). Box and Whisker plots generated using GraphPad Prism® software version 5.04 copyright © 1992 to 2014 (GraphPad® Software Inc., CA, USA). Whiskers represent the minimum and maximum raw expression values. Significance was determined in Partek® Genomics Suite™ software version 6.6 © copyright 2013 (Partek® Inc., St Louis, MO, USA) [p<0.05* and p<0.001***]. Fold-changes (FC) and probability (p)-values provided in panels c) full length isoform A and d) truncated isoform B. Primer sequences for qRT-PCR and their binding sites on the cDNA template are represented in Green.

Abbreviations: 3' - three prime, 5' - five prime, *C9ORF72* - chromosome 9 open reading frame 72, cDNA - complementary DNA, ECACC - European Collection of Cell Cultures, F' - forward primer sequence, LCL - lymphoblastoid cell line, qRT-PCR - quantitative real-time PCR, R' - reverse primer sequence, RMA - Robust Multi-array Average, ST - sense target and UTR - untranslated region.



			C9ORF72	*ACTB*	ΔcT	ΔΔcT	Conc.	-SD	+SD	Fold	p-value
Control	C006	LC0455	21.98	13.81	8.17						
	C021	LCa0076	22.44	14.57	7.87						
	C026	BC6295	22.52	13.05	9.47						
	C031	SC3709	21.97	13.76	8.21						
	C036	SMa0156	22.48	13.30	9.18						
	C037	BC6448	22.76	13.41	9.35						
	C099	SC3282	22.20	14.28	7.92						
	Mean		22.34	13.74	8.60	0.00	1.00	1.63	0.61		
	SD				0.71						
C9ORF72+	F046	LP0008	22.49	13.69	8.80						
	F106	BP6029	22.65	13.71	8.94						
	S059	SP3041	23.20	12.73	10.47						
	S110	SP3298	23.12	13.77	9.35						
	S121	SP3420	23.16	13.85	9.31						
	S132	SP3413	22.94	13.61	9.33						
	S186	SP3431	22.84	13.87	8.97						
	Mean		22.91	13.60	9.31	0.71	0.61	0.90	0.41	1.64	0.029
	SD				0.56						

Figure 5.24 Reduced *C9ORF72* Transcript Variant I/III (Isoform A) Levels Detected by qRT-PCR in a Subpopulation of ECACC LCL's in the Discovery Cohort Relative concentrations were measured against the standard housekeeping gene *ACTB.* Means and SEM plotted using GraphPad® Prism software version 5.04 copyright © 1992 to 2014 (GraphPad Software Inc., USA). Probability values calculated in Microsoft Excel 2010 (Microsoft Corporation, UK) with a one tailed student's t-test applied. Gene expression changes were confirmed if the direction of change was the same as the microarray with p<0.05*.

Abbreviations: *ACTB* - actin, beta, BC - Birmingham control, BP - Birmingham patient, Ca - Cambridge, C - control, *C9ORF72* - chromosome 9 open reading frame 72, cT - cycle threshold, Δ - delta, ECACC - European Collection of Cell Cultures, F - familial, LC - London control, LCL - lymphoblastoid cell line, LP - London patient, Ma - Manchester, qRT-PCR - quantitative real-time PCR, SC - Sheffield control, S - sporadic, SD - standard deviation, SEM - standard error of the mean and SP - Sheffield patient.

and an additional 28 controls (total n=35). In order to achieve maximum statistical power cDNA synthesis reactions were performed on pooled RNA samples with 5X 200ng starting material in each pool to efficiently run as many samples as possible on a single 96-well plate (Section 2.3.2.6.3).

Contrary to those previously discussed, these latest findings suggest overall there is no discernable difference in the abundance of isoform A or B (Figure 5.25) specific transcripts between LCL's carrying the G_4C_2 repeat and controls. It was of interest to note, however, the presence of two distinct groupings on the qRT-PCR scatter plot for isoform A (Figure 5.25a) with the first cluster, highlighted in yellow, appearing to have a significantly higher level of expression than controls [⇧1.20-fold, ($p<0.01$ **) (🟨)] and a second cluster, highlighted in green, appearing to have a significantly lower level of expression than the controls [⇩1.23-fold, ($p<0.01$**) (🟩)]. Further qRT -PCR analyses on a small number of individually selected targets was performed in order to ascertain whether or not the differences observed in *C9ORF72* expression could be correlated with a fast (survival <2yrs) versus slow (survival ≥4yrs) disease progression. However, no evidence in support of this hypothesis was obtained.

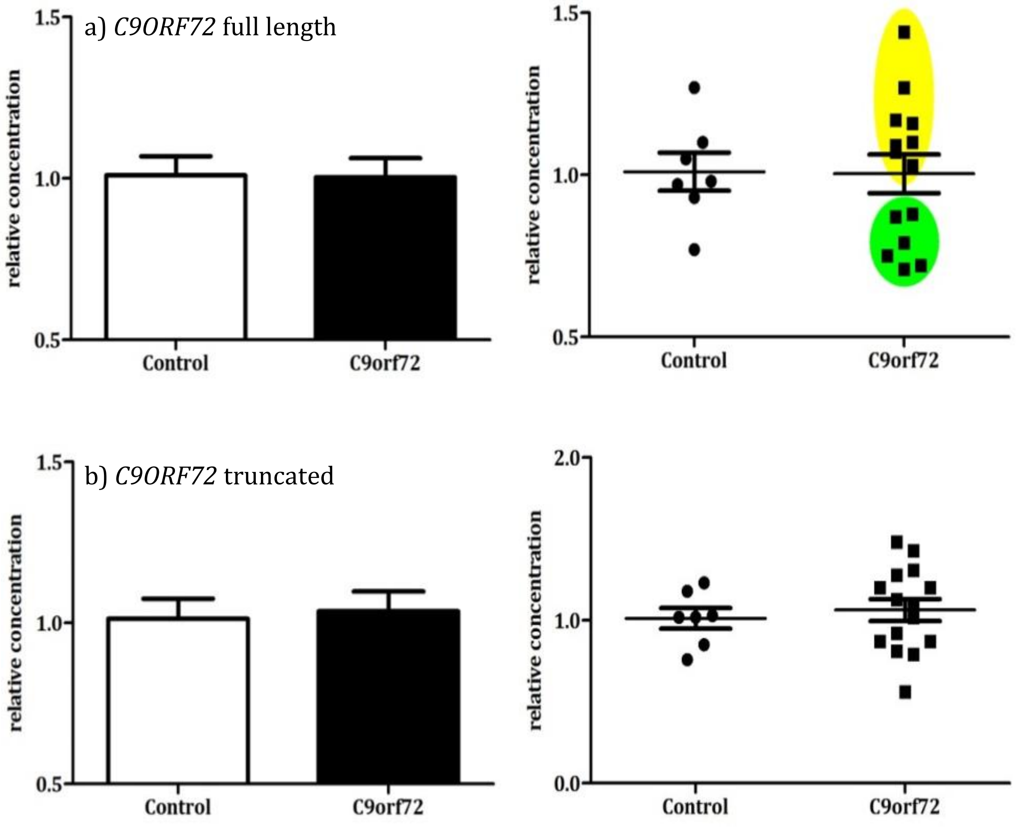


Figure 5.25 qRT-PCR of Pooled RNA *C9ORF72* Full Length Variants I/III (Isoform A) and Truncated Variant II (Isoform B) Specific Transcripts Relative concentrations measured against the standard housekeeping gene *18SrRNA*. The box (left) and scatter plots (right) were generated using GraphPad® Prism software version 5.04 copyright © 1992-2014 (GraphPad Software Inc., USA). The probability values were calculated in Microsoft Excel 2010 (Microsoft Corporation, UK) applying a one tailed student's t-test.

Abbreviations: *18SrRNA* - 18S ribosomal RNA, *C9ORF72* - chromosome 9 open reading frame 72 and qRT-PCR - quantitative real-time PCR.

5.2.4 qRT-PCR Validation of *C9ORF72* RNA Binding Partners

An RNA pull-down assay was developed in house by Dr Matthew Walsh (SITraN) and colleagues from the Department of Molecular Biology & Biotechnology and Chemical Engineering at the Life Science Interface (ChELSI) institute, University of Sheffield as a detection method for the identification of key candidate binding partners (Cooper-Knock et al 2014b) of the hexanucleotide expansion recently discovered in *C9ORF72* (DeJesus-Hernandez et al 2011, Renton et al 2011) (Section 1.2.5.4). Briefly, *in vitro* transcribed 3' biotinylated molecules of RNA containing 5X repeats of the GGGGCC sequence (AAAAUU for the control experiments) were pre-incubated with protein extracts derived from post-mortem cerebellar granule neurones or human neuronal SH-SY5Y cell lines (Cooper-Knock et al 2014b); including, both cellular lysates, and nuclear separated fractions prior to irradiation with UV light. The RNA-protein complexes which form are captured with streptavidin Sepharose® and eluted by RNase digestion. Peptide products are then analysed using mass spectrometry. Across the three different extracts (i.e. total, nuclear and cerebellum), this approach identified 103 unique protein species including forty which are encoded by genes found to be dysregulated in the ECACC *C9ORF72*vctrl analysis of the LCL's [Partek® unadjusted $p<0.05$, FC ≥ ±1.20] (Table 5.9). Nine candidates (*EIF4H, PURA, HNRNPA0, HNRNPF, HNRNPH2, NUDT21, FUS, RBM3* and *RPL22*) were selected for qRT-PCR using either traditional SYBR® Green technology (Section 2.3.1.6) or IDT PrimeTime® Mini qPCR Assays (Section 2.3.2.6.6). Of these nine, 77.8% (n=7/9) validated including purine-rich element binding protein A (*PURA*) ($p<0.01$**) (Figure 5.26), *HNRNPA0* ($p<0.01$ **), *FUS* ($p<0.01$**), *NUDT21* ($p<0.01$**) (Figure 5.12), *HNRNPF* ($p<0.01$**) (Figure 5.13) (Section 5.2.1.3.3), *EIF4H* ($p<0.001$***) and *RPL22* ($p<0.01$**) (Section 5.2.1.4.1) (Figure 5.15). *HNRNPH2* was not significant (Section 5.2.1.3.3) (Figure 5.13) and for *RBM3* a small trend in the same direction as the microarray was observed (Figure 5.12) (Section 5.2.1.3.3).

Additional transcripts encoding a further eleven of Dr Matthew Walsh's $GGGGCC_{(5)}$

Symbol	**Gene Name**	**Direction**	**Fold**	**p-value**	**Nuclear**	**Cerebellum**	**Total**	**Reference**
ATP5B***	ATP synthase, H^+ transporting, mitochondrial F1 complex, beta polypeptide	⇧	1.11	0.013			X	
CALM1	calmodulin 1 (phosphorylase kinase, delta)	⇧	1.24	3.01E-03		X		
CPSF6***	cleavage and polyadenylation specific factor 6, 68kDa	⇩	1.12	8.08E-04			X	
DNAJC9	DnaJ (Hsp40) homolog, subfamily C, member 9	⇧	1.22	0.012			X	
EIF4H	eukaryotic translation initiation factor 4H	⇧	1.31	5.01E-03			X	
FUS	fused in sarcoma	⇧	1.23	7.50E-04	X	X	X	(Mori et al 2013b)
HDGFRP3	hepatoma-derived growth factor, related protein 3	⇧	1.49	1.56E-03		X		
HNRNPA0	heterogeneous nuclear ribonucleoprotein A0	⇧	1.23	2.35E-07	X			
HNRNPA2B1	heterogeneous nuclear ribonucleoprotein A2/B1	⇧	1.09	0.038	X		X	(Mori et al 2013b)
HNRNPAB	heterogeneous nuclear ribonucleoprotein A/B	⇧	1.26	6.49E-05	X			
HNRNPD	heterogeneous nuclear ribonucleoprotein D (AU-rich element RNA binding protein 1, 37kDa)	⇧	1.19	2.65E-04	X			
HNRNPF	heterogeneous nuclear ribonucleoprotein F	⇧	1.22	6.15E-04	X		X	
HNRNPH2	heterogeneous nuclear ribonucleoprotein H2 (H')	⇧	1.28	0.024	X		X	(Lee et al 2013b)
HNRNPR	heterogeneous nuclear ribonucleoprotein R	⇧	1.19	7.78E-04	X	X		(Mori et al 2013b)
HNRNPUL1	heterogeneous nuclear ribonucleoprotein U-like 1	⇧	1.12	3.20E-03			X	
HMGA1***	high mobility group AT-hook 1	⇧	1.16	0.011	X			
ILF2	interleukin enhancer binding factor 2, 45kDa	⇧	1.19	1.52E-03	X	X		(Mori et al 2013b)
MYH9***	myosin, heavy chain 9, non-muscle	⇩	1.08	0.040			X	
MYL6***	myosin, light chain 6, alkali, smooth muscle and non-muscle	⇧	1.19	0.041			X	
NACA***	nascent polypeptide-associated complex alpha subunit	⇧	1.18	0.017			X	
NCL	nucleolin	⇧	1.13	0.015	X	X	X	
NPM1***	nucleophosmin (nucleolar phosphoprotein B23, numatrin)	⇧	1.06	0.034			X	
NUDT21	nudix (nucleoside diphosphate linked moiety X)-type motif 21	⇧	1.20	6.68E-05			X	
_PA2G4_	proliferation-associated 2G4, 38kDa	⇧	1.13	0.012			X	

*PURA****	purine-rich element binding protein A	⇧	1.20	1.39E-05		X		(Sareen et al 2013, Xu et al 2013)
*PURB****	purine-rich element binding protein B	⇧	1.14	0.020		X	X	
RBM3	RNA binding protein motif (RNP1, RRM) protein 3	⇧	1.22	9.22E-05	X		X	
*RPL22****	ribosomal protein L22	⇧	1.40	1.06E-04			X	
SEPT2	septin 2	⇧	1.10	7.82E-03			X	
SERBP1	SERPINE1 mRNA binding protein 1	⇧	1.11	0.027			X	
SFPQ	splicing factor proline/glutamine-rich	⇧	1.14	0.028	X			(Mori et al 2013b)
SFRS3	serine/arginine-rich splicing factor 3	⇧	1.20	0.015		X		
*SRP14****	signal recognition particle 14kDa (homologous Alu RNA binding protein)	⇧	1.34	1.75E-03		X	X	
TAF15	TAF RNA polymerase II, TATA box binding protein (TBP)-associated factor, 60kDa	⇧	1.18	4.39E-04			X	
THOC4	THO complex 4	⇧	1.17	0.027			X	
*TRMT112****	tRNA methyltransferase 11-2 homolog (*S. cerevisiae*)	⇧	1.14	0.017			X	
U2AF2	U2 small nuclear RNA auxiliary factor 2	⇧	1.19	1.76E-03	X		X	
XRCC6	X-ray repair complementing defective repair in Chinese hamster cells 6	⇩	1.16	0.011	X		X	
YWHAG	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, gamma polypeptide	⇧	1.19	9.41E-04		X		
YWHAH	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta polypeptide	⇧	1.27	1.70E-03		X		
Total					**15**	**12**	**27**	

Table 5.9 RNA Pull-Down List of MW Predicted GGGGCC$_{(5)}$ Binding Partners (n=40/103) which are Differentially Expressed in *C9ORF72+* LCL's from the ECACC Microarray Study [Partek® unadjusted p<0.05, FC ≥ ±1.20] *C9ORF72* specific gene expression changes not detectable in non*C9ORF72*-related_SALS cases or neurologically normal, healthy control subjects are denoted by three asterisks inserted immediately after the gene symbol in column 1. Candidates taken forward for qRT-PCR validation are shaded in grey.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, ECACC - European Collection of Cell Cultures, FC - fold-change, LCL - lymphoblastoid cell line, MW - Dr Mathew Walsh, qRT-PCR - quantitative real-time PCR and S - sporadic.

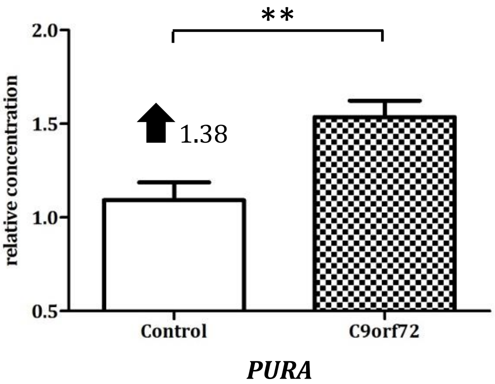


Figure 5.26 *PURA* qRT-PCR Validation Relative concentrations were measured against the standard housekeeping gene *18SrRNA*. Means and SEM plotted in GraphPad® Prism software version 5.04 copyright © 1992-2014 (GraphPad Software Inc., USA). Probability values were calculated in Microsoft Excel 2010 (Microsoft Corporation, UK) with a one tailed student's t-test applied. Gene expression changes confirmed if the direction of change (arrow) was the same as the microarray with p<0.05* (p<0.01**).

Abbreviations: *18SrRNA* - 18S ribosomal RNA, *C9ORF72* - chromosome 9 open reading frame 72, *PURA* - purine-rich element binding protein A, qRT-PCR - quantitative real-time PCR and SEM - standard error of the mean.

RNA binding partners were also predicted to be aberrantly spliced in the ECACC LCL analysis of *C9ORF72*vctrl (Table 5.10) [Partek® unadjusted p-value (fold-change) ≥ 0.05 and p-value (alt. splicing) <0.05]. These were comprised of: calmodulin 1 (*CAL M1*), a murine biomarker of ALS in the SOD1^{G93A} transgenic animal model (Calvo et al 2012) [AS-ANOVA p<0.0001]; heterogeneous nuclear ribonucleoprotein H1 (*HNRNP H1*) [AS-ANOVA p<0.01] and H3 (2H9) (*HNRNPH3*) [AS-ANOVA p<0.05]; chromatin architectural factor high mobility group AT-hook 1 (*HMGA1*) (Malini et al 2011, Sgarra et al 2010) [AS-ANOVA p<0.05]; cell-cycle regulated SFRS protein kinase 2 (*SRP K2*) [AS-ANOVA p<0.05]; splicing factors, arginine/serine-rich 1 (SF2) (*SFRS1*) [AS-ANOVA p<0.01], 2 (SC35) (*SFRS2*) [AS-ANOVA p<0.0001], 5 (Srp40) (*SFRS5*) [AS-AN OVA p<0.0001] and 7, 35kDa (9G8) (*SFRS7*) [AS-ANOVA p<0.0001]; actin filament binding protein tropomyosin 2, beta (*TPM2*) [AS-ANOVA p<0.001] and transcriptional co-activator PC4 and SFRS1 interacting protein 1 (*PSIP1*) [AS-ANOVA p<0.0001], that stimulates homologous recombination, as well as mechanisms of DSB repair, to inhibit the induction of apoptosis in response to environmental stress (Daugaard et al 2012).

Symbol	**Gene**	**p-value (alt.splicing)**	**Nuclear**	**Cerebellum**	**Total**	**Reference**
*CALM1****	calmodulin 1 (phosphorylase kinase, delta)	9.71E-09		X		
*HMGA1****	high mobility group AT-hook 1	0.049	X			
HNRNPH1	heterogeneous nuclear ribonucleoprotein H1 (H)	4.18E-03	X	X	X	
HNRNPH3	heterogeneous nuclear ribonucleoprotein H3 (2H9)	1.56E-03	X		X	
PSIP1	PC4 and SFRS1 interacting protein 1	2.04E-07		X		
SFRS1	splicing factor, arginine/serine-rich 1 (splicing factor 2, alternate splicing factor)	9.94E-03	X	X	X	(Reddy et al 2013)
SFRS2	splicing factor, arginine/serine-rich 2	6.22E-05	X	X	X	(Lee et al 2013b)
*SFRS5****	splicing factor, arginine/serine-rich 5	8.59E-14			X	
SFRS7	splicing factor, arginine/serine-rich 7, 35kDa	6.17E-06		X		
SRPK2	SFRS protein kinase 2	0.047		X		
TPM2	tropomyosin 2 (beta)	1.97E-04			X	
Total			**5**	**7**	**6**	

Table 5.10 RNA Pull-Down List of MW Predicted GGGGCC$_{(5)}$ Binding Partners (n=11/103) which are Aberrantly Spliced in the *C9ORF72+* LCL's from the ECACC Microarray Study [Partek® unadjusted p-value (fold-change) ≥0.05 and p-value (alt. splicing) <0.05] *C9ORF72* specific alternative splicing events not detectable in non*C9ORF72*-related_SALS cases or neurologically normal, healthy control subjects are denoted by three asterisks inserted immediately after the gene symbol in column 1.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, ECACC - European Collection of Cell Cultures, LCL - lymphoblastoid cell line, MW - Dr Mathew Walsh, S - sporadic and SFRS - splicing factor, arginine/serine-rich.

Graphical representations from the easyExon 1.0.4 Java-based platform copyright © 2006 to 2014 (National Yang-Ming University, Taiwan) (Chang et al 2008) of *CALM1, SRPK2, SFRS5, SFRS7* and *HNRNPH1* are illustrated in Figure 5.27. Again, changes in mean probeset signal intensities between different sample types [*C9ORF72+* (Red) and Ctrl (Blue)] appeared modest and with large values for the SEM, it was decided not to pursue selected targets for qRT-PCR validation (Section 5.2.2).

5.3 DISCUSSION

5.3.1 Frequency of the G_4C_2 Repeat in a Large Caucasian Cohort

Patient derived LCL's [120-FALS and 500-SALS] selected from the National MNDA DNA Bank, which were later recruited to the ECACC discovery (n=370) (Section 4. 1.1) and replication (n=250) (Section 4.1.2) cohorts were screened for the *C9ORF72* expansion, using the repeat-primed PCR method described by Renton et al (2011); with a minor adjustment made to the ratio of forward, reverse and anchor primers (Cooper-Knock et al 2012b). G_4C_2 repeat lengths of more than 30 copies were detected at an overall frequency of 14.4% (n=89/620), incorporating 40.8% of FALS (n=49/120) [42-FALS, 1-FALS+PD and 6-PBP (familial)] and a further 8.2% of SALS (n=41/500) [40-SALS and 1-PBP (sporadic)]. These figures were consistent with a number of previously published statistics for other Caucasian populations from the Northern States of America and Canada (DeJesus-Hernandez et al 2011) or Western Europe including: Italy (Xi et al 2012); Belgium (Debray et al 2013, Gijselinck et al 2012, Renton et al 2011, van Rheenen et al 2012); Germany (Majounie et al 2012); Spain (Garcia-Redondo et al 2013) and the UK (Beck et al 2013, Cooper-Knock et al 2012b). Global incidence rates vary but have generally been considered to be highest in Scandinavia [Finland 46.4% of FALS (n=52/112) and 21.1% of SALS (n=61/ 289); Sweden 57.1% of FALS (n=8/14) and 12.2% of SALS (n=9/74) (Majounie et al 2012, van der Zee et al 2013)] and lowest across Asia and the Far East [China 6.7% of FALS (n=1/15) and 0.9% of SALS (n=1/113); Japan 3.4% of FALS (n=2/58) and 0.4% of SALS (n=2/552) and Taiwan 18.2% of FALS (n=4/22) and 2.0% of SALS (n =2/102) (Jiao et al 2014, Konno et al 2013, Liu et al 2013a, Ogaki et al 2012, Tsai et

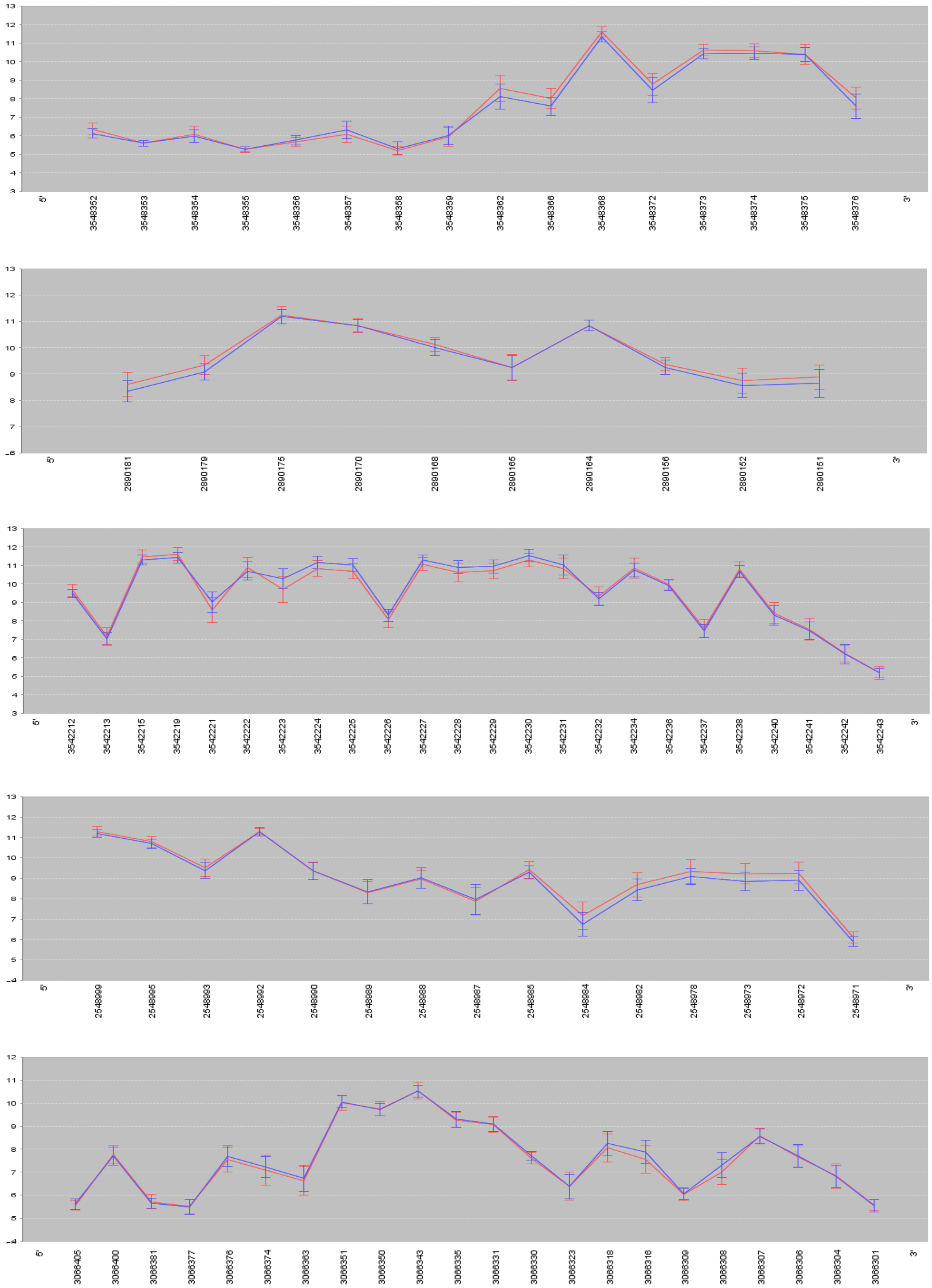


Figure 5.27 Graphical Representations of *C9ORF72+* GGGGCC$_{(5)}$ RNA Binding Partners Top 5 Most Significant Aberrant Splicing Events [Partek® unadjusted p-value (fold-change) ≥0.05 and p-value (alt. splicing) <0.05] Lists of AS transcripts predicted in Partek® Genomics Suite™ software version 6.6 copyright © 2013 (Partek® Inc., St Louis, MO, USA). The mean probeset signal intensities and SEM were plotted using the easyExon 1.0.4 Java-based platform copyright © 2006 to 2014 (microarray.ym.edu.tw/easyExon) (National Yang-Ming University, Taiwan) (Chang et al 2008).

Key: *C9ORF72+* 🟥 and Ctrl 🟦

al 2012, Zou et al 2013b)].

The minor allele (A) of surrogate marker rs3849942 and a 42- or 82-SNP haplotype commonly shared by G_4C_2 repeat carriers of all ethnicities has led to the hypothesis that the expansion has descended from a single common ancestor originating from Finland around 500 A.D. (i.e. ~100 to 250 generations ago which roughly coincides with the fall of the Roman empire and the start of the Viking's invasion of Europe), rather than recurrent *de novo* mutations having occurred throughout history (Mok et al 2012, Pliner et al 2014, Smith et al 2013).

5.3.2 *C9ORF72* and Mutations in Other ALS-FTLD Causative Genes

The frequent observation of incomplete penetrance in ALS-FTLD pedigrees with an apparent AD mode of transmission provides evidence which supports an oligogenic model of the disease (van Blitterswijk et al 2012a). There have been several reports in the literature of patients carrying more than one mutation in multiple ALS-FTLD causative genes. *C9ORF72* for example has been found in combination with *TARDBP* in <2.0% of cases (Chio et al 2012c), *FUS* or *SOD1* in <0.9% of cases (van Blitterswijk et al 2012a) and *OPTN* in ~0.4% of cases (Cooper-Knock et al 2012b, Millecamps et al 2012); among others listed in Table 5.11, relating to ALS, and in combination with *TARDBP* in 1.3% of cases (Kaivorinne et al 2014), *PSEN2* in 1.9% of cases (Ferrari et al 2012), *PGRN* in 1.4% of cases (Lashley et al 2014, Mignarri et al 2014) and *MAPT* in 0.5% of cases (King et al 2013, van Blitterswijk et al 2013b) relating to FTLD.

Across the ECACC discovery (Section 4.1.1) and replication (Section 4.1.2) cohorts of LCL's there were two examples of oligogenic inheritance including: One involving a single *C9ORF72+* FALS patient with an *OPTN* mutation which occurs at a higher than previously reported frequency of 0.8% (Section 5.3.2.1) (Cooper-Knock et al 2012b) and a second involving an *C9ORF72+* SALS patient with an *TARDBP* mutation which occurs at a lower than previously reported frequency of 0.2% (Section 5.3.2.2) (Chio et al 2012c). Concurrence of the G_4C_2 repeat with a second genetic variant of pathological significance in ALS and/or FTLD is predicted to have arisen at a much greater incidence than what would ordinarily be expected by chance ($p=1.6x10^{-7}$) (van Blitterswijk et al 2012a). It is also likely that this is a fairly conservative estimate since

	Frequency	Reference(s)	Comments
ALS Loci			
Common Co-occurrences			
TARDBP	~1.5-1.8%	(Chio et al 2012c)	(Section 1.2.5.2.1)
VAPB	0.9%	(van Blitterswijk et al 2012b)	(Section 1.2.5.1.5)
FUS	<0.9%	(van Blitterswijk et al 2012a)	(Section 1.2.5.2.2)
SOD1	<0.9%	(van Blitterswijk et al 2012a)	(Section 1.2.5.1.1)
Rarer Co-occurrences			
ANG	~0.2-1.1%	(Williams et al 2013)	(Section 1.2.5.2.3)
OPTN	0.4%	(Cooper-Knock et al 2012b, Millecamps et al 2012)	(Section 1.2.5.1.7)
UBQLN2	0.4%	(Kenna et al 2013)	(Section 1.2.5.2.6)
CHMP2B	0.2%	(Kenna et al 2013)	(Section 1.2.5.2.8)
FTLD Loci			
PSEN2	1.9%	(Ferrari et al 2012)	(Section 1.2.5.3.3)
PGRN	1.4%	(Lashley et al 2014, Mignarri et al 2014)	(Section 1.2.5.3.2)
TARDBP	1.3%	(Kaivorinne et al 2014)	(Section 1.2.5.2.1)
MAPT	0.5%	(King et al 2013, van Blitterswijk et al 2013b)	(Section 1.2.5.3.1)

Table 5.11 Oligogenic Frequencies of the *C9ORF72* G_4C_2 Repeat Expansion in ALS and FTLD

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *ANG* - angiogenin, *C9ORF72* - chromosome 9 open reading frame 72, *CHMP2B* - charged multivesicular protein 2B, FTLD - frontotemporal lobar degeneration, *FUS* - fused in sarcoma, *MAPT* - microtubule associated protein tau, *OPTN* - optineurin, *PGRN2* - progranulin 2, *PSEN2* - presenilin 2, *SOD1* - copper/zinc superoxide dismutase 1, *TARDBP* - trans-active response (TAR) DNA binding protein, *UBQLN2* - ubiquilin 2 and *VAPB* - vesicle associated membrane protein (VAMP) associated protein B.

many previously published studies (Blasco et al 2013, Hewitt et al 2010, Kuhnlein et al 2008b) have routinely excluded cases where there is a known mutational change from any further genetic screening (Sreedharan et al 2008).

5.3.2.1 *C9ORF72* and *OPTN*

Sheffield patient [F056-(SP3462)] is one of the familial ALS cases known to carry the expansion in *C9ORF72* which was also identified as having a heterozygous c.964G>A (p.E322K) missense mutation in exon 10 of the *OPTN* gene. The single base substitution is localised to a highly conserved coiled-coil region of the mature peptide sequence (Bury et al 2015). *In silico* analysis predicts that a switch at the position of the 322nd amino acid from the small, acidic residue glutamate to the substantially larger and basic residue, lysine would serve to decrease overall stability and is likely to be pathogenic. Although initially reported as a non-synonymous SNP, the minor allele (A) of rs523747 (Sugihara et al 2011) has only been found very infrequently across Sub-Saharan Africa: 0.028 Yoruba in Ibadan, Nigeria (YRI) (n=5/176); 0.062 Luhya in Webuye, Kenya (LWK) (n=12/194). The change could not be detected in 375 age and gender matched neurologically normal, healthy control subjects screened from the North of England (Bury et al 2015) or 180 (Utah) residents (CEU reference population) with ancestry from Northern and Western Europe. It was also absent from Han Chinese, Beijing (CHB) and Japanese, Tokyo (JPT) populations attained as part of the International HapMap or 1000Genomes Project.

The female index case had a strong family history of MND and dementia. Her father, aged 74yrs, and a male paternal cousin aged 34yrs, were both known to be affected. The proband [F056-(SP3462)] was a non-smoker. She presented at fifty with a predominantly bulbar phenotype and symptoms of EL. Signs of dysarthria & dysphagia also developed, 6 months prior to the individual having received a formal diagnosis of ALS (Section 1.1.3). Despite treatment with Riluzole, contiguous advancement led to severe muscle wasting and paralysis which eventually culminated in respiratory failure and death approximately 2½ years after the initial onset of disease.

The neuropathology of this case closely resembled that of "classical ALS" (Section 1. 1.5.1) with the presence of ubiquitinated, p62 and TDP-43 positive inclusion bodies within residual MN's of the primary motor cortex, brainstem and AH of the SC (Bury et al 2015). In less abundance, there were also a number of OPTN immunoreactive, p62 positive, but TDP-43 negative skein-like or compact inclusions, described elsewhere by Maruyama et al (2010) and Hortobagyi et al (2011); concentrated within the frontal neocortex, hippocampus and cerebellum. These were found to colocalise with approximately 5% of aggregated poly-GA DPR proteins, produced by the RAN mediated translation of sense and antisense *C9ORF72* transcripts (Bury et al 2015) (Ash et al 2013, Mackenzie et al 2014, Mori et al 2013c, Proudfoot et al 2014). OPTN labelling was also apparent in 10 of 12 G_4C_2 repeat carriers without a mutation and in two FALS cases including: One individual with a heterozygous c.338T>C (p.I133T) missense substitution in exon 4 of *SOD1* (Ince et al 1996) (Section 1.2.5.1.1) and a second with a heterozygous c.1570A>T (p.R524W) missense substitution in exon 15 of *FUS* (Hewitt et al 2010) (Section 1.2.5.2.2). Therefore, OPTN immunostaining is not necessarily specific for *OPTN* mutation carriers.

The c.964G>A (p.E322K) mutation has also been identified in two Caucasian siblings from a German ALS and glaucoma pedigree who were reported to carry, on the same allele, a second non-synonymous variant in *OPTN* [rs11258194 c.293T>A (p.M98K) found at a frequency of 6.7% (n=6/90) in the North of England; situated in the Rab8 binding site of the coiled coil I domain (Bury et al 2015)], in addition to, a previously established heterozygous c.1055A>G (p.N352S) missense substitution in exon 5 of *TARDBP* (Weishaupt et al 2013) (Section 1.2.5.2.1). The female index case initially presented with elevated intraocular pressure (IOP); though this later turned out to be normal. At the age of 39 she developed progressive descending tetraparesis that began in the right upper limb with symptoms of mild bulbar involvement, abnormal deep tendon reflexes, fasciculations and severe muscular atrophy, in the absence of overt cognitive impairment. Respiratory function deficits were also prominent with NIPPV support (Section 1.1.4) being required for a minimum of 18 hours daily after the first 7 years. The patient and her brother, who so far has remained healthy, are still reported to be alive at the age of 52 and 57yrs, respectively. Consequently, there was no autopsy material available for conducting neuropathological investigations (Weishaupt et al 2013).

5.3.2.2 *C9ORF72* and *TARDBP*

A second Sheffield patient [S352-(SP3484)] with an apparently sporadic form of the disease was also known to carry the *C9ORF72* expansion (Section 4.1.2.3) in addition to a novel heterozygous c.962C>T (p.A321V) missense substitution in exon 6 of the *TARDBP* gene (Kirby et al 2010). The alanine to valine change at the position of the 321st amino acid was predicted to be pathological from *in silico* analysis and is also known to occur within a highly conserved C-terminal glycine rich domain that binds several of the hnRNP proteins, namely A0 (⇧1.23-fold, p<0.001), A2B1 (⇧1.09-fold, p<0.05) and R (⇧1.19-fold, p<0.001) (Table 5.10); reported to be up-regulated in the microarray (Section 5.2.4) and qRT-PCR (Figure 5.12) analyses of *C9ORF72*-related gene expression changes observed in the ECACC LCL's (Buratti et al 2005, Romano et al 2014, He et al 2014, Yu et al 2012). Functional studies were conducted *in vitro* using p.G287S, A321V and M337V affected patient (n=3) and control (n=6) derived fibroblast cell cultures to measure the abundance of *CDK6* (cyclin-dependent kinase 6) specific mRNA transcripts in response to WT or mtTDP-43 protein. A significant increase in the level of CDK6 ($p<0.05$) was observed in patient fibroblasts compared to controls suggesting normal repression of *CDK6* transcription had been impaired (Kirby et al 2010).

The female index case reported no prior family history of MND or dementia. Both of her parents died of malignancy and her two remaining siblings, aged 37 and 41yrs, respectively were healthy at the time of the initial study; although the youngest has since received a diagnosis of ALS. The proband [S352-(SP3484)] was a non-smoker. She presented at thirty-seven with progressive weakness and loss of dexterity in the left-hand. EMG recordings established more widespread denervation consistent with a diagnosis of MND. Towards the advanced stages of the disease the individual also developed signs of dyspnoea. Riluzole was being administered, in combination with Vitamin E supplements, for 4 years 9 months before the onset of respiratory failure which culminated in her death at the age of forty-two. Clinically overt symptoms of cognitive or behavioural dysfunction were distinctly lacking in this case which is uncommon in instances involving a hexanucleotide G_4C_2 repeat expansion in *C9ORF72.* Since the individual in question was screened from cases in the local Sheffield Blood Bank it meant post-mortem material was unavailable for neuropathological investigation (Kirby et al 2010).

One interesting remark that was also observed by Chio et al (2012c) is with respect to an emerging theme in which individuals who have acquired an oligogenic form of inheritance are more likely to become symptomatic at an earlier age. In the ECACC LCL's, patient carriers of two or more mutations in ALS-FTLD causative genes were on average 17½ years younger [43½ versus 61yrs (two-tailed student's t-test p=0. 041)] than the mean of the non*C9ORF72*-related_SALS cases and ~12½ years younger than the mean of the *C9ORF72* FALS and SALS cases combined. Although [F056-(SP3462)] and [S352-(SP3484)] represent only a small sample size of (n=2) it does, nevertheless, raise an important question as regards to whether an individual's genetic burden can act as a modifier of disease severity/progression (Chio et al 2012c, van Blitterswijk et al 2013b).

5.3.3 Clinical Features Relating to the *C9ORF72* Phenotype

Expression Console™ assessment of post-hybridization QC parameters (Table 5.2) (Section 5.1.2) of *C9ORF72+* LCL's recruited to the ECACC discovery cohort, as well as, selected samples from the ECACC replication cohort [i.e. meeting the criteria for inclusion into Chapter 6: '*C9ORF72* Survival Study'] resulted in 38 individuals being included in the final microarray analysis, along with an additional 56 non*C9ORF72*-related_SALS cases and 26 neurologically normal, age and gender matched, healthy controls (Table 5.1). A discussion of technical tissues relating to the storage, handling and processing of peripheral EBV-transformed B-lymphocytes (LCL's) for GEP is provided at the end of Chapter 4 (Section 4.4).

Core presentations associated with the expansion, generally speaking, mimic those of "classical ALS" (Cooper-Knock et al 2012b, Gijselinck et al 2012, Murray et al 2011), bvFTLD or the combined ALS-FTLD syndrome (Section 1.2.1) (Cooper-Knock et al 2014a). Instances involving PLS (~0.5%) (Section 1.2.2.2) and PMA (<2%) (Section 1.2.2.3) have been reported elsewhere in the literature but are exceedingly rare and were absent from the ECACC LCL's (van Rheenen et al 2012). Approximately 50.0% of patient carriers are diagnosed with spinal onset ALS which is comparable to the proportion of sporadic cases and consistent with our findings (Table 5.1) (Woollacott & Mead 2014). Several groups have observed a greater than expected incidence of bulbar predominant involvement (Chio et al 2012a, Cooper-Knock et al 2014a, Debray et al 2013, Ratti et al 2012, Snowden et al 2013, Stewart et al 2012). However, this has not always been the case and could not be replicated in the ECACC LCL's (Table 5.1) (Byrne et al 2012). A high prevalence of cognitive and behavioural impairment, with or without a family history of dementia, is anticipated in *C9ORF72*-related versus non*C9ORF72*-related ALS (Boeve et al 2012, Byrne et al 2012, Cooper-Knock et al 2012b, Garcia-Redondo et al 2013, Gijselinck et al 2012, Millecamps et al 2012, Sabatelli et al 2012). Although this was not necessarily true of the LCL's our conclusions were limited by the lack of available information for the Birmingham and

London cases (Section 5.1.1.1); which collectively comprised one third of the cohort. There are also reports of a higher than expected chance of other motor and extramotor phenotypes associating the with the *C9ORF72* expanded repeat including ALZ (<1%) (Section 1.4.1.2.3) (Kohli et al 2013) and PD (~4%) (Section 1.2.1) (Cooper-Knock et al 2013a). Normally a slight male preponderance is apparent is cases involving "classical ALS" with M:F ratios ranging between 1.2 and 1.5:1 (Section 1.1.2) (Leblond et al 2014). Conversely, in *C9ORF72+* familial and apparently sporadic ALS patients this has been shown to be closer to 1.00:1 (Woollacott & Mead 2014) with marginally more females than males having been identified in the familial LCL's of the ECACC microarray cohort (Table 5.1).

In comparison to non*C9ORF72*-related_SALS, LCL carriers of >30 copies of the G_4C_2 repeat were symptomatic at an earlier age [Average 56±10.9yrs versus 61±11.9yrs (student's t-test $p<0.05$*)] which supports the previously published findings of Byrne et al (2012), Cooper-Knock et al (2012b), Garcia-Redondo et al (2013) and Xi et al (2012). In the ECACC microarray cohort the largest effect size was observed for the female patients [Average 52±12.1yrs versus 64±12.3yrs (student's t-test $p<0.01$ **)] with no significant difference reported for the male patients [Average 60±7.7yrs versus 59±11.3yrs (student's t-test $p>0.05$)]. A gender bias has also been described in a study conducted by Williams et al (2013); albeit in the reverse direction with an earlier age at symptom onset recorded for male *C9ORF72*-related versus non*C9ORF72*-related ALS cases. In addition there have been several reports in the literature of the G_4C_2 repeat being associated with a shorter survival (Byrne et al 2012, Cooper-Knock et al 2012b, Debray et al 2013, Garcia-Redondo et al 2013, Irwin et al 2013, Millecamps et al 2012, Ratti et al 2012, Stewart et al 2012). In the ECACC LCL's, this was the case across all of the *C9ORF72+* (n=89) and non*C9ORF72*-related_SALS (n=531) patients in the discovery and replication cohorts combined [Hazard ratio 0.85 (95% CI 0.68-1.08) with Median survival of 29 months for *C9ORF72+* FALS and SALS and 34 months for non*C9ORF72*-related_SALS (Wilcoxon t-test p=0.009)] [APPENDIX FIGURE B1] but was not the case for selected samples in the *C9ORF72* (n=38) and non*C9ORF72*-related_SALS (n=56) study [Hazard ratio 0.89 (95% CI 0.59-1.33) with Median survival of 24 months for *C9ORF72+* FALS and SALS and 27 months for non *C9ORF72*-related_SALS (Wilcoxon t-test p=0.264)] (Figure 5.28).

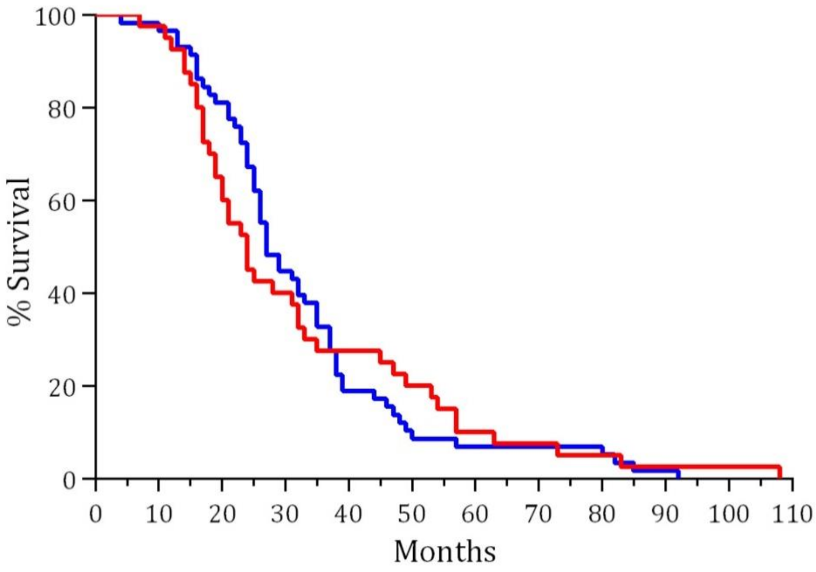


Figure 5.28 Kaplan-Meier Survival Curve for LCL's in the ECACC *C9ORF72* (Red) and Non*C9ORF72*-Related_SALS (Blue) Study

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, ECACC - European Collection of Cell Cultures, LCL - lymphoblastoid cell line and S - sporadic.

5.3.4 Microarray Profiles Associated with the G_4C_2 Repeat

On the Affymetrix Human Exon 1.0ST GeneChip® Arrays an overall up-regulation in the level of gene transcription was apparent with 650 (59.3%) of 1,096 [unadjusted p<0.05, FC ≥ ±1.20] or 755 (64.4%) of 1,173 [ANOVA F-test p<0.05, FC ≥ ±1.20] DE transcripts detected using Partek® Genomics Suite™ (Section 5.2.1.1.1) and Qlucore Omics Explorer (Section 5.2.1.5.1) exhibiting an significant increase in expression in the immortalised EBV-transformed B-lymphocytes (LCL's) of *C9ORF72+* FALS (n=18) and SALS (n=20) patients compared to a subset of 26, age as well as gender, matched neurologically normal, healthy control subjects selected from the ECACC discovery cohort. These gene lists were almost identical with a 90% overlap portrayed by the GeneVenn diagram depicted in Figure 5.16 (Section 5.2.1.5.1). Such a high degree of concordance increases our confidence that the algorithms deployed by each of these computational analyses programs produces consistent and reliable readouts which reflect biologically meaningful alterations in gene expression and not just artifactual findings associated with the different sample types. In DAVID, functional annotation clustering consistently ranked RNA processing (GO: 0006396) (Section 5.2.1.3) and

Translation (GO: 006412) (Section 5.2.1.4) as the top two most highly enriched gene ontology categories with EASE scores of 7.5 or above and FDR corrected probability values below 10^{-08} [Partek® Genomics Suite™ (Table 5.3); Qlucore Omics Explorer (Table 5.7)].

Among the transcripts highlighted were a significant proportion of those encoding RRM containing proteins predicted to bind the G_4C_2 repeat [n=40/103 identified in an RNA pull-down assay performed by Dr Matthew Walsh and colleagues from the University of Sheffield (Table 5.10) (Section 5.2.4)]. These comprised several of the hnRNP proteins (n=8/40) [*HNRNPA0* (⇧$_{reg}$) (p<0.01**) and *HNRNPF* (⇧$_{reg}$) (p<0.01 **) confirmed in the ECACC LCL's by qRT-PCR between pooled *C9ORF72+* cases and control samples (Figure 5.12)] in addition to the ALS causative gene *FUS* (Section 1. 1.8.2.2) (⇧$_{reg}$) which was also confirmed in the ECACC LCL's by qRT-PCR (p<0.01**) and further validated by western blot analysis in a similar assay conducted by Mori et al (2013b) using nuclear extracts derived from human embryonic kidney (HEK-293) cell lines. The authors also corroborated four more candidate binding partners of *C9ORF72* including: *HNRNPA2B1* (⇧1.09-fold, p<0.05) and *R* (⇧1.19-fold, p<0.001) with genetic alterations in the former, PrLD, having recently been implicated in the pathogenesis of ALS and MSP (Table 1.2) (Section 1.2.5.2.10); interleukin enhancer binding factor 2, 45kDa (ILF-2) [*ILF2* ⇧1.19-fold (p<0.01) *C9ORF72*vctrl; ⇧1.13-fold (p<0.01) non*C9ORF72*-related_SALSvctrl] which forms the minor constituent of the nuclear factor of activated T-cells (NFAT) complex (Karmakar et al 2010, Kiesler et al 2010) [a heterodimeric association between the ILF-2 (NF45) and ILF-3 (NF90) transcription factors found, through its association with the DNA-dependent protein kinase (DNA-PK), to be important in modulating non-homologous end joining (NHEJ) during the repair of DSB (Shamanna et al 2011)] and a second DNA damage response protein, polypyrimidine tract binding (PTB)-associated splicing factor (PSF) [*SFPQ* (splicing factor proline/glutamine rich) ⇧1.14-fold (p<0.05) *C9ORF72*vctrl; ⇧1.24-fold (p<0.001) non*C9ORF72*-related_SALS vctrl] (Ha et al 2011, Krietsch et al 2012, Rajesh et al 2011, Salton et al 2010) which has been demonstrated *in vivo* using the zebrafish ortholog (whitesnake) (Lowery et al 2007) to be essential for cell survival and brain organogenesis throughout normal embryonic development.

Pre-mRNA processing factors hnRNPH1/2 [*HNRNPH2* ⇧1.28-fold (p<0.05) *C9ORF72* vctrl; not significant in a PrimeTime Mini qPCR Assay (Figure 5.12)] and F [*HNRNPF* ⇧1.22-fold (p<0.001) *C9ORF72*vctrl; up-regulation confirmed in a traditional SYBR Green qRT-PCR Assay (Figure 5.12)] were demonstrated by RNA fluorescence *in situ* hybridization (FISH) and immunohistochemistry (IHC) to co-localise with up to 30% (Cooper-Knock et al 2014b) or 70% (Lee et al 2013b), respectively of the G_4C_2 repeat containing intranuclear RNA foci detected in human post-mortem cerebellum tissue derived from a minimum of three *C9ORF72+* ALS and/or FTLD patients in each study. In the former instance, Cooper-Knock et al (2014b) also showed co-localisation of hn RNPH1/F with ~20% of G_4C_2 repeat containing RNA foci identified in the residual MN's of the ventral horn of the SC [i.e. the most vulnerable neuronal cell population susceptible to degeneration in ALS (Morrison et al 1996)].

Lee et al (2013b) proceeded to transfect neuroblastoma SH-SY5Y cell lines with enhanced green fluorescent protein (EGFP) tagged expression vectors containing either 8X (control), 38X or 72X constructs of the *C9ORF72* intronic G_4C_2 repeat in which a positive correlation was observed between the size of the expansion and the amount of RNA foci that had formed. RNase/DNase treatment proved ineffective in ablating these toxic accumulations; consistent with an earlier finding that the hexanucleotide repeat can form stable stem-loop structures in the DNA sequence which are capable of generating uni- or multi-molecular RNA G-quadruplexes *in vitro* (Fratta et al 2012, Reddy et al 2013). In a time course experiment the authors witnessed a substantial reduction in the number of neuronal SH-SY5Y cells that contained RNA foci over a 24 and 72hr period. Of the remaining cells which still expressed EGFP, analysis conducted using fluorescence-activated cell sorting (FACS), highlighted a three- (38X) and five- (72X) fold increase in the abundance of the apoptotic marker (annexin V) compared to the 8X control lines. Moreover, immunocytochemistry (ICC) also found activation of caspase 3 (CASP3) to be significantly enhanced in the presence of RNA foci induced by the expansion in neuronal SH-SY5Y cell lines. Accordingly, evidence of PARP cleavage was detected in cells transfected with the 38X or 72X constructs but not the 8X control lines. Interestingly, in the LCL's both *CASP3* [*CASP3* (caspase-3, apoptosis-related cysteine peptidase) ⇧1.42-fold (p<0.0001) *C9ORF72*vctrl and ⇧ 1.30-fold (p<0.001) non*C9ORF72*-related_SALSvctrl] and *PARP9* [*PARP9* (poly(ADP -ribose) polymerase family, member 9) ⇧1.32-fold (p<0.01) *C9ORF72*vctrl and ⇧1.24

-fold (p<0.05) non*C9ORF72*-related_SALSvctrl] were increased more in the *C9ORF72*-related cases than the non*C9ORF72*-related_SALS cases, compared to controls. The findings of Lee et al (2013b) were further substantiated *in vivo* when the same EGFP tagged expression vectors were introduced into the zebrafish. Embryos injected with the 38X or 72X constructs were found to contain a considerably greater proportion of apoptotic cells than controls that were CASP3 active and which stained positively for the universal marker of DNA fragmentation, TUNEL (terminal deoxynucleotidyl transferase dUTP nick end labelling).

Another binding partner identified by Dr Mathew Walsh, PURA [⇧1.20-fold, (p<0.01) *C9ORF72*vctrl; up-regulation confirmed in a traditional SYBR Green qRT-PCR Assay (Figure 5.26)] has also been recapitulated by Xu et al (2013), using *in vitro* and *in vivo* model systems, to interact with the G_4C_2 repeat in a manner that is both dose-dependent and sequence specific. In this study the authors transfected 3X (control) or 30X (disease) constructs and EGFP-alone tagged expression vectors into the common fruit fly (*Drosophila melanogaster*) and mouse neuroblastoma (Neuro-2a) cell line. Thirty copies of the aberrantly expanded sequence in *C9ORF72* proved sufficient to cause neurotoxicity and death, which is conserved between mammals and invertebrates. Targeting 30X constructs to the retina in *Drosophila* severely affected eye morphology and locomotor activity, with ommatidia irregularities and loss of pigmentation. In addition, ubiquitinated p62 and TDP-43 positive inclusions immunoreactive for PURA were also shown to be present, as seen in human post-mortem derived cerebellum tissue from patient carriers expressing the *C9ORF72* expansion with FTLD-U pathology. Furthermore, overexpression of PURA in the fruit fly and Neuro-2a model mitigated neurodegeneration associated with the G_4C_2 repeat and rescued cell viability. PURA is a transcriptional activator that is highly abundant in the brain and is known to play a prominent role in regulating the cell cycle and differentiation (White et al 2009). Recently, WES has revealed *de novo* mutations in *PURA* to be a genetic cause of neurodevelopmental delay and learning disabilities in children (n= 4/1,133) screened as part of the Deciphering Developmental Disorders (DDD) UK study group (Hunt et al 2014), with other complications including: neonatal hypotonia; seizures/seizure-like movements and difficulties in feeding.

Using a slightly different approach, Donnelly et al (2013) identified the CNS-enrich ed RNA editing regulator, adenosine deaminase, RNA-specific, B2 (ADARB2) [*ADAR B2* ⇩1.36-fold, ($p<0.05$) *C9ORF72*vctrl; ⇩1.34-fold, ($p<0.05$) non*C9ORF72*-related_S ALSvctrl] as one of 19 ORF's on a custom proteome array, which exhibited a consistly high affinity for the G_4C_2 expanded repeat (6.5X) in *C9ORF72+* ALS patient derived skin fibroblast induced pluripotent stem cell (iPSC) differentiated MN's in comparison to GC scrambled control lines. Sequestration of ADARB2 into toxic intranuclear RNA foci formed by the G_4C_2 repeat is expected to lead to a reduction in the rate of GluR2 AMPA receptor adenosine (A) to inosine (I) editing of the glutamine/arginine (Q/R) site (Donnelly et al 2013); thereby conferring an increased susceptibility to excitotoxic stress (Hideyama et al 2012) (Section 1.2.4.2).

5.3.5 Reduced *C9ORF72* Expression Confirmed in a Subset of LCL's

A significant reduction in the abundance of isoform a (full length) [Variant I (NM_00 1256054) and III (NM_018325) (Figure 5.22)] specific mRNA transcripts pertaining to the *C9ORF72* gene was confirmed [⇩1.62-fold, ($p<0.01$) *C9ORF72*vctrl (Figure 5. 24)] in a traditional SYBR® Green qRT-PCR Assay using an initial subset of the LCL's (n=14) selected from the ECACC discovery cohort (Section 5.2.3) (Cooper-Knock et al 2013b). Other groups have also reported similar findings in human post-mortem derived frontal cortex and cerebellum tissue (Belzil et al 2013, Ciura et al 2013, DeJesus-Hernandez et al 2010, Donnelly et al 2013, Gijselinck et al 2012, Waite et al 20 14); which is supportive of a loss of function/haploinsufficiency mechanism of neurotoxicity.

In zebrafish and *C. elegans* models, antisense oligonucleotide mediated knockdown of the *C9ORF72* ortholog *in vivo* has been shown to cause axonal degeneration of the MN's leading to age-dependent motility deficits & hypersensitivity to environmental stress (Ciura et al 2013, Therrien et al 2013). Overexpression of human WT protein in the zebrafish was subsequently found to have ameliorated these effects (Ciura et al 2013). Several epigenetic events involving the trimethylation of specific lysine residues in histone molecules H3 and H4 for example (Belzil et al 2013) or the hypermethylation of a cysteine-phosphate-guanine (CpG) island (Xi et al 2014, Xi et al 20 13) in close proximity to the expansion are also expected to play a key role in controlling the negative regulation of *C9ORF72* gene expression (Belzil et al 2014).

Contrary to these findings, however, no observable difference in the overall levels of isoform a (full length) or isoform b (truncated) [Variant II (NM_145005) (Figure 5.22)] specific transcripts was apparent in an extended qRT-PCR assay using pooled RNA samples from the entire population of *C9ORF72+* LCL's with a RIN score of 7.5 or above in the combined ECACC discovery and replication cohorts (n=75) (Figure 5.25). Another study conducted by Sareen et al (2013) using *C9ORF72+* ALS and ALS-FTLD patient and control (n=4) derived skin biopsy material to generate fibroblast cell lines and MN cultures differentiated from iPSC's also failed to detect a significant change in the overall abundance of *C9ORF72* mRNA transcripts (RNA-seq and qRT-PCR) [qRT-PCR primers designed in exon 2 to target all three transcript variants] or protein expression (western blot analysis). The use of an informative SNP, which was found to occur naturally within the population at a frequency of 17% (rs10757668), enabled the authors to distinguish between those sequences originating from the WT allele and those emanating from the expansion carrying allele in two of their *C9ORF72* cases (Sareen et al 2013). Five prime rapid amplification of cDNA ends (5'-RACE) identified predominantly exon 1b containing transcripts [Variant III (NM_018325) (Figure 5.22)] in WT and control, versus, increased transcriptional start site variability and a greater proportion of exon 1a containing transcripts [Variant I (NM_001256054) and II (NM_145005) (Figure 5.22)] in the mutants. This paradoxical shift towards the transcription of variants containing the six base pair repeat is supportive of the notion that *C9ORF72* mediated neurodegeneration may also arise through a toxic gain of function as well as a loss of function mechanism. RNA FISH detected aberrantly formed aggregates of >30 copies of the expanded G_4C_2 sequence in discrete & punctate nuclear RNA foci in approximately a fifth of *C9ORF72+* ALS and and ALS+FTLD iPSC differentiated MN cultures which exhibited co-localisation with two previously discussed proteins of interest: Namely, hnRNPA1 a well-established binding partner of TDP-43 (Buratti et al 2005) that has recently been identified through exome sequencing and linkage analysis (Kim et al 2013) to be a rare cause of AD inherited adult-onset ALS (ALS20) (Table 1.2) and MSP (Section 1.2.5.2.10) and PURA (Table 5.10) [⇧1.20-fold, (p<0.001) *C9ORF72*vctrl] which was confirmed by qRT-PCR in the ECACC LCL's (Figure 5.26) (Sareen et al 2013).

Others have subsequently recognised RAN translation as an unconventional mode of protein synthesis that generates aggregate prone poly-GA (glycine-alanine), poly-GP (glycine-proline) or poly-GR (glycine-arginine) peptides which have been shown to colocalise with p62 positive, TDP-43 negative NCI's in human post-mortem CNS tissue; a characteristic molecular hallmark of *C9ORF72* pathology (Section 1.2.5.4) (Almeida et al 2013a, Ash et al 2013, Gendron et al 2013b). Furthermore, emerging evidence suggests that bidirectional transcription of the six base pair repeat occurs which would be responsible for producing bosh sense as well as antisense transcripts and DPR's (Gendron et al 2013a, Mori et al 2013a, Zu et al 2013).

RNA foci and RAN translated products have also been linked to the pathogenesis of several other neurodegenerative conditions that are associated with a microsatellite repeat expansion including: Myotonic dystrophy type 1 (DM1) (Jiang et al 2004, Zu et al 2011); fragile X tremor/ataxia syndrome (FXTAS) (Tassone et al 2004, Todd et al 2013); Huntinton-disease like 2 (HDL2) (Rudnicki et al 2007) and spinocerebellar ataxia type 8 (SCA8) (Chen et al 2009, Daughters et al 2009, Moseley et al 2006) (Wojciechowska & Kryzosiak 2011). In DM1 patients, for example, nuclear RNA foci containing CTG expanded dystrophia myotonica-protein kinase (*DMPK*) sequester a number of RNA binding proteins, including muscleblind-like regulator 1 (*MBNL1*) in order to disrupt their normal physiological function (Childs-Disney et al 2013, Mykowska et al 2011, Osborne et al 2009); leading to alterations in gene expression and a dysregulation of splicing.

In summary, RNA processing appears to be a major pathway that has been shown to be disrupted in relation to the newly discovered intronic hexanucleotide G_4C_2 repeat expansion identified in *C9ORF72*. Transcriptional profiling of the ECACC LCL's using Human Exon 1.0ST GeneChip® Arrays highlighted a significant increase in the overall expression of many of these genes in comparison to non*C9ORF72*-related_SALS cases and controls. The up-regulation observed on the microarray could possibly reflect a compensatory mechanism in which the cells are trying to overcome sequestration of the C9ORF72 protein and RNA binding partners in toxic RNA foci that are known to accumulate inside the cell.

CHAPTER 6: *C9ORF72* SURVIVAL STUDY

The principal aim of this chapter was to identify genetic factors which are associated with a fast (<2yrs survival) versus slow (≥4yrs survival) disease progression in the peripheral LCL's of patients carrying a large, pathogenic hexanucleotide G_4C_2 repeat expansion in the newly identified *C9ORF72* gene. As more microarrays were being run and as further clinical information from the MNDA became available throughout the course of the project additional cases from the ECACC discovery and replication cohorts, meeting the selection criteria outlined above, were included. Given recently emerging evidence from the SOD1^{G93A} mouse (Alves et al 2011, Cervetto et al 2013, Gunther et al 2014, Heiman-Patterson et al 2005, Naumenko et al 2011) it was also of interest to determine whether there were any gender specific effects of survival on the global GEP's of patients carrying the *C9ORF72* expansion.

6.1 *C9ORF72* Long versus Short Survival Cohort

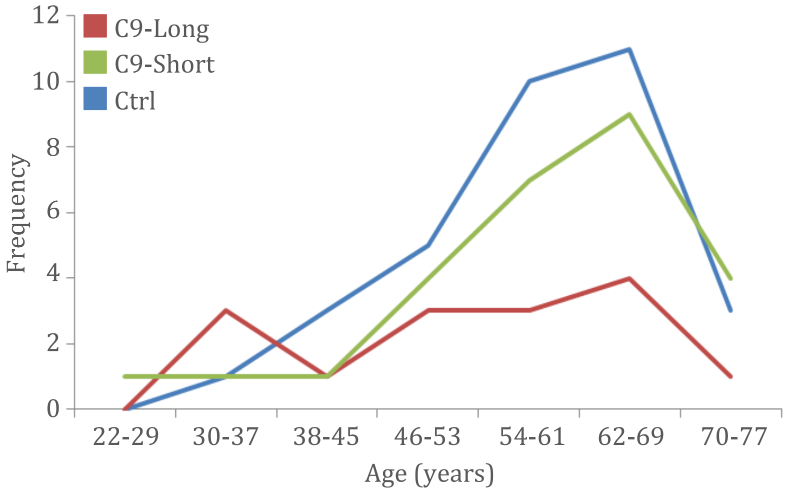
6.1.1 ECACC EBV-Transformed B-Lymphocytes

6.1.1.1 Clinical Characteristics

6.1.1.1.1 Control Cases

Neurologically normal, age and gender matched, healthy control LCL's (n=33/100) [19-M, 14-F] selected from the ECACC discovery cohort were largely recruited from patient partners or their unrelated carers (Section 4.1.1). These were comprised of 10 Birmingham (30.3%) cases including one from Liverpool [C02-(BLi0245)], one from Oxford [C090-(BOx0073)] and one from Belfast City Hospital [C020-(BBe000 6)]; 8 London (24.2%) cases including two from Cambridge [C019-(LCa0022) and C021-(LCa0076)], one from Poole General Hospital [C017-(LPo0027)] and one from Southampton General Hospital [C015-(LSh0032)] and 15 Sheffield (45.5%) cases including one from Manchester [C01-(SMa0033)], two from Preston [C010-(SPr00 14) and C022-(SPr0086)] and five from Newcastle [C04-(SNc0091), C011-(SNc00

45), C029-(SNc0023), C076-(SNc0106) and C085-(SNc0035)]. Age at consultation ranged between 36 and 71 years with a mean of 58.1±10yrs. The M:F ratio was 1.36: 1 (Figure 6.1).



	C9-Long	C9-Short	Control
M:F	0.67:1	2.00:1	1.36:1
Age	53.7±12yrs	58.4±11yrs	58.1±10yrs
Total	**15**	**27**	**33**

Figure 6.1 Age Frequency Distribution of Patient and Control LCL's in the *C9ORF72* Long (≥4yrs) versus Short (<2yrs) Survival Study

Abbreviations: *C9ORF72* (C9) - chromosome 9 open reading frame 72, Ctrl - control, F - female, LCL - lymphoblastoid cell line and M - male.

6.1.1.1.2 C9ORF72+ Short Survival Cases

Patient derived, expansion carrying LCL's (n=27/88) [18-M, 9-F] with a survival of less than two years (i.e. defined as having a fast disease progression) comprised 16 FALS and 11 SALS selected from the ECACC discovery (Section 4.1.1) and replication (Section 4.1.2) cohorts. These consisted of 6 Birmingham (22.2%) cases including one from Liverpool [F072-(BLi0251)], one from Oxford [F078-(BOx0029)] and one from Bristol Frenchay Hospital [F048-(BBr0015)]; 10 London (37.0%) cases and 11 Sheffield (40.8%) cases including one from Preston [F025-(SPr0059)]. The M:F ratio was 2.00:1 (Figure 6.1).

MALES The majority of male *C9ORF72+* short (<2yrs) survival cases, 94.4% (n=17/ 18) were diagnosed according to the World Federation of Neurology's amended EEC of 1998 with either definite (n=8/17) [3-familial, 5-sporadic] or probable (n=9/17) [5-familial, 4-sporadic] ALS (Figure 1.1) including one incidence of concomitant PD [F114-(SP3560)] (Section 1.2.1). The remaining 5.6% (n=1/18) of the cohort were diagnosed with PBP [F100-(SP3070)] (Section 1.2.2.1). Age at symptom onset ranged between 45 and 71 years with a mean of 58.4±11yrs. Disease duration ranged from 6½ to 22 months with a mean of 1.35±0.3yrs (Table 6.1). Limb onset accounted for 61.1% of cases (n=11/18) [2-FALS, 1-FALS+PD and 8-SALS], bulbar onset a further 22.2% (n=4/18) [3-FALS and 1-SALS] and a mixed presentation 11.1% (n=2/18) [1-FALS and 1-PBP (familial)]. Information regarding site of onset was not available for the remaining 5.6% of the cohort (n=1/18) [1-FALS]. The ALSFRS-R scores ranged between 0 (severe disability) and 46 (near normal function) with an average of 27.6 ±15 for 88.9% of male *C9ORF72+* short (<2yrs) survival cases (n=16/18) [7-FALS, 1-FALS+PD, 7-SALS and 1-PBP (familial)].

For the Sheffield cases some additional clinical information could be extracted from the local database. Of these, 14.3% (n=1/7) [1-SALS] were prone to EL and a further 14.3% (n=1/7) [1-SALS] displayed symptoms of dyspnoea without requiring NIPPV support. One individual presenting with a family history of dementia was diagnosed with the rare FA variant of the disease [S042-(SP3122)] (Section 1.2.1). Dysarthria and dysphagia were also apparent in 42.9% of the cohort (n=3/7) [1-FALS, 1-FALS +PD and 1-SALS] with PEG feeding becoming a necessary intervention in 33.3% of these latter cases (n=1/3) [1-FALS+PD] (Section 1.1.4). Two patients (28.6%) were non-ambulant with a further 14.3% unable to walk without assistance (n=1/7) [1-SALS]. Current smokers comprised 14.3% of the cohort (n=1/7) [1-PBP (familial)], non-smokers 57.1% (n=4/7) [1-FALS+PD and 3-SALS] and for the remaining 28.6% (n=2/7) [2-SALS] this information was not disclosed.

FEMALES Similarly, the majority of female *C9ORF72+* short (<2yrs) survival cases, 88.9% (n=8/9) were also diagnosed (Section 1.1.3) (Figure 1.1) with either definite (n=4/8) [4-familial] or probable (n=4/8) [2-familial, 2-sporadic] ALS including one incidence of concomitant FTLD [F115-(SP3118)]. The remaining 11.1% (n=1/9) of the cohort was diagnosed with PBP [F041-(LP0440)]. Age at symptom onset ranged between 28 and 71 years with a mean of 55.1±15yrs. Disease duration ranged from 14 to 23 months with a mean of 1.65±0.3yrs (Table 6.1). Limb onset accounted for

	Survival (<2yrs)				Survival (≥4yrs)			
	MALE	**FEMALE**	**ALL**	**CONTROL**	**MALE**	**FEMALE**	**ALL**	**CONTROL**
M:F	n/a	n/a	2.00:1	2.25:1	n/a	n/a	0.67:1	0.67:1
Age								
range	45-71yrs	28-71yrs	28-71yrs	36-71yrs	43-65yrs	35-71yrs	35-71yrs	36-71yrs
mean	58yrs	55yrs	58yrs	59yrs	57yrs	52yrs	54yrs	54yrs
Onset								
Limb	11 (61.1%)	1 (11.1%)	12 (44.5%)	n/a	6 (100.0%)	7 (77.8%)	13 (86.6%)	n/a
Bulbar	4 (22.2%)	5 (55.6%)	9 (33.3%)	n/a	0 (0.0%)	2 (22.2%)	2 (13.4%)	n/a
Mixed	2 (11.1%)	3 (33.3%)	5 (18.5%)	n/a	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a
Respiratory	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a
unknown	1 (5.6%)	0 (0.0%)	1 (3.7%)	n/a	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a
Diagnosis								
ALS	16 (88.8%)	7 (77.8%)	23 (85.2%)	n/a	5 (83.3%)	8 (88.9%)	13 (86.6%)	n/a
ALS+FTLD	0 (0.0%)	1 (11.1%)	1 (3.7%)	n/a	1 (16.7%)	0 (0.0%)	1 (6.7%)	n/a
ALS+PD	1 (5.6%)	0 (0.0%)	1 (3.7%)	n/a	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a
PBP	1 (5.6%)	1 (11.1%)	2 (7.4%)	n/a	0 (0.0%)	1 (11.1%)	1 (6.7%)	n/a
PLS	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a
PMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a	0 (0.0%)	0 (0.0%)	0 (0.0%)	n/a
ALSFRS-R								
range	0-46	18-38	0-46	n/a	33-45	30-45	30-45	n/a
mean	28	27	27	n/a	40	38	39	n/a
Survival								
range	0.5-1.8yrs	1.2-1.9yrs	0.5-1.7yrs	n/a	4.1-8.9yrs	4.1-6.9yrs	4.1-8.9yrs	n/a
mean	1.4yrs	1.6yrs	1.5yrs	n/a	6.2yrs	5.1yrs	5.4yrs	n/a
Total	**18 (18)**	**9 (8)**	**27 (26)**	**26 (24)**	**6 (6)**	**9 (8)**	**15 (14)**	**15 (15)**

Table 6.1 Clinical Summary of Male and Female *C9ORF72+* LCL's in the ECACC Long (≥4yrs) versus Short (<2yrs) Survival Study with Age and Gender Matched Controls The National MNDA DNA Bank didn't have a suitable match for familial sample F24 (SP3148) of 28yrs explaining the small discrepancy in age range and M:F ratio between patients and controls of the short survivors group. In total 33 individuals were selected as neurologically normal, healthy controls with a different subset of this pool used for each of the downstream comparative analyses. Affymetrix® post-QC numbers are provided in brackets and highlighted in red.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, ECACC - European Collection of Cell Cultures, F - familial, F - female, FRS-R - Revised Functional Rating Scale, FTLD - frontotemporal lobar degeneration, LCL - lymphoblastoid cell line, M - male, MNDA - Motor Neurone Disease Association, n/a - not applicable, PD - Parkinson's disease, PBP - Progressive Bulbar Palsy, PLS - Primary Lateral Sclerosis, PMA - Progressive Muscular Atrophy, QC - quality control, S - sporadic and SP - Sheffield patient.

11.1% (n=1/9) [1-SALS], bulbar onset a further 55.6% (n=5/9) [1-FALS+FTLD, 3-FALS and 1-PBP (familial)] and a mixed presentation the remaining 33.3% of cases (n=3/9) [2-FALS and 1-SALS]. The ALSFRS-R scores ranged between 18 (moderate disability) and 38 (mild disability) with an average of 27.0±7 for 77.8% of female *C9ORF72+* short (<2yrs) survival cases (n=7/9) [4-FALS, 1-FALS+FTLD, 1-SALS and 1-PBP (familial)].

For the Sheffield cases some additional clinical information could be extracted from the local database. Of these, 50.0% (n=2/4) [1-FALS and 1-SALS] were prone to EL, with one familial patient also suffering from hypersialorrhea and a further 50.0% (n=2/4) [1-FALS and 1-FALS+FTLD] displaying symptoms of dyspnoea that did not require NIPPV support. Dysarthria and dysphagia were apparent in 75.0% (n=3/4) [1-FALS, 1-FALS+FTLD and 1-SALS] of the cohort without PEG feeding becoming a necessary intervention. All patients were ambulant with the majority, 75.0% able to walk unaided and only one sporadic individual requiring assistance. Current or ex-smokers were absent in this instance with non-smokers comprising three-quarters (n=3/4) [1-FALS, 1-FALS+FTLD and 1-SALS] of cases and for the remaining 25.0% (n=1/4) [1-FALS] this information was not disclosed.

6.1.1.1.3 C9ORF72+ Long Survival Cases

Patient derived, expansion carrying LCL's (n=15/88) [6-M, 9-F] with a survival of at least four years following the initial onset of symptoms (i.e. defined as having a slow disease progression) were comprised of 9 FALS and 6 SALS selected from the ECACC discovery (Section 4.1.1) and replication (Section 4.1.2) cohorts. These consisted of 4 Birmingham (26.7%) cases; 4 London (26.7%) including one from Southampton General Hospital [F102-(LSh0038)] and one from Plymouth Derriford Hospital [F0 29-(LPy0018)] and 7 Sheffield (46.6%) cases including one from Newcastle [S203-(SNc0059)] and one from Manchester [F081-(SMa0006)]. The M:F ratio was 0.67:1 (Figure 6.1).

MALES All of the male *C9ORF72+* long (≥4yrs) survival cases (n=6/6) [4-familial, 2-sporadic] were diagnosed with probable ALS including one incidence of concomitant FTLD [S191-(SP3042)] (Section 1.2.1). Age at symptom onset ranged between 43 and 65 years with a mean of 56.7±8yrs (Table 6.1). Disease duration ranged from 49 to 107 months with a mean of 6.18±2.3yrs for 66.7% of the cohort (n=4/6) [2-FALS, 1-SALS and 1-SALS+FTLD]. For the remaining 33.3% of cases (n=2/6) [2-FALS] the individuals were still reported to be alive as of June 2013 with a minimum disease duration of 4 [F047-(BP6502)] or 6 [F013-(BP6494)] years, respectively. All of the patients presented focally with asymmetric upper and/or lower limb weakness. The ALSFRS-R scores ranged between 33 (mild disability) and 45 (near normal function) with an average of 39.8±5 for 100.0% of male *C9ORF72+* long (≥4yrs) survival cases (n=6/6) [4-FALS, 1-SALS and 1-SALS+FTLD].

For the three Sheffield cases some additional clinical information regarding smoking status could be extracted from the local database. Two thirds of patients (n=2/3) [1-SALS and 1-SALS+FTLD] were non-smokers and for the remaining 33.3% of cases (n=1/3) [1-FALS] this information was not disclosed.

FEMALES The vast majority of female *C9ORF72+* long (≥4yrs) survival cases, 88.9% (n=8/9) were also diagnosed with either definite (n=4/8) [2-familial, 2-sporadic] or probable (n=4/8) [2-familial, 2-sporadic] ALS. One additional familial patient [F029-(LPy0018)] comprising the remaining 11.1% of the cohort was diagnosed with PBP. Age at symptom onset ranged between 35 and 71 years with a mean of 51.7±14yrs. Disease duration ranged from 49 to 83 months with a mean of 5.09±0.9yrs (Table 6. 1). Limb onset accounted for 77.8% (n=7/9) [4-FALS and 3-SALS] and bulbar onset the remaining 22.2% of cases (n=2/9) [1-SALS and 1-PBP (familial)]. The ALSFRS-R scores ranged between 30 (mild disability) and 45 (near normal function) with an average of 38.1±6 for 100.0% of female *C9ORF72+* long (≥4yrs) survival cases (n=9/ 9) [4-FALS, 4-SALS and 1-PBP (familial)].

For the Sheffield cases some additional clinical information could be extracted from the local database. Of these, 25.0% (n=1/4) [1-SALS] suffered from dyspnoea that did not require NIPPV support. Dysarthria and dysphagia was also apparent in a further 25.0% (n=1/4) [1-SALS] of the cohort with PEG feeding (Section 1.1.4) becoming a necessary intervention in this latter instance. The majority of patients, 75.0% were ambulant with only one familial case unable to walk without assistance. Current or ex-smokers were absent, with three quarters having never smoked (n=3/4) [1-FALS and 2-SALS] and for the remainder of the cohort (n=1/4) [1-SALS] this information was not disclosed.

6.1.1.2 Therapeutics Used to Treat the Cohort

6.1.1.2.1 C9ORF72+ Short Survival Cases

Riluzole, administered at a dose of 50mg twice daily, was being used to treat 83.3% of male (n=15/18) [5-FALS, 1-FALS+PD and 10-SALS] and 66.7% of female (n=6/9) [3-FALS, 1-FALS+FTLD and 2-SALS] *C9ORF72+* short (<2yrs) survival cases. A small proportion of individuals, 4.8% (n=1/21) [1-SALS] experienced adverse side effects and the medication was withdrawn. Vitamin C and/or E (n=5/27) [1-FALS and 4-SALS] or multivitamin supplements (n=1/27) [1-SALS] were collectively being taken by 22.2% (n=6/27) of the cohort. Conversely, 14.8% of patients (n=2/27) [3-FALS and 1-PBP (familial)] chose not to receive any kind of disease modifying therapy and for the remaining 7.4% (n=2/27) [1-FALS and 1-PBP (familial)] this information was not available.

6.1.1.2.2 C9ORF72+ Long Survival Cases

The glutamate antagonist, Riluzole was also being used to treat 83.3% of male (n=5/6) [3-FALS, 1-SALS and 1-SALS+FTLD] and 88.9% of female (n=8/9) [4-FALS, 1-PBP (familial) and 3-SALS] *C9ORF72+* long (≥4yrs) survival cases. Vitamin C and/or E (n=5/15) [4-SALS and 1-SALS+FTLD] or multivitamin supplements (n=2/15) [2-FALS] were collectively being taken by 46.7% (n=7/15) of the cohort. As well as Riluzole, several patients were also participants of the minocycline [F073-(BP6165)], BDNF [F091-(SP3534)] or ONO-2506 (Arundic acid) [S203-(SNc0059)] drug trials [APPENDIX TABLE B4]. Conversely, the remaining 13.3% (n=2/15) [1-FALS and 1-SALS] of the cohort chose not to receive any kind of disease modifying therapy.

6.1.1.3 Genetic Status of the Cohort

All of the FALS and SALS patients (n=42/88) [24-M, 18-F] in the ECACC microarray cohort that met the criteria for inclusion into the *C9ORF72+* long (≥4yrs) (Section 6.

1.1.1.3) versus short (<2yrs) (Section 6.1.1.1.2) survival study were identified from a repeat-primed PCR screen as carriers of more than 30 copies of the expanded G_4C_2 sequence in intron 1 of the *C9ORF72* gene (Cooper-Knock et al 2012b) (Section 1.1.8.4). Additionally, in the slow progressing female cases there was also one example of oligogenic inheritance involving an apparently sporadic Sheffield sample [S352-(SP3484)] with a deleterious c.962C>T (p.A321V) missense mutation in exon 6 of the *TARDBP* gene (Kirby et al 2010) (Section 5.3.2.2).

6.1.2 Affymetrix® Expression Console™ QC Metrics

In vitro transcribed biotinylated ss-cDNA targets of ~40-70nt were hybridised onto Human Exon 1.0ST GeneChip® Arrays (Section 2.3.2.3 and 2.3.2.4). Affymetrix® QC metrics were assessed in Expression Console™ software version 1.3.0.187 (Section 4.3.2). Two female controls (n=2/33) [C076-(SNc0106) and C079-(SC3279)] and a further two SALS patients, including one from the *C9ORF72+* short (<2yrs) survival group (n=1/27) [S123-(BP6021)] and a second (n=1/15) [S352-(SP3484)] from the *C9ORF72+* long (≥4yrs) survival group, scored poorly against three or more of the parameters summarised in Table 6.2 (Figure 6.2, 6.3 and 6.4). The aforementioned cases (n=4/75), therefore, which represent 5.3% of the initial cohort, were removed from any subsequent downstream comparative analyses (Table 6.1). This generated a final cohort comprised of 40 FALS and SALS patients with a fast (n=26) [18-M, 8-F] versus slow (n=14) [6-M, 8-F] disease progression and 31, age and gender matched, neurologically healthy control subjects.

	Affymetrix® Expression Console™ QC Metrics						
	bac_spike	bgrd_mean	%P	AUC	all_probeset_mean	RLE	PPMCC
C056	🟩	🟥	🟩	🟩	🟩	🟩	🟩
C076	🟩	🟩	🟥	🟥	🟩	🟥	🟥
C079	🟩	🟩	🟩	🟩	🟥	🟥	🟥
C090	🟩	🟩	🟩	🟩	🟩	🟥	🟥
S123	🟩	🟩	🟩	🟥	🟥	🟥	🟥
S352	🟩	🟩	🟩	🟥	🟥	🟥	🟥

Table 6.2 Affymetrix® Expression Console™ Summary of Failed LCL Samples in the *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study

Key: 🟩 Passed 🟥 Failed

Abbreviations: AUC - area under the receiver operating curve (ROC), bac_spike - bacterial spike in controls, bgrd - background, *C9ORF72* - chromosome 9 open reading frame 72, C - control, LCL - lymphoblastoid cell line, PPMCC - Pearson's product moment correlation coefficient, P - present calls, QC - quality control, RLE - relative log expression and S - sporadic.

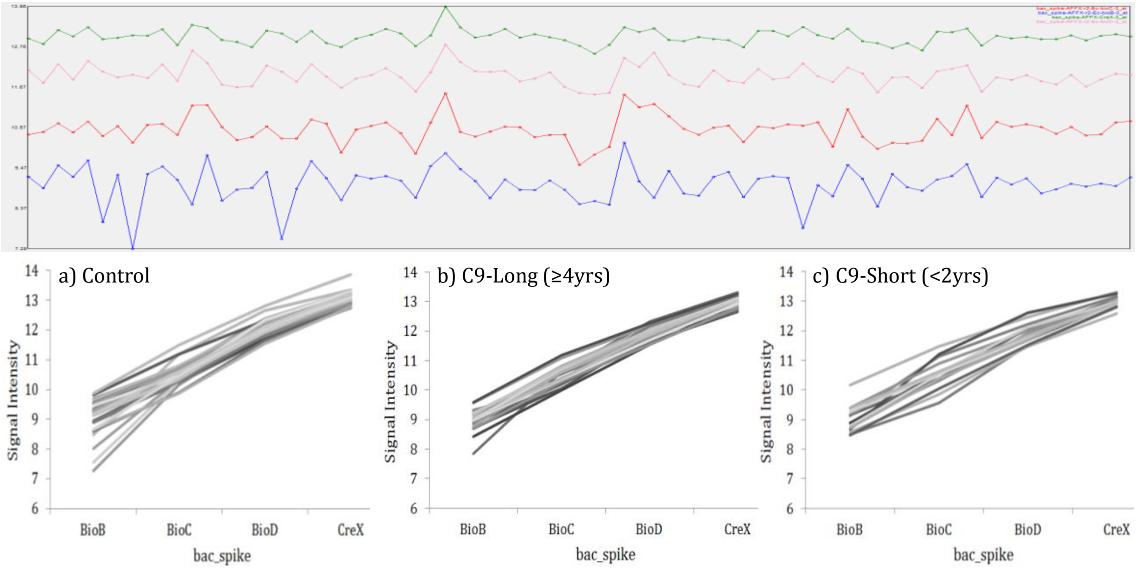


Figure 6.2 Eukaryotic Hybridization Controls for LCL Samples in the *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study Bacterial derived genes of the *E. coli* biotin synthesis pathway [BioB (blue), BioC (red) and BioD (pink)] and the recombinase gene CreX (green) from the P1 bacteriophage were spiked in at increasing concentrations (top panel) [1.5pM (limit of detection), 5pM, 25pM and 100pM] immediately prior to labelling to monitor the efficiency of the hybridization reaction. In the bottom panel mean signal intensities for each of the probesets spotted onto the Affymetrix® Human Exon 1.0ST GeneChip® Arrays are provided for a) controls (n=33), b) *C9ORF72+* long (≥4yrs) survival cases (n=27) and c) *C9ORF72+* short (<2yrs) survival cases (n=15). Assessment of Affymetrix® QC metrics was performed using Expression Console™ software version 1.3.0.187.

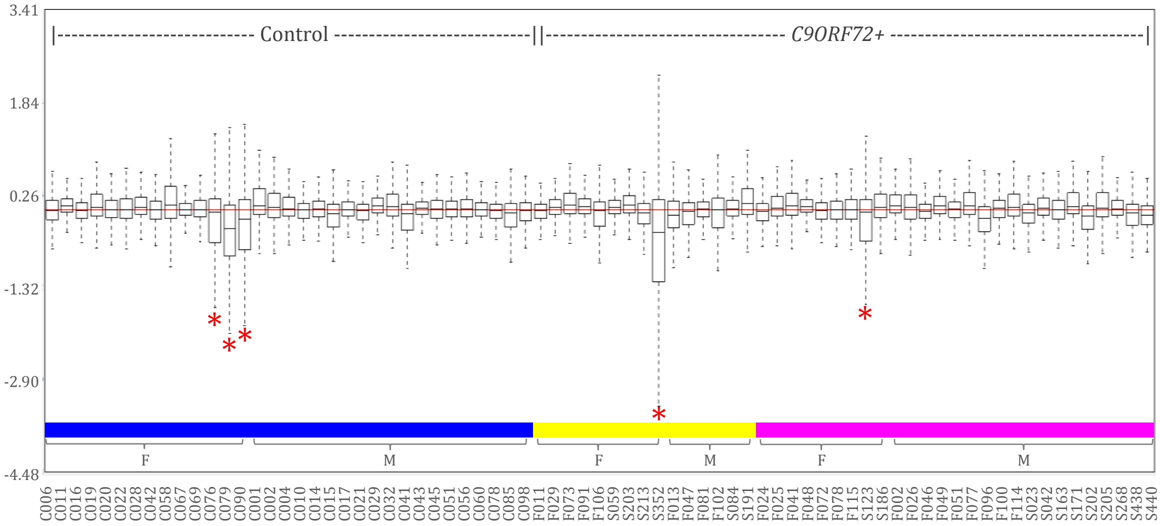


Figure 6.3 Mean Absolute RLE Boxplots for LCL Samples in the *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study Relative log expression means and standard deviations for age and gender matched M (male) and F (female) control subjects (blue) and *C9ORF72+* FALS and SALS patients with either a fast (<2yrs) (pink) or slow (≥4yrs) (yellow) disease progression. Whiskers represent the minimum and maximum average probeset signal intensities for each array at the level of the whole transcript. Asterisks (red) highlight significant outliers. Assessment of Affymetrix® QC metrics was performed using Expression Console™ software version 1.3.0.187.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, C - control, F - familial, LCL - lymphoblastoid cell line, QC - quality control, RLE - relative log expression, S - sporadic and ST - sense-target.

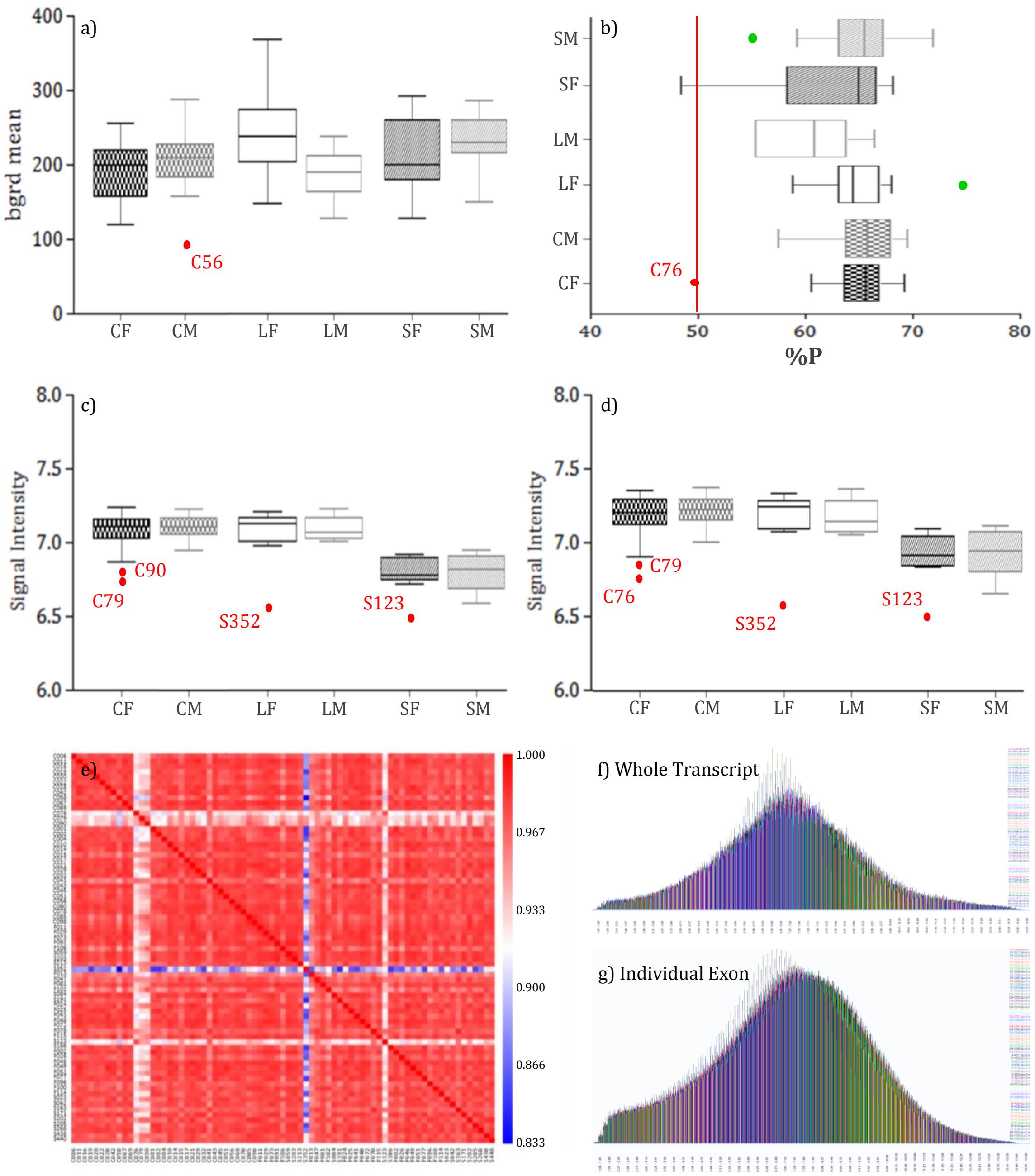


Figure 6.4 Expression Console™ Summary of the QC Metrics Assessed for LCL Samples in the *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study In the top four panels box and whisker plots were generated for male (M) [■] and female (F) [■] control cases (checkerboard) or *C9ORF72+* FALS and SALS with a long (L) (≥4yrs) (unfilled) versus short (S) (<2yrs) (diagonally stripped) survival using GraphPad Prism® software version 5.04 and applying a Tukey multiple comparison test: a) average background (bgrd) signal, b) %P calls, c) mean probeset signal intensities at transcript level and d) mean probeset signal intensities at individual exon level. Samples flagged as outliers are highlighted in red. Note that for %P calls statistically outlying cases with at least fifty percent of probesets called as present were still included in downstream comparative analyses; these are represented in green. The coloured matrix in e) represents Pearson's product Moment correlation coefficient (r) in which each pair-wise comparison is assigned a value on a scale of 0.8333 (blue) to 1.000 (red) with a high score indicative of a strong linear relationship between the X and Y variables. Signal histogram plots are provided at f) transcript and g) individual exon level in the bottom right-hand panels. Each series of coloured bars represents the distribution of log2 transformed, average GC-RMA normalised signal intensities for a single array in the experiment. Assessment of Affymetrix® QC metrics was performed using Expression Console™ software version 1.3.0.187.

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, C - control, F - familial, LCL - lymphoblastoid cell line, P - present calls, QC - quality control, RMA - Robust Multi-array Average and S - sporadic.

6.2 Human Exon 1.0ST GeneChip® Array Profiling

Affymetrix® CEL files, 94.7% (n=71/75) [C9-Long (n=14), C9-Short (n=26) and Ctrl (n=31)] were imported into Partek® Genomics Suite™ software version 6.6 (Section 2.3.2.5.2). Raw expression values were log2 transformed and a GC-RMA background normalisation procedure applied using core metaprobesets (n=287,329). At whole transcript level these relate to over twenty-two thousand unique clusters pertaining to full length protein coding mRNA sequences in the RefSeq or GenBank® database. Post-normalised pivot tables were exported as text files which were reconfigured in Microsoft® Excel 2010 and the data visualised using Qlucore Omics Explorer software version 2.3. ANOVA F-tests were filtered on 'Sample Type' [Multi-group comparisons between C9-Long v C9-Short v Ctrl and Two-group comparisons between C9-Long v Ctrl, C9-Short v Ctrl and C9-Long v C9-Short] in order to generate lists of variables or gene transcripts that best separate the groupings on a PCA plot or hierarchically clustered HeatMap. Bias attributed to the effects of any potential confounders such as 'Age' (continuous) and 'Gender' (nominal) were removed by eliminating these as factors.

DE transcripts identified between the ECACC *C9ORF72+* LCL cases with a fast versus slow disease progression and a subset of neurologically healthy controls, that were matched for age and gender, were detected at the 5% significance level (unadjusted p<0.05) by performing a 2-way ANCOVA statistical test in Partek® Genomics Suite™ software version 6.6. Lists were filtered to remove unannotated transcripts (n=4,377/22,011) and a FC threshold ≥ ±1.20 applied (Section 2.3.2.5.2). Where multiple Affymetrix® transcript cluster ID's were present for a single gene the identification number producing the most significant outcome with the greatest level of coverage (i.e. highest number of probesets and/or exon clusters) was retained. However, if the direction of change was opposing then both transcripts were removed.

Once generated, the lists of DE transcripts [Partek® unadjusted p<0.05, FC ≥ ± 1.20] could also be imported into DAVID bioinformatics resource version 6.7. Functional annotation clustering analysis was performed on GOTERM_BP_FAT and GOTERM_MF_FAT gene ontology (GO) terms applying a *Homo sapiens* background and filtering using 'Medium' classification stringency (Section 2.3.2.5.4). Categories with an EASE score above 1.30 and Benjamini-Hochberg FDR uncorrected $p<0.05$ were considered statistically significant. Transcripts identified as being significantly up (⇧)/down (⇩) regulated under different experimental conditions were analysed independently.

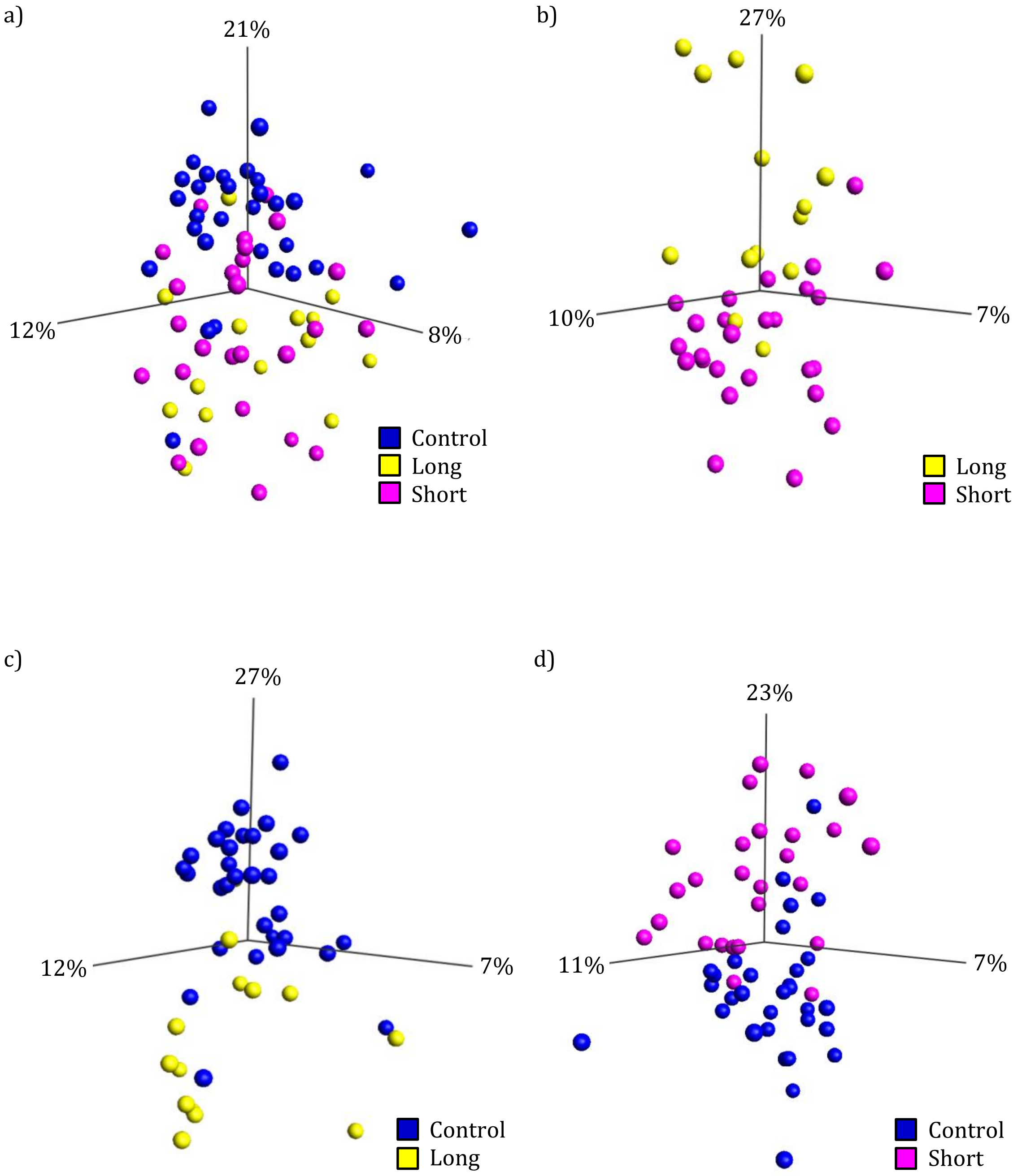
6.2.1 ALL Samples Combined

6.2.1.1 Clustering Analysis

A multi-group comparative analysis conducted at the 5% significance level [ANOVA F-test $p<0.05$, FC ≥ ±1.20] using Qlucore Omics Explorer software version 2.3 of all LCL cases (n=40) and controls (n=31) (Blue) in the ECACC *C9ORF72+* long (≥4yrs) (Yellow) versus short (<2yrs) (Pink) survival study (Figure 6.5a) identified 2,792 of 22,011 variables that explain up to 21% of the variance in GEP's generated between patient and control samples along the y-axis of the first principal component (PC1) and 12% (PC2) or 8% (PC3), respectively of the variance between a fast versus slow disease progression which is represented by the x and z-axes of the second and third principal components.

Two-group comparative analyses performed at the same 5% significance threshold [ANOVA F-test $p<0.05$, FC ≥ ±1.20] identified corresponding lists of 1,162 (C9-Long v C9-Short), 2,805 (C9-Long v Ctrl) or 2,374 (C9-Short v Ctrl) variables, respectively which may explain up to 27% of the variance in GEP's generated between *C9ORF72+* LCL's with a long (≥4yrs) (Yellow) versus short (<2yrs) (Pink) survival (Figure 6.5b) or controls (Blue) (Figure 6.5c) and a further 23% of the variance that is generated between *C9ORF72+* short (<2yrs) survival cases and controls (Figure 6.5d).

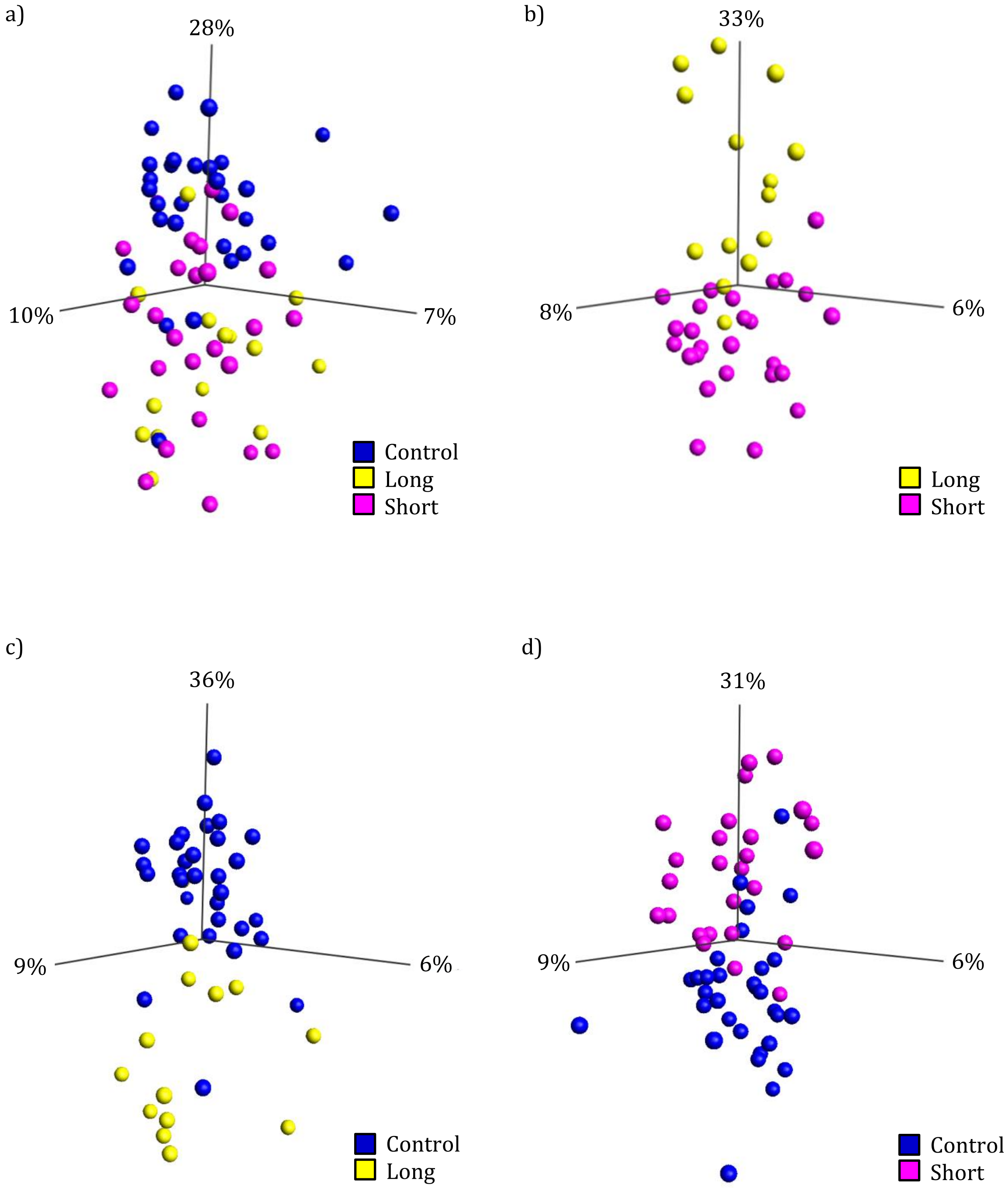
Clustering analysis was also conducted in Qlucore Omics Explorer software version 2.3 at a higher stringency of applying a 1% significance threshold [ANOVA F-test $p< 0.01$, FC ≥ ±1.20] (Figure 6.6a-d). However, given that the lists of variables which are generated were markedly reduced in number and since the sample groupings on the



#	ANOVA	Comparison	Eliminated Factors	p-value	Fold	Variables
a)	Multi-Group	🟨 🟪 🟦	‘Age’ and ‘Gender’	<0.05	±1.20	2,792/22,011
b)	Two-Group	🟨 🟪	‘Age’ and ‘Gender’	<0.05	±1.20	1,162/22,011
c)	Two-Group	🟨 🟦	‘Age’ and ‘Gender’	<0.05	±1.20	2,805/22,011
d)	Two-Group	🟪 🟦	‘Age’ and ‘Gender’	<0.05	±1.20	2,374/22,011

Figure 6.5 Qlucore Omics Explorer Clustering Analysis [ANOVA F-test p<0.05, FC ≥ ±1.20] of ALL Samples Combined in the *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study

Abbreviations: ANOVA - analysis of variance, *C9ORF72* - chromosome 9 open reading frame 72 and FC - fold-change.



#	ANOVA	Comparison	Eliminated Factors	p-value	Fold	Variables
a)	Multi-Group	🟨 🟪 🟦	'Age' and 'Gender'	<0.01	±1.20	968/22,011
b)	Two-Group	🟨 🟪	'Age' and 'Gender'	<0.01	±1.20	227/22,011
c)	Two-Group	🟨 🟦	'Age' and 'Gender'	<0.01	±1.20	1,069/22,011
d)	Two-Group	🟪 🟦	'Age' and 'Gender'	<0.01	±1.20	812/22,011

Figure 6.6 Qlucore Omics Explorer Clustering Analysis [ANOVA F-test p<0.01, FC ≥ ±1.20] of ALL Samples Combined in the *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study

Abbreviations: ANOVA - analysis of variance, *C9ORF72* - chromosome 9 open reading frame 72 and FC - fold-change.

PCA plots proved no more distinct than those which have already been discussed, a decision was made to adhere to the original 5% threshold used also in Chapter 5 for the analysis of the *C9ORF72* and non*C9ORF72*-related_SALS study (Section 5.2.1.5).

6.2.1.2 DAVID Enrichment of Partek® Generated Gene Lists

6.2.1.2.1 C9ORF72+ LongvShort Survival

A direct comparison between *C9ORF72+* long (≥4yrs) versus short (<2yrs) survival of all samples combined at the 5% significance level [Partek® unadjusted $p<0.05$, FC ≥ ±1.20] identified 628 DE transcripts in Partek® Genomics Suite™ software version 6.6. These included 301 genes (47.9%) that were significantly up-regulated (⇧) and a further 327 genes (52.1%) which were significantly down-regulated (⇩). In DAVID these corresponded to 624 mapped ID's [299 genes ⇧ and 325 genes ⇩] which were found to be enriched for GO categories that are associated with gene transcription, negative regulation of apoptosis and vesicle-mediated transport (Table 6.3a) as well as the cell cycle, DNA damage response mechanisms and Golgi-mediated trafficking (Table 6.3b) [APPENDIX TABLE B13].

a) ALL Samples C9-Long v C9-Short ⇧$_{reg}$ [Partek® unadjusted $p<0.05$, FC≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0006355	regulation of transcription, DNA-templated	2.32	50	2.50E-05
2	GO:0045892	negative regulation of transcription, DNA-templated	2.22	18	7.40E-04
3	GO:0043066	negative regulation of apoptotic process	2.00	14	3.30E-03
4	GO:0016192	vesicle-mediated transport	1.71	20	1.40E-03

b) ALL Samples C9-Long v C9-Short ⇩$_{reg}$ [Partek® unadjusted $p<0.05$, FC≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0007067	mitotic nuclear division	2.84	14	2.40E-04
2	GO:0045841	negative regulation of mitotic metaphase/ anaphase transition	1.70	4	9.30E-04
3	GO:0006974	cellular response to DNA damage stimulus	1.51	15	9.90E-03
4	GO:0048193	Golgi vesicle transport	1.30	8	0.011

Table 6.3 DAVID Enrichment of ALL Samples Combined in the ECACC *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study

Abbreviations: # - rank, ⇧$_{reg}$ - up-regulated, ⇩$_{reg}$ - down-regulated, *C9ORF72* - chromosome 9 open reading frame 72, DAVID - Database for Annotation, Visualisation and Integrated Discovery, EASE - enrichment score, ECACC - European Collection of Cell Cultures, FC - fold-change and GO - gene ontology.

6.2.1.2.2 C9ORF72+ LongvCtrl and ShortvCtrl Survival

The GeneVenn diagram which is depicted in Figure 6.7 [Partek® unadjusted p<0.05, FC ≥ ±1.20] highlights 1,218 DE transcripts between *C9ORF72+* long (≥4yrs) survival cases and controls including 742 genes (60.9%) that were significantly up-regulated and 476 genes (39.1%) which were significantly down-regulated. Additionally, 751 DE transcripts were highlighted between the *C9ORF72+* short (<2yrs) survival cases and controls including 436 genes (58.1%) that were significantly up-regulated and 315 genes (41.9%) which were significantly down-regulated. Among the transcripts highlighted were 1,007 genes found to be specifically dysregulated in the *C9ORF72+* long (≥4yrs) survival cases [604 genes ⇧ and 403 genes ⇩] and a further 540 genes which were found to be specifically dysregulated in *C9ORF72+* short (<2yrs) survival cases [297 genes ⇧ and 243 genes ⇩]. Of the 211 commonly shared transcripts that represent 17.3% or 28.1% of the aforementioned gene lists, respectively (Figure 6.7) only one, heat shock 70kDa protein 1A (*HSPA1A*) [C9-Longvctrl ⇩1.44-fold, p<0.05; C9-Shortvctrl ⇧1.33-fold, p<0.05], exhibited opposing directions of change.

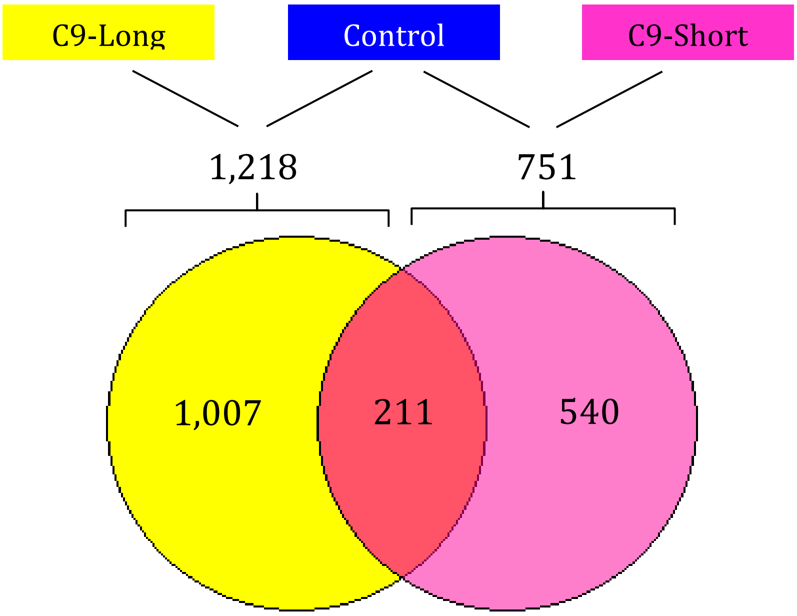


Figure 6.7 GeneVenn of ALL Samples Combined in the ECACC *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study Lists of DE transcripts generated using Partek® Genomics Suite™ software version 6.6 copyright © 2013 (Partek® Inc., St Louis, MO, USA). GeneVenn application freely available online at genevenn.sourceforge.net (University of Southern Mississippi, USA) (Pirooznia et al 2007).

Abbreviations: *C9ORF72* (C9) - chromosome 9 open reading frame 72, DE - differentially expressed and ECACC - European Collection of Cell Cultures.

Importation of the *C9ORF72+* long (≥4yrs) specific gene list (n=1,007) into DAVID returned 998 mapped ID's [598 genes ⇧ and 400 genes ⇩] which were found to be enriched for GO categories associated with translation & ribosome biogenesis, gene transcription, RNA processing, response to ROS and regulation of apoptosis (Table 6.4a) in addition to metabolism, solute: cation symporter activity and organisation of the lysosome (Table 6.4b) [APPENDIX TABLE B14].

a) ALL Samples C9-Long Specific ⇧$_{reg}$ [Partek® unadjusted p<0.05, FC≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0006412	translation	5.52	38	4.30E-11
2	GO:0003743	translation initiation factor activity	4.74	12	3.90E-06
3	GO:0034062	RNA polymerase activity	2.28	7	2.60E-03
4	GO:0044265	cellular macromolecule catabolic process	2.07	39	2.40E-03
5	GO:0004721	phosphoprotein phosphatase activity	2.01	15	1.10E-03
6	GO:0006351	transcription	1.92	103	1.00E-05
7	GO:0043933	macromolecular complex subunit organisation	1.88	40	8.60E-04
8	GO:0006396	RNA processing	1.79	38	1.90E-05
9	GO:0000302	response to reactive oxygen species	1.76	9	2.90E-03
10	GO:0006351	transcription, DNA-dependent	1.75	20	3.10E-03
11	GO:0006119	oxidative phosphorylation	1.62	11	1.30E-03
12	GO:0042254	ribosome biogenesis	1.61	13	5.90E-04
13	GO:0042981	regulation of apoptotic process	1.53	42	2.60E-03
14	GO:0051262	protein tetramerisation	1.38	7	1.50E-03

b) ALL Samples C9-Long Specific ⇩$_{reg}$ [Partek® unadjusted p<0.05, FC ≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0015923	mannosidase activity	4.30	6	8.80E-06
2	GO:0009311	oligosaccharide metabolic process	3.19	8	3.30E-06
3	GO:0016125	sterol metabolic process	2.87	11	6.00E-05
4	GO:0015293	symporter activity	2.26	10	2.00E-03
5	GO:0009100	glycoprotein metabolic process	2.09	15	1.20E-04
6	GO:0046942	carboxylic acid transport	1.89	10	4.40E-03
7	GO:0006643	membrane lipid metabolic process	1.84	8	1.70E-03
8	GO:0015294	solute:cation symporter activity	1.53	8	3.30E-03
9	GO:0009267	cellular response to starvation	1.42	5	4.60E-03
10	GO:0007040	lysosome organisation	1.32	5	1.80E-03
11	GO:0016052	carbohydrate catabolic process	1.31	7	0.032

Table 6.4 DAVID Enrichment of ALL Samples Combined C9-Long Specific Gene Lists

Abbreviations: # - rank, ⇧$_{reg}$ - up-regulated, ⇩$_{reg}$ - down-regulated, C9 - chromosome 9 open reading frame 72, DAVID - Database for the Annotation, Visualisation and Integrated Discovery, EASE - enrichment score, FC - fold-change and GO - gene ontology.

Conversely, importation of the *C9ORF72+* short (<2yrs) specific gene list (n=540) returned 535 mapped ID's [294 genes ⇧ and 241 genes ⇩] enriched for GO categories associated with DNA metabolism, DNA replication and the cell cycle and regulation of cellular response to stress (Table 6.5a) as well as cell motility, modulation of the immune response, protein kinase activity, nucleotide binding and organisation of the cytoskeleton (Table 6.5b) [APPENDIX TABLE B15].

a) ALL Samples C9-Short Specific ⇧$_{reg}$ [Partek® unadjusted $p<0.05$, FC≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0006259	DNA metabolic process	3.24	22	3.80E-05
2	GO:0006261	DNA-dependent DNA replication	1.65	6	2.00E-03
3	GO:00fv07049	cell cycle	1.53	23	4.30E-03
4	GO:0080135	regulation of cellular response to stress	1.41	7	5.20E-03

b) ALL Samples C9-Short Specific ⇩$_{reg}$ [Partek® unadjusted $p<0.05$, FC≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0051270	regulation of cell motion	2.66	12	2.70E-05
2	GO:0051249	regulation of lymphocyte activation	2.00	9	5.00E-04
3	GO:0002706	regulation of lymphocyte mediated immunity	1.96	5	4.40E-03
4	GO:0031589	cell-substrate adhesion	1.82	7	1.30E-03
5	GO:0032147	activation of protein kinase activity	1.71	8	5.20E-04
6	GO:0030247	polysaccharide binding	1.38	7	0.013
7	GO:0001883	purine nucleoside binding	1.36	30	0.028
8	GO:0007010	cytoskeleton organisation	1.34	12	0.019
9	GO:0002683	negative regulation of immune system process	1.31	7	5.60E-04

Table 6.5 DAVID Enrichment of ALL Samples Combined C9-Short Specific Gene Lists

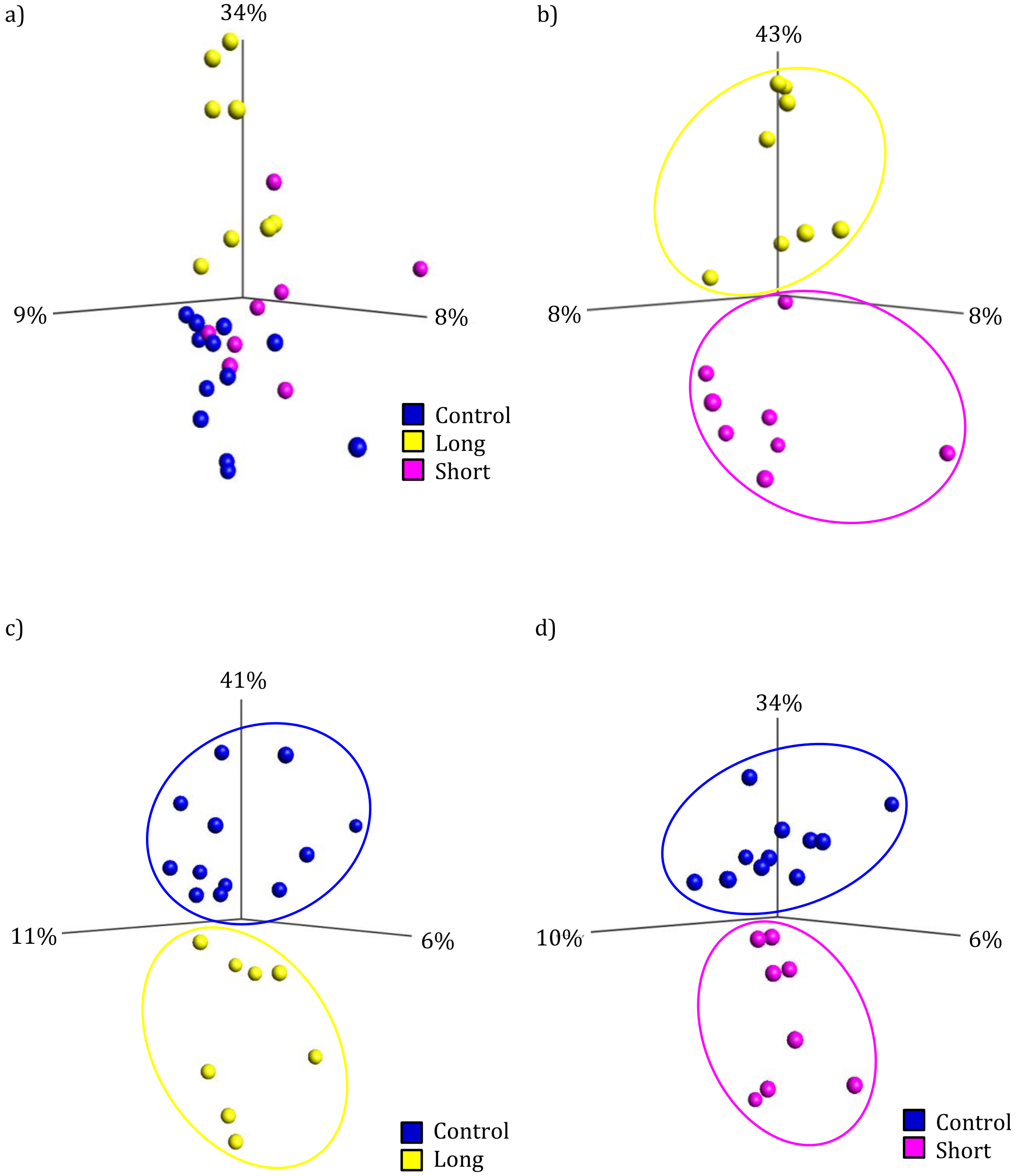
Abbreviations: # - rank, ⇧$_{reg}$ - up-regulated, ⇩$_{reg}$ - down-regulated, C9 - chromosome 9 open reading frame 72, DAVID - Database for the Annotation, Visualisation and Integrated Discovery, EASE - enrichment score, FC - fold-change and GO - gene ontology.

6.2.2 FEMALE Samples

6.2.2.1 Clustering Analysis

A Qlucore Omics Explorer multi-group comparative analysis [ANOVA F-test $p<0.05$, FC ≥ ±1.20] of female only LCL cases (n=16) and controls (n=12) (Blue) in the ECACC *C9ORF72+* long (≥4yrs) (Yellow) versus short (<2yrs) (Pink) survival study (Figure 6.8a) identified 1,216 of 22,011 variables that explain up to 34% of the variance in GEP's generated between patient and control samples along the y-axis of PC1 and 9% or 8%, respectively, of the variance between a fast versus slow disease progression along the x and z-axes of PC2 and PC3.

Two-group comparative analyses, which were also conducted at the 5% significance threshold [ANOVA F-test $p<0.05$, FC ≥ ±1.20], identified clearly defined genetic sub-



#	ANOVA	Comparison	Eliminated Factor	p-value	Fold	Variables
a)	Multi-Group	🟨 🟪 🟦	'Age'	<0.05	±1.20	1,216/22,011
b)	Two-Group	🟨 🟪	'Age'	<0.05	±1.20	1,038/22,011
c)	Two-Group	🟨 🟦	'Age'	<0.05	±1.20	2,028/22,011
d)	Two-Group	🟪 🟦	'Age'	<0.05	±1.20	402/22,011

Figure 6.8 Qlucore Omics Explorer Clustering Analysis [ANOVA F-test p<0.05, FC ≥ ±1.20] of FEMALE ONLY Samples in the *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study

Abbreviations: ANOVA - analysis of variance, *C9ORF72* - chromosome 9 open reading frame 72 and FC - fold-change.

groups that form distinct clusters on the PCA plots depicted in Figure 6.8b-d. These generated corresponding lists of 1,038 (C9-Long v C9-Short), 2,028 (C9-Long v Ctrl) and 402 (C9-Short v Ctrl) variables, respectively which may explain up to 43% of the variance in GEP's generated between *C9ORF72+* LCL's with a long (≥4yrs) (Yellow) versus short (<2yrs) (Pink) survival (Figure 6.8b) in addition to 41% of the variance between *C9ORF72+* long (≥4yrs) survival cases versus controls (Blue) (Figure 6.8c) and a further 34% of the variance between *C9ORF72+* short (<2yrs) survival cases versus controls (Figure 6.8d).

6.2.2.2 DAVID Enrichment of Partek® Generated Gene Lists

6.2.2.2.1 C9ORF72+ LongvShort Survival

A Partek® Genomics Suite™ analysis [unadjusted p<0.05, FC ≥ ±1.20] of female only samples conducted at the 5% significance threshold identified 550 DE transcripts in a direct comparison between *C9ORF72+* LCL cases with a long (≥4yrs) versus short (<2yrs) survival including 292 genes (53.1%) which were significantly up-regulated (⇧) and a further 258 genes (46.9%) that were significantly down-regulated (⇩). In DAVID these corresponded to 548 mapped ID's [291 genes ⇧ and 257 genes ⇧] which were found to be enriched for GO categories associated with gene transcription and the induction of apoptosis (Table 6.6a) as well as regulation of the cell cycle, phospholipid biosynthesis and protein N-linked glycosylation (Table 6.6b) [APPENDIX TABLE B16].

a) FEMALE Samples C9-Long v C9-Short ⇧$_{reg}$ [Partek® unadjusted p<0.05, FC≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0006355	regulation of transcription, DNA-templated	2.22	62	5.30E-04
2	GO:0006915	induction of apoptosis	2.21	15	5.50E-04

b) FEMALE Samples C9-Long v C9-Short ⇩$_{reg}$ [Partek® unadjusted p<0.05, FC≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0022402	cell cycle process	2.08	18	2.00E-03
2	GO:0008654	phospholipid biosynthesis process	1.75	7	2.80E-03
3	GO:0006487	protein N-linked glycosylation	1.65	5	3.10E-03
4	GO:0010564	regulation of cell cycle process	1.48	7	4.90E-03

Table 6.6 DAVID Enrichment of FEMALE ONLY Samples in the ECACC *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study

Abbreviations: # - rank, ⇧$_{reg}$ - up-regulated, ⇩$_{reg}$ - down-regulated, *C9ORF72* - chromosome 9 open reading frame 72, DAVID - Database for Annotation, Visualisation and Integrated Discovery, EASE -

enrichment score, ECACC - European Collection of Cell Cultures, FC - fold-change and GO - gene ontology.

6.2.2.2.2 C9ORF72+ LongvCtrl and ShortvCtrl Survival

The GeneVenn diagram which is depicted in Figure 6.9 [Partek® unadjusted $p<0.05$, FC ≥ ±1.20] highlights 1,325 DE transcripts between *C9ORF72+* long (≥4yrs) survival cases and controls including 849 genes (64.1%) that were significantly up-regulated and 476 genes (35.9%) which were significantly down-regulated. Additionally, 212 DE transcripts were highlighted between the *C9ORF72+* short (<2yrs) survival cases and controls including 151 genes (71.2%) that were significantly up-regulated and 61 genes (28.8%) which were significantly down-regulated. Among the transcripts highlighted were 1,250 genes found to be specifically dysregulated in the *C9ORF72+* long (≥4yrs) survival cases [787 genes ⇧ and 463 genes ⇩] and a further 137 genes which were found to be specifically dysregulated in *C9ORF72+* short (<2yrs) survival cases [90 genes ⇧ and 47 genes ⇩]. Commonly shared transcripts (n=75) represent 5.7% or 35.4% of the aforementioned gene lists, respectively and included the stress granule and nucleolar protein, SGNP (alternative name DNAPTP6) [*DNAPTP6* (DNA polymerase-transactivated protein 6) C9-Longvctrl ⇧1.45-fold, $p<0.05$; C9-Shortvctrl ⇩1.62-fold, $p<0.01$] which was the only transcript to exhibit opposing directions of change on the microarray.

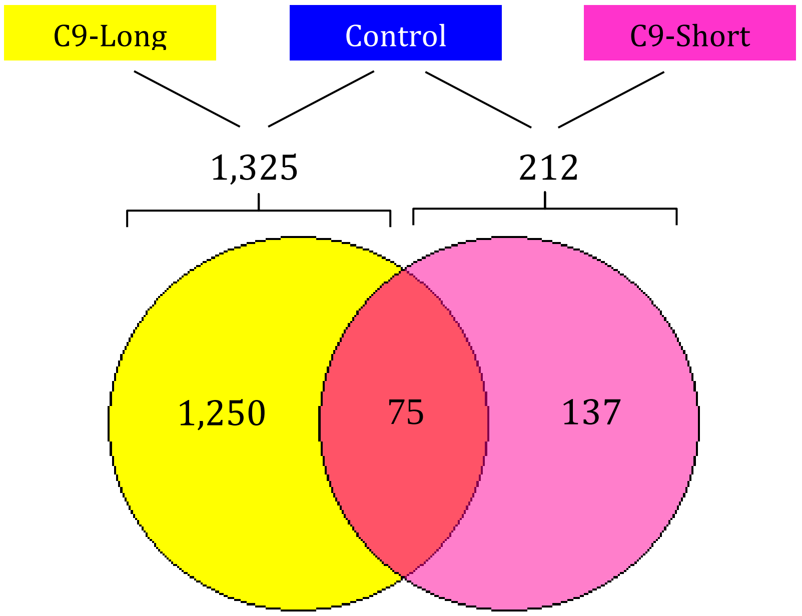


Figure 6.9 GeneVenn of FEMALE ONLY Samples in the ECACC *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study Lists of DE transcripts generated using Partek® Genomics Suite™ software version 6.6 copyright © 2013 (Partek® Inc., St Louis, MO, USA). GeneVenn application freely available online at genevenn.sourceforge.net (University of Southern Mississippi, USA) (Pirooznia et al 2007).

Abbreviations: *C9ORF72* (C9) - chromosome 9 open reading frame 72, DE - differentially expressed and ECACC - European Collection of Cell Cultures.

Importation of the female *C9ORF72+* long (≥4yrs) specific gene list (n=1,250) into DAVID returned 1,242 mapped ID's [784 genes ⇧ and 458 genes ⇩] that were found to be enriched for GO categories associated with the initiation of translation, protein transport/degradation, energy metabolism, ribonucleoprotein complex biogenesis, regulation of the cell cycle, gene transcription and induction of apoptosis (Table 6. 7a) as well as transmembrane transporter activity, protein N-linked glycosylation and homeostasis (Table 6.7b) [APPENDIX TABLE B17].

a) FEMALE Samples C9-Long Specific ⇧$_{reg}$ [Partek® unadjusted p<0.05, FC≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0044265	cellular macromolecule catabolic process	4.31	60	3.10E-06
2	GO:0003743	translation initiation factor activity	3.59	13	9.40E-06
3	GO:0019001	guanyl nucleotide binding	3.09	32	5.70E-04
4	GO:0015031	protein transport	2.45	60	1.40E-05
5	GO:0006511	ubiquitin-dependent protein catabolic process	2.14	26	6.40E-05
6	GO:0022613	ribonucleoprotein complex biogenesis	2.09	18	2.40E-03
7	GO:0006351	transcription, DNA-templated	2.06	123	5.20E-04
8	GO:0032268	regulation of cellular protein metabolic process	1.83	34	6.10E-03
9	GO:0006091	generation of precursor metabolites and energy	1.81	28	6.50E-04
10	GO:0019787	small conjugating protein ligase activity	1.77	16	5.50E-03
11	GO:0000278	mitotic cell cycle	1.70	35	3.90E-05
12	GO:0006915	induction of apoptosis	1.57	27	1.90E-03
13	GO:0065003	macromolecular complex assembly	1.40	43	0.011
14	GO:0003899	DNA-directed RNA polymerase activity	1.30	6	0.037

b) FEMALE Samples C9-Long Specific ⇩$_{reg}$ [Partek® unadjusted p<0.05, FC ≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0006487	protein N-linked glycosylation	3.33	9	1.10E-05
2	GO:0015175	neutral amino acid transmembrane transporter activity	2.85	6	9.90E-05
3	GO:0008610	lipid biosynthetic process	2.64	25	2.00E-06
4	GO:0008203	cholesterol metabolic process	1.79	10	4.80E-04
5	GO:0015297	antiporter activity	1.74	7	4.90E-03
6	GO:0009267	cellular response to starvation	1.50	5	7.90E-03
7	GO:0019842	vitamin binding	1.46	11	9.10E-04
8	GO:0042592	homeostatic process	1.44	32	4.10E-03
9	GO:0022890	inorganic cation transmembrane transporter	1.40	5	0.012

activity

Table 6.7 DAVID Enrichment of FEMALE ONLY C9-Long Specific Gene Lists

Abbreviations: # - rank, ⇧reg - up-regulated, ⇩reg - down-regulated, C9 - chromosome 9 open reading frame 72, DAVID - Database for the Annotation, Visualisation and Integrated Discovery, EASE - enrichment score, FC - fold-change and GO - gene ontology.

Conversely, importation of the female *C9ORF72+* short (<2yrs) specific gene list (n= 137) returned 136 mapped ID's [89 genes ⇧ and 47 genes ⇩] which were found not to contain any GO categories that could be considered statistically significant [EASE score ≥1.30, Benjamini-Hochberg FDR uncorrected p<0.05 (Section 2.3.2.5.4)] with 'Medium' classification stringency defined in the DAVID online functional annotation enrichment analysis described in Section 6.2 [APPENDIX TABLE B18].

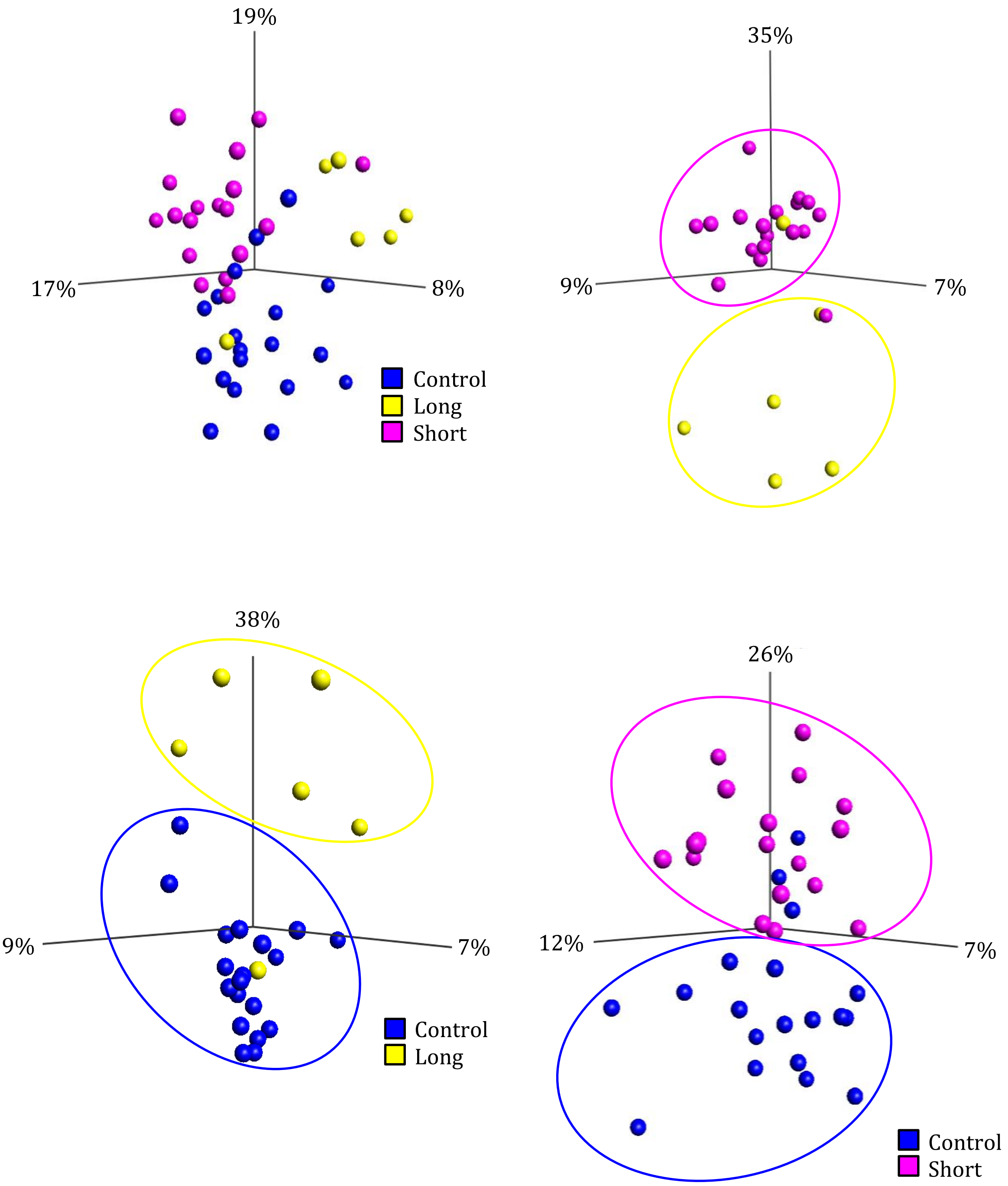
6.2.3 MALE Samples

6.2.3.1 Clustering Analysis

A Qlucore Omics Explorer multi-group comparative analysis [ANOVA F-test p<0.05, FC ≥ ±1.20] of male only LCL cases (n=24) and controls (n=21) (Blue) in the ECACC *C9ORF72+* long (≥4yrs) (Yellow) versus short (<2yrs) (Pink) survival study (Figure 6.10a) identified 2,410 of 22,011 variables that explain up to 19% of the variance in GEP's generated between patient and control samples along the y-axis of PC1 and a further 17% or 8%, respectively of the variance between a fast versus slow disease progression along the x and z-axes of PC2 and PC3.

Two-group comparative analyses, which were also conducted at the 5% significance threshold [ANOVA F-test p<0.05, FC ≥ ±1.20], identified corresponding lists of 1,376 (C9-Long v C9-Short), 2,131 (C9-Long v Ctrl) and 2,470 (C9-Short v Ctrl) variables, respectively that explain up to 35% of the variance in GEP's generated between the *C9ORF72+* LCL's with a long (≥4yrs) (Yellow) versus short (<2yrs) (Pink) survival (Figure 6.10b) in addition to 38% of the variance between *C9ORF72+* long (≥4yrs) survival cases versus control (Blue) (Figure 6.10c) and a further 26% of the variance between *C9ORF72+* short (<2yrs) survival cases versus controls (Figure 6.10d).

6.2.3.2 DAVID Enrichment of Partek® Generated Gene Lists



#	ANOVA	Comparison	Eliminated Factor	p-value	Fold	Variables
a)	Multi-Group	🟨 🟪 🟦	'Age'	<0.05	±1.20	2,410/22,011
b)	Two-Group	🟨 🟪	'Age'	<0.05	±1.20	1,376/22,011
c)	Two-Group	🟨 🟦	'Age'	<0.05	±1.20	2,131/22,011
d)	Two-Group	🟪 🟦	'Age'	<0.05	±1.20	2,470/22,011

Figure 6.10 Qlucore Omics Explorer Clustering Analysis [ANOVA F-test p<0.05, FC ≥ ±1.20] of MALE ONLY Samples in the *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study

Abbreviations: ANOVA - analysis of variance, *C9ORF72* - chromosome 9 open reading frame 72 and FC - fold-change.

6.2.3.2.1 C9ORF72+ LongvShort Survival

A Partek® Genomics Suite™ analysis conducted at the 5% significance threshold of male only samples identified 1,024 DE transcripts [unadjusted $p<0.05$, FC ≥ ±1.20] in a direct comparison between the *C9ORF72+* LCL cases with a long (≥4yrs) versus short (<2yrs) survival. These included 551 genes (53.8%) which were significantly up-regulated (⇧) and 473 genes (46.2%) that were significantly down-regulated (⇩). In DAVID, 1,015 mapped ID's [546 genes ⇧ and 469 genes ⇩] were returned which were found to be enriched for GO categories associated with DNA helicase activity, negative regulation of gene transcription, hormone receptor binding and ubiquitin-mediated proteolysis (Table 6.8a) as well as aspects of RNA processing/metabolism, Golgi vesicle transport, initiation of translation, response to cellular stress and the modulation of immunity (Table 6.8b) [APPENDIX TABLE B19].

a) MALE Samples C9-Long v C9-Short ⇧$_{reg}$ [Partek® unadjusted $p<0.05$, FC≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0006355	regulation of transcription, DNA-templated	4.27	122	3.30E-09
2	GO:0010629	negative regulation of gene expression	2.47	29	5.30E-04
3	GO:0019941	modification-dependent protein catabolic process	2.01	29	3.70E-03
4	GO:0008026	ATP-dependent helicase activity	1.91	10	2.50E-03
5	GO:0051427	hormone receptor binding	1.50	8	0.016
6	GO:0043933	macromolecular complex subunit organisation	1.49	22	1.30E-03

b) MALE Samples C9-Long v C9-Short ⇩$_{reg}$ [Partek® unadjusted $p<0.05$, FC≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0043933	macromolecular complex subunit organisation	2.60	35	4.90E-04
2	GO:0006396	RNA processing	2.39	33	1.80E-05
3	GO:0034660	ncRNA metabolic process	2.20	17	3.70E-04
4	GO:0048193	Golgi vesicle transport	2.01	11	2.30E-03
5	GO:0017076	purine nucleotide binding	1.94	71	9.10E-04
6	GO:0008104	protein localisation	1.68	44	5.70E-05
7	GO:0015780	nucleotide-sugar transport	1.38	3	9.60E-03
8	GO:0050662	coenzyme binding	1.37	11	0.017
9	GO:0016876	ligase activity, forming aminoacyl-tRNA and related compounds	1.36	5	0.031
10	GO:0051028	mRNA transport	1.36	7	0.026
11	GO:033554	cellular response to stress	1.35	25	0.014
12	GO:006446	regulation of translation initiation	1.33	5	0.022
13	GO:0032395	MHC class II receptor activity	1.32	4	0.012

Table 6.8 DAVID Enrichment of MALE ONLY Samples in the ECACC *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study

Abbreviations: # - rank, ⇧$_{reg}$ - up-regulated, ⇩$_{reg}$ - down-regulated, ATP - adenosine triphosphate, *C9ORF72* - chromosome 9 open reading frame 72, DAVID - Database for Annotation, Visualisation and Integrated Discovery, EASE - enrichment score, ECACC - European Collection of Cell Cultures, FC - fold-change, GO - gene ontology, MHC - major histocompatibility complex, mRNA - messenger RNA, ncRNA - non-coding RNA and tRNA - transfer RNA.

6.2.3.2.2 C9ORF72+ LongvCtrl and ShortvCtrl Survival

The GeneVenn diagram which is depicted in Figure 6.11 [Partek® unadjusted p<0.05, FC ≥ ±1.20] highlights 1,045 DE transcripts between *C9ORF72+* long (≥4yrs) survival cases and controls including 705 genes (78.9%) that were significantly up-regulated and 340 genes (21.1%) which were significantly down-regulated. Additionally, 1,067 DE transcripts were highlighted between the *C9ORF72+* short (<2yrs) survival cases and controls including 639 genes (59.9%) that were significantly up-regulated and 428 genes (40.1%) which were significantly down-regulated. Among the transcripts highlighted were 894 genes found to be specifically dysregulated in the *C9ORF72+* long (≥4yrs) survival cases [609 genes ⇧ and 285 genes ⇩] and a further 916 genes that were found to be specifically dysregulated in *C9ORF72+* short (<2yrs) survival cases [544 genes ⇧ and 372 genes ⇩]. Commonly shared transcripts (n=151), which represent 14.5% or 14.2% of the aforementioned gene lists, respectively included calcium binding protein 1 (*CABP1*) [C9-Longvctrl ⇧1.36-fold, p<0.05; C9-Shortvctrl ⇩1.34-fold, p<0.01] which was the only transcript to exhibit opposing directions of change on the microarray.

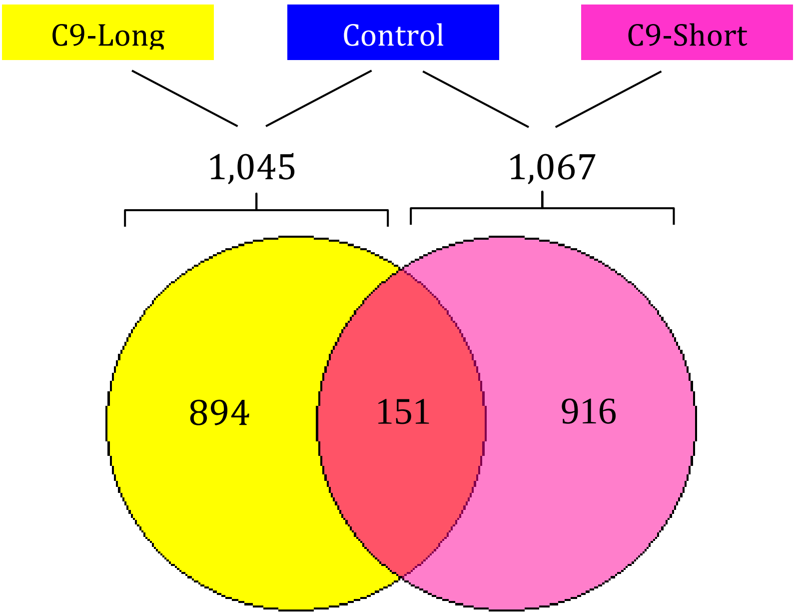


Figure 6.11 GeneVenn of MALE ONLY Samples in the ECACC *C9ORF72+*

Long (≥4yrs) versus Short (<2yrs) Survival Study Lists of DE transcripts were generated using Partek® Genomics Suite™ software version 6.6 copyright © 2013 (Partek® Inc., St Louis, MO, USA). GeneVenn application freely available online at genevenn.sourceforge.net (University of Southern Mississippi, USA) (Pirooznia et al 2007).

Abbreviations: *C9ORF72* (C9) - chromosome 9 open reading frame 72, DE - differentially expressed and ECACC - European Collection of Cell Cultures.

Importation of the male *C9ORF72+* long (≥4yrs) specific gene list (n=894) into DAVID returned 879 mapped ID's [598 genes ⇧ and 281 genes ⇩] which were found to be enriched for GO categories associated with structural constituents of the ribosome, GTPase activity, ubiquitin-mediated proteolysis, gene transcription, DNA helicase activity and ncRNA processing (Table 6.9a) as well as Golgi vesicle transport and the modulation of immunity (Table 6.9b) [APPENDIX TABLE B20].

a) MALE Samples C9-Long Specific ⇧$_{reg}$ [Partek® unadjusted p<0.05, FC≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0003735	structural constituent of ribosome	4.26	19	3.70E-06
2	GO:0003924	GTPase activity	2.68	19	8.20E-05
3	GO:0030163	protein catabolic process	2.46	35	8.30E-04
4	GO:0003714	transcription corepressor activity	2.41	15	1.40E-04
5	GO:0070035	purine NTP-dependent helicase activity	1.71	9	0.010
6	GO:0034470	ncRNA processing	1.57	13	0.013
7	GO:0034622	cellular macromolecular complex assembly	1.40	20	4.50E-03

b) MALE Samples C9-Long Specific ⇩$_{reg}$ [Partek® unadjusted p<0.05, FC ≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0048193	Golgi vesicle transport	1.42	7	0.017
2	GO:0032395	MHC class II receptor activity	1.31	3	0.032

Table 6.9 DAVID Enrichment of MALE ONLY C9-Long Specific Gene Lists

Abbreviations: # - rank, ⇧$_{reg}$ - up-regulated, ⇩$_{reg}$ - down-regulated, C9 - chromosome 9 open reading frame 72, DAVID - Database for the Annotation, Visualisation and Integrated Discovery, EASE - enrichment score, FC - fold-change, GTPase - guanosine triphosphatase, ncRNA - non-coding RNA and NTP - nucleotide triphosphate.

Conversely, importation of the male *C9ORF72+* short (<2yrs) specific gene list (n=9 16) returned 906 mapped ID's [536 genes ⇧ and 370 genes ⇩] which were enriched for GO categories associated with ncRNA metabolism, structural constituents of the ribosome, DNA damage response, cellular respiration, unfolded protein binding and mitochondrial release of cytochrome c (Table 6.10a), in addition to, organisation of the cytoskeleton, cell adhesion, cell junction assembly, GTPase mediated signalling, regulation of cellular component movement and skeletal system development (Table 6.10b) [APPENDIX TABLE B21].

a) MALE Samples C9-Short Specific ⇧$_{\text{reg}}$ [Partek® unadjusted $p<0.05$, FC≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0034660	ncRNA metabolic process	4.31	21	6.60E-06
2	GO:0003735	structural constituent of ribosome	3.14	17	1.10E-05
3	GO:0006974	cellular response to DNA damage stimulus	3.12	24	3.10E-04
4	GO:0045333	cellular respiration	1.99	10	1.50E-03
5	GO:0004526	ribonuclease P activity	1.94	4	2.00E-03
6	GO:0051289	protein homotetramerization	1.67	5	5.40E-03
7	GO:0016879	ligase activity, forming carbon-nitrogen bonds	1.53	15	3.80E-03
8	GO:0001836	release of cytochrome c from mitochondria	1.46	4	0.020
9	GO:0010212	response to ionizing radiation	1.38	7	6.30E-03
10	GO:0006396	RNA processing	1.37	34	2.40E-05
11	GO:0007264	small GTPase mediated signal transduction	1.36	16	0.024
12	GO:0051082	unfolded protein binding	1.30	8	0.035

b) MALE Samples C9-Short Specific ⇩$_{\text{reg}}$ [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

#	GO term	Functional Category	EASE	Count	p-value
1	GO:0007010	cytoskeleton organisation	5.27	27	5.60E-07
2	GO:0007155	cell adhesion	3.77	32	2.30E-05
3	GO:0051270	regulation of cellular component movement	3.69	17	1.50E-06
4	GO:0031267	small GTPase binding	2.43	9	9.00E-04
5	GO:0030695	GTPase regulator activity	2.17	23	1.90E-05
6	GO:0032147	activation of protein kinase activity	2.05	12	1.60E-05
7	GO:0046983	protein dimerization activity	1.92	21	5.80E-03
8	GO:0031418	L-ascorbic acid binding	1.84	4	7.90E-03
9	GO:0019838	growth factor binding	1.82	9	1.20E-03
10	GO:0009101	glycoprotein biosynthetic process	1.73	10	4.20E-03
11	GO:0016702	oxidoreductase activity, acting on single donors with incorporation of molecular oxygen, incorporation of two atoms of oxygen	1.59	6	9.90E-03
12	GO:0009611	response to wounding	1.56	20	9.20E-03
13	GO:0034329	cell junction assembly	1.55	5	8.60E-03
14	GO:0048567	ectodermal digestive tract morphogenesis	1.47	3	0.016
15	GO:0001883	purine nucleoside binding	1.42	47	6.10E-03
16	GO:0001501	skeletal system development	1.40	15	4.60E-03
17	GO:0031349	positive regulation of defence response	1.36	6	0.015

Table 6.10 DAVID Enrichment of MALE ONLY C9-Short Specific Gene Lists

Abbreviations: # - rank, ⇧$_{\text{reg}}$ - up-regulated, ⇩$_{\text{reg}}$ - down-regulated, C9 - chromosome 9 open reading frame 72, DAVID - Database for the Annotation, Visualisation and Integrated Discovery, EASE - enrichment score, FC - fold-change, GTPase - guanosine triphosphatase and ncRNA - non-coding RNA.

6.3 DISCUSSION

In the *C9ORF72+* long (≥4yrs) versus short (<2yrs) survival study there was a slight trend towards a younger age of symptom onset predicting a slower disease course (Table 6.1) [*C9ORF72+* long (≥4yrs) 53.7±12yrs (n=14) and *C9ORF72+* short (<2yrs) 58.4±11yrs (n=26) for all samples combined; unpaired student's t-test p>0.05 (not significant)] which supports the previously published findings of Lee et al (2013a), Magnus et al (2002), Mandrioli et al (2006), Williams et al (2013) and Yoshida et al (1986). A significantly higher percentage of spinal onset cases were apparent in the *C9ORF72+* long (≥4yrs) survival cohort; consistent with the reports of Louwerse et al (1997), Pupillo et al (2014), Tysnes et al (1994) and Zoccolella et al (2008). Across the *C9ORF72+* short (<2yrs) survival cohort males had a similar proportion of spinal (55.6%) and bulbar (22.2%) onset cases in comparison to the wider ALS population (Korner et al 2011) (Section 1.2.1). In contrast, female patients had a considerably greater incidence of bulbar (44.4%) or mixed (33.3%) presentation, which has also been observed elsewhere in the literature (Beghi et al 2007, Chancellor et al 1993, del Aguila et al 2003, Kristensen & Melgaard 1977, Salemi et al 1989, Scotton et al 2012). Other prognostic factors that correlate negatively with survival include EEC (i.e. definite versus probable/suspected ALS), low ALSFRS-R scores [*C9ORF72+* long (≥4yrs) 38.5±5 (n=14) and *C9ORF72+* short (<2yrs) 27.4±13 (n=26) for all samples combined; unpaired student's t-test (p<0.01**)] and a short diagnostic delay (Table 6.1) (Hardiman et al 2011, Kaufmann et al 2005, Lo Coco et al 2007, Louwerse et al 1997, Pupillo et al 2014, Zoccolella et al 2008).

Another interesting observation is that more patients in the *C9ORF72+* long (≥4yrs) survival cohort had received Riluzole therapy (86.7%) and were taking Vitamin C/E or multivitamin supplements (46.7%) at the time of biosample collection compared to patients in the *C9ORF72+* short (<2yrs) survival cohort which had percentages of 77.8% and 22.2%, respectively (Section 1.1.4).

Initially, in an analysis of all samples combined [Partek® unadjusted p<0.05, FC ≥ ± 1.20], a direct comparison was drawn between ECACC LCL's carrying the *C9ORF72* expanded allele which have a fast (Section 6.1.1.1.2) versus slow (Section 6.1.1.1.3) disease progression, to identify genetic modifiers of survival that may or may not be influenced by the underlying pathogenesis of ALS (Section 6.2.1.2.1) (de Magalhaes et al 2009, Fraser et al 2005, Glass et al 2013, Kwon et al 2010). These included DE transcripts which were found to be enriched for DAVID returned GO categories that are associated with gene transcription, negative regulation of apoptosis and vesicle-mediated transport from the list of up-regulated changes (Table 6.3a) as well as the cell cycle, DNA damage response pathways and Golgi-mediated transport from the list of down-regulated changes (Table 6.3b). Dysregulation of vesicular trafficking in relation to the *C9ORF72+* long (≥4yrs) survival cases has also been observed in post-mortem brain tissue from 30 participants recruited to a human ageing study (Lu et al 2004). A diminished response to DNA damage and the possibility of cell cycle arrest are also interesting findings, especially given prior links between genomic instability and cellular senescence in premature ageing disorders such as Werner's syndrome and Hutchinson-Gilford progeria syndrome (Kudlow et al 2007, Lei et al 2012, Scaffidi et al 2005, Serio 2011).

In a subsequent analysis of *C9ORF72+* long (≥4yrs) and short (<2yrs) survival cases versus neurologically normal, age and gender matched, healthy controls (n=31) a GeneVenn diagram depicted in Figure 6.7 highlighted many more genetic modifiers of a fast or slow disease progression which were specific to ALS (Section 6.2.1.2.2). These included DE transcripts enriched for GO categories that are associated with RNA processing (Section 5.2.1.3) (also seen to have increased with age in skin cells derived from a large number of female MZ and dizygotic (DZ) twins (n=856) (Glass et al 2013)) and translation or ribosome biogenesis identified previously from the analysis of Chapter 5 (Section 5.2.1.4) in addition to RNA polymerase activity, gene transcription, oxidative phosphorylation, response to ROS (Section 1.2.4.1) and the regulation of apoptosis from the list of up-regulated changes and cellular response to starvation, solute: cation symporter activity, carboxylic acid transport, multiple metabolic pathways as well as organisation of the lysosome from the list of down-regulated changes (Table 6.4). Evidence of an elevated response to ROS specifically occurring in relation to the *C9ORF72+* long (≥4yrs) survival cases was a significant finding given the importance of oxidative stress in the neurodegenerative disease process; particularly in instances of SOD1-linked ALS (Section 1.2.5.1.1) (Barber et al 2006, Cluskey & Ramsden 2001) and in view of the well-established free radical theory of ageing (Beckman & Ames 1998, Harman 1956, Hekimi & Guarente 2003, Hughes & Reynolds 2005). Contrastingly, for the *C9ORF72+* short (<2yrs) survival cases DAVID returned GO categories which were associated with DNA metabolism, cellular response to stress and the cell cycle from the list of up-regulated changes (Table 6.5a) as well as cell-substrate adhesion, cell motion, protein kinase activity, polysaccharide binding, regulation of the immune response [a noteworthy feature given the potential role for non-cell autonomous mediated toxicity in ALS (Section 1.2.4.6) (Appel et al 2011, Ilieva et al 2009)] and cytoskeletal organisation from the list of down-regulated changes (Table 6.5b). The fact that *C9ORF72+* short (<2yrs) survival cases appear to be going into the cell cycle is interesting since it is also a phenomenon that has been discussed in transcriptional profiling of MN's, a disease relevant tissue, isolated from the transgenic SOD1^{G93A} mouse model (Ferraiuolo et al 2007).

In the literature a number of key genetic determinants of survival in ALS have been recorded including vascular endothelial growth factor A (*VEGFA*) (Anand et al 2012, Gupta et al 2011, Vijayalakshmi et al 2014, Wang et al 2007), unc-13 homolog A (*C. elegans*) (*UNC13A*) (Section 1.2.5.1.11) (Chio et al 2013b), zinc finger protein 512B (*ZNF512B*) (Tetsuka et al 2013), activating transcription factor 3 (*ATF3*) (Seijffers et al 2014), kinesin-associated protein 3 (*KIFAP3*) (Landers et al 2009), EPH receptor A4 (*EPHA4*) (Van Hoecke et al 2012) and glutamate receptor, metabotropic 1 (*GRM1*) (Milanese et al 2014). With the exception of *VEGFA* [⇩1.28-fold, $p<0.05$ C9-LongvCtrl and ⇩1.27-fold, $p<0.05$ C9-LongvShort], a potent angiogenic factor which has been demonstrated through its activation of the anti-apoptotic PI3K-Akt pathway to delay disease onset and to slow down the rate of progression in the transgenic SOD1^{G93A} mouse, none of the other genes mentioned above were found to be dysregulated in the ECACC LCL's possibly owing, at least in part, to the fact that some or all of these genes may not be expressed in B-lymphocytes (Azzouz et al 2004, Storkebaum et al 2005).

A notable gender imbalance between the *C9ORF72+* long (≥4yrs) and short (<2yrs) [M:F ratio 0.67:1 and 2.00:1, respectively (Figure 6.1)] survival cases prompted an independent analysis [Partek® unadjusted $p<0.05$, FC ≥ ±1.20] of male (Section 6.2.3) and female (Section 6.2.2) only samples. In a former, direct comparison between male G_4C_2 repeat carriers which have a fast versus slow disease progression DAVID identified GO categories associated with gene transcription (common to all samples combined), ATP helicase activity and ubiquitin-mediated proteolysis from the list of up-regulated changes (Table 6.8a) in addition to RNA processing, a major pathway implicated in the pathogenesis of a number of neurodegenerative diseases (Section 1.2.4.9) (Anthony & Gallo 2010), ncRNA metabolism, Golgi vesicle transport, mRNA transport/translation, protein localisation and cellular response to stress from the list of down-regulated changes (Table 6.8b). In an identical analysis of female G_4C_2 repeat carriers, DAVID identified GO categories associated with gene transcription and the induction of apoptosis from the list of up-regulated changes (Table 6.6a) as well as the cell cycle (common to all samples combined), phospholipid biosynthesis and protein N-linked glycosylation from the list of down-regulated changes (Table 6.6b). Dysregulation of the cell cycle has also been seen in a meta-analysis of more than 20 ageing studies combining datasets from humans and animal (mouse and rat) models (de Magalhaes et al 2009).

Of the *C9ORF72+* long (≥4yrs) specific categories ribosome biogenesis (common to all samples combined), GTPase activity and ncRNA metabolism (opposing direction to above C9-LongvShort analysis) were found to be significantly up-regulated (Table 6.9a) whereas Golgi vesicle transport and major histocompatibility complex (MHC) class II receptor activity were significantly down-regulated in male cases relative to controls (Table 6.9b). In contrast, female *C9ORF72+* long (≥4yrs) specific categories included gene transcription/translation (common to all samples combined), protein transport, ubiquitin-mediated proteolysis, RNP complex biogenesis, the regulation of apoptosis, energy metabolism and the cell cycle (opposing direction to above C9-LongvShort analysis) which were significantly up-regulated (Table 6.7a) as well as cholesterol metabolism, protein N-linked glycosylation, vitamin binding and cellular response to starvation (common to all samples combined) (Table 6.7b) which were significantly down-regulated in relation to controls. Perturbations in the latter were interesting findings in respect to the fact that a higher proportion of *C9ORF72+* long (≥4yrs) survival cases were taking vitamin C/E or multivitamin supplements (Section 6.1.1.2) and given the connection between poor nutritional status and shortened life expectancy in those patients who develop more severe symptoms of dysarthria and dysphagia during the clinical course of the disease (Scotton et al 2012).

Of the *C9ORF72+* short (<2yrs) specific categories none were found to be enriched for the analysis of the female only samples (Section 6.2.2.2.2). In male cases relative to controls, DE transcripts associated with ncRNA metabolism, structural constituent of the ribosome and small GTPase mediated signal transduction (i.e. similar to those in the *C9ORF72+* long (≥4yrs) specific list) along with cellular respiration, response to DNA damage stimulus, RNA processing and mitochondrial release of cytochrome c (Section 1.2.4.8) were identified as being significantly up-regulated (Table 6.10a) whereas the organisation of the cytoskeleton, cell adhesion and activation of protein kinase activity (similar to all samples combined) were found to be significantly down -regulated (Table 6.10b).

The *C9ORF72+* ALS common lists, represented by the intersection of the GeneVenn diagram depicted in Figures 6.7, 6.9 and 6.11, were also interrogated to determine whether any transcripts of interest occur in opposing directions of change between cases with a fast versus slow disease progression. These included: chaperonin, heat shock 70kDa protein 1A (*HSPA1A*) [⇩1.44-fold, $p<0.05$ C9-LongvCtrl and ⇧1.33-fold, $p<0.05$ C9-ShortvCtrl] from an analysis of all samples combined which is interesting given a potential therapeutic role for Arimoclomol in an ongoing phase II clinical trial (Kalmar et al 2014); neuron specific calcium binding protein 1 (*CABP1*) [⇧1.36-fold, $p<0.05$ C9-LongvCtrl and ⇩1.34-fold, $p<0.01$ C9-ShortvCtrl] in the male only group, which modulates the activity of inositol 1,4,5-triphosphate receptors (Li et al 2009, Li et al 2013a) and has been shown to be highly expressed in human brain tissue and the retina (Wingard et al 2005) as well as stress granule and nucleolar protein, SGNP [*DNAPTP6* (DNA polymerase transactivated protein 6) ⇧1.45-fold, $p<0.05$ C9-Long vCtrl and ⇩1.62-fold, $p<0.01$ C9-ShortvCtrl] from the female only group which is considered important for the regulation of ribosomal biogenesis and translational control in response to OS (Section 1.2.4.1) (Zhu et al 2008).

Overall, similar proportions of up and down-regulated genes (Partek®) [unadjusted $p<0.05$, $FC \geq \pm1.20$] or variables (Qlucore) [ANOVA F-test $p<0.05$, $FC \geq \pm1.20$] were identified in all three comparisons with the molecular signatures from GEP analyses most likely reflecting a combination of the underlying neurodegenerative processes and transcriptional changes that occur in response to ageing. These may be difficult to dissect apart fully especially since ALS is a late onset disorder in which patients do not typically manifest symptoms of the disease before their sixth or seventh decade (Calvo et al 2014b, Kinsley & Siddique 2001).

Despite the female only samples demonstrating a clearer degree of separation on the PCA plot (Figure 6.8 in comparison to Figures 6.5, 6.6 and 6.10) (i.e. fewer variables having a larger effect size and explaining more of the variance in GEP's along the y-axis of the first principal component) lists of Partek® generated DE transcripts were notably smaller and underpowered to detect biologically enriched GO categories in the DAVID functional annotation clustering analysis tool (lower EASE scores, poor gene counts and weaker p-values with the exception of the *C9ORF72+* short (<2yrs) specific changes which failed to return a significant result altogether); possibly due to the limited sample numbers in this group. Not only that, in some instances it has also been difficult to obtain accurate survival data with the dates of onset provided in the local or national databases normally accurate to within 3 to 6 months which partially stems from the insidious nature of the disease (Nzwalo et al 2014, Paganoni et al 2014). In future studies these issues could be addressed by recruiting a larger patient cohort and widening the gap between the thresholds for defining a fast (<12 months) versus slow (>5yrs) progression which was not possible in the scope of this project.

CHAPTER 7: CONCLUDING REMARKS

Since the advent of the Human Genome Project (Watson 1990), launched almost 25 years ago, microarray analysis has become an invaluable tool (Bombard et al 2014, Lohmann et al 2013, Moroi & Heckenlively 2008, Waldman & Terzic 2008) which is paving the way towards a more personalised health care system in the UK and elsewhere. Its technology offers the end user a rapid, high-throughput approach to global GEP (Agostini et al 2012, Wu et al 2012b) that is accurate, reproducible and unbiased. Using a single GeneChip® or array, it has become possible to take a snap shot of the level of gene expression pertaining to a vast number of mRNA targets and/or splice variants within a particular tissue or cell of interest at any given point in time (Sharp et al 2006b). Though the generation of patient specific molecular profiles or gene signatures it is anticipated that clinicians will soon be able to sub-classify complex aetiologies into genetically defined sub-groups which correlate with certain aspects of the phenotypic information available to them; thus providing more informative ways of stratifying diverse patient populations. This aims to improve diagnostic and prognostic decision making, as well as, being able to more reliably predict an individual's response to novel therapeutic or treatment strategies as already demonstrated in respect to paediatric septic shock (Wong et al 2010, Wong et al 2014), I BD (van Lierop et al 2013) and Acute Myeloid Leukemia (Haferlach et al 2010, Tsutsumi et al 2004); a heterogeneous disorder of neoplasms which has led to the invention of the world's first diagnostic DNA chip, the AML-profiler™ (Skyline Diagnostics, The Netherlands).

The MN's which degenerate in ALS remain inaccessible during life. There are also a number of limitations associated with the use of post-mortem material; not least of all that the GEP's generated will inevitability only reflect the very terminal stages of disease progression (i.e. the point at which the majority of vulnerable neuronal cell populations will have already been lost from the system which makes it difficult to establish cause or effect) (Cooper-Knock et al 2012a, Sharp et al 2006a, Sutherland et al 2011). Therefore, great benefits are to be had in sampling surrogate peripheral tissues that lend themselves to better standardisation of technical procedures. Whole blood, for example, represents a particularly attractive source of RNA, owing to the longitudinal sampling method it supports and the overall ease with which it can be collected (Burczynski & Dorner 2006). The fact that it interacts with and permeates every other tissue & organ of the mammalian body is suggestive of circulating blood constituting a rich biosensor pool which has the potential to act as a sentinel of the neurodegenerative disease process (Kennedy et al 2008, Pahl 2005). It has become apparent, however, that the sheer abundance of erythrocyte derived alpha and beta haemoglobin transcripts (~70% total RNA) (Winn et al 2010) produces interference on the microarray which masks the detection of other, less abundant transcripts of equal biological importance within the sample (Feezor et al 2004, Wright et al 2008). The initial aim of this project in evaluating, following PAXgene® RNA extraction, the use of two globin reduction strategies, concluded that the Ambion® GLOBINClear™ protocol (Dr Rohini Raman) and NuGEN Ovation® Whole Blood Solution were both highly variable and inefficient, with inconsistent findings reported across identical SALS patient and control samples collected at the same time in separate PAXgene® Blood RNA Collection Tubes. Given these challenges it was hypothesised, therefore, that immortalised EBV-transformed B-lymphocytes (LCL's) which represent a more homogeneous cell population would be advantageous in the detection of robust GE changes that can reliably aid in the sub-classification of disease using a large bank of frozen LCL pellets obtained from the ECACC held at the HPA (Public Health England, UK). In light of a pathogenic non-coding G_4C_2 hexanucleotide repeat expansion, of > 30 copies, having recently been identified in *C9ORF72* (Renton et al 2011, DeJesus-Hernandez et al 2011), which is now thought to account for up to 43% of FALS and around 7% of SALS cases (Cooper-Knock et al 2012b) (Section 1.2.5.4), it was also of interest to: 1) elucidate further mechanism(s) of neurotoxicity associated with the expansion and 2) determine genetic modifiers of a fast (<2yrs survival) versus slow (≥4yrs survival) disease progression in *C9ORF72*-related cases of ALS.

Due to time constraints, and various delays in obtaining samples from the National MNDA DNA Bank, along with the relevant and most up-to-date clinical information (e.g. gender, age and site of onset, EEC, ALSFRS-R, Riluzole status and time to death) and mutational screening data, particularly of the *C9ORF72* gene, it meant not all of the LCL samples recruited to the original ECACC discovery (Section 4.1.1) and replication (Section 4.1.2) cohorts (n=820) [120-FALS, 500-SALS and 200-CTRL] could be analysed in the scope of this study. Across the LCL's that were processed and had subsequently passed the Affymetrix® QC metrics assessed in Expression Console™ software version 1.3.0.187, there was an overall increase in the level of gene transcription which was observed in respect to *C9ORF72* (59.3%, n=650/1,096) and non*C9ORF72*-related_SALS (63.9%, n=1,148/1,796) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20] cases compared to a subset of neurologically healthy, age and gender matched, controls. In DAVID, functionally enriched gene ontology (GO) categories included translation which was specific to the *C9ORF72* expansion, as well as RNA processing, DNA metabolism, RNP complex biogenesis and regulation of the cell cycle that were found to be a more common feature of the broader ALS phenotype. The differential expression of a number of key validation targets including several *C9ORF72* binding partners (*NUDT21, RPL22, EIF4H, PURA, HNRNPA0/F* and *FUS*) (Section 5.2.4) of the G_4C_2 repeat were subsequently confirmed by qRT-PCR (traditional SYBR® Green or IDT Prime Time® Mini qPCR Assays) using pooled RNA samples with a RIN score of 7.5 or above, from the microarray plus additional *C9ORF72+* cases (n=75) and controls (n=35) from the ECACC discovery and replication cohorts.

The *C9ORF72* gene itself was down-regulated in a subset of the LCL's (Section 5.2.3) (Cooper-Knock et al 2013b); however this could not be replicated across the rest of the cohort. This could, at least partially, be due to the presence of alternative splice variants encoding different protein isoforms (a/b) which exert contradictory effects depending upon the location of the expanded G_4C_2 repeat sequence with respect to exons 1a [Variant I (NM_001256054) full length 481a.a. and Variant II (NM_145005) truncated 222a.a.] and 1b [Variant III (NM_018325) full length 481a.a. (Figure 5.22)]. From the literature it can be speculated that in exon 1b containing transcripts the expansion is situated within the core promotor region which is expected to lead to a significant reduction in its expression whereas, in exon 1a containing transcripts the expansion is known to reside in intron 1 which results in aberrant transcription of the hexanucleotide G_4C_2 repeat (Renton et al 2011, DeJesus-Hernandez et al 2011). On the Human Exon 1.0ST GeneChip® Arrays and by qRT-PCR it was not possible to distinguish between full length transcript Variants I and III (isoform a); thus providing some explanation as to why no overall effect was observed in the LCL's or iPSC derived MN cultures in a subsequent study conducted by Sareen et al (2013).

Whether pathogenicity of the expansion arises from a loss of function (haploinsufficiency) or gain of function mechanism mediated by the formation of toxic RNA foci (Donnelly et al 2013) or RAN translated DPR proteins (Gendron et al 2013b) is not fully understood. However, an up-regulation in the expression of *C9ORF72* binding partners of the G_4C_2 repeat and other RNA processing related genes supports a role for RNA toxicity whereby the cells are attempting to compensate for the sequestration of these proteins by aberrantly formed foci in the cytoplasm (Cooper-Knock et al 2014b).

One limitation of the PhD was the technology and software constraints in analysing alternative splicing events that are estimated to affect more than 90% of the human genome (Pan et al 2008, Wang et al 2008). On Human Exon 1.0ST GeneChip® Arrays probeset (exon level) signal intensities are normalised to the mean intensity value for the gene as a whole rather than the overall mRNA levels for all the transcripts on the microarray which is used as an index of the extent to which a particular exon is included or excluded in relation to the global expression of the relevant gene that it represents a constituent part of. This means whilst detailed information regarding the total number of splice variants and the proportion of these variants that contain each of the individual exons is available, the precise manner in which the inclusion or exclusion of one probeset relates to another is lacking (Highley et al 2014). The recent launch of the Transcriptome Analysis Console 2.0 software (Affymetrix® Ltd., UK) is expected to simplify the interpretation of future experiments, along with the release of the Human Transcriptome GeneChip® Array 2.0 which will provide even greater coverage with over six million probes [~150 probes/gene, 10 probes/exon and 4 probes/exon-exon splice junction].

In the ECACC analysis of a fast (<2yrs survival) versus slow (≥4yrs survival) disease progression sample sizes were too small to be able to draw meaningful conclusions. Clinical data pointed towards a possible effect of gender which is supported in the literature from manipulation of the murine $SOD1^{G93A}$ mouse model (Alves et al 2011, Cervetto et al 2013, Gunther et al 2014, Heiman-Patterson et al 2005, Naumenko et al 2011, Pan et al 2012); although other factors, such as correlations with expansion length, will need to be considered in conducting future work.

FUTURE WORK

- Due to time constraints it was not feasible to wait for all of the arrays in the ECACC discovery and replication cohorts to be processed before commencing the downstream comparative analyses described in Chapter 5: '*C9ORF72* GEP Study' and Chapter 6: '*C9ORF72* Long (≥4yrs) versus Short (<2yrs) Survival Study'. However, now that more CEL files have become available it would be of interest to re-run the bioinformatics pipelines using an independent validation cohort in order to confirm the reproducibility of our findings. Further corroboration of the microarray data could come from western blotting, to verify protein level changes, and functional *in vitro* studies using live LCL cultures; although the later would require additional ethical approval to be put in place. Checking to see whether DE or alternatively spliced transcripts detected in the ECACC EBV-transformed B-lymphocytes correlate with those identified from laser capture micro-dissected MN's (i.e. representing the most vulnerable cell population affected by the neurodegenerative disease process) would be an important next step in confirming the utility of peripheral tissues in performing GEP in ALS.

- Re-analyse the exon level data using the Transcriptome Analysis Console (TAC), recently launched by Affymetrix® Ltd., UK which aims to simplify the analysis of functional gene networks/pathways and alternative splicing events. Packages are now also available within R [e.g. work carried out by Cooper-Knock et al (2015b) using FIRMA ('finding isoforms using robust multichip analysis') concluded that there was no significant difference in the overall number of alternative splicing events pertaining to the same bank of ECACC LCL's between *C9ORF72* and non*C9ORF72*-related ALS, however, splicing associated with the G_4C_2 hexanucleotide repeat was found to be less consistent and more prone to errors which correlated with disease severity].

- Where possible, obtain more accurate survival data for the *C9ORF72+* LCL's in the ECACC discovery and replication cohorts. It may be the case that some patients who were still reported to be alive in June 2013 have now passed the threshold for inclusion into the *C9ORF72+* Long (≥4yrs) versus Short (<2yrs) Survival Study. Also investigate whether any additional cell lines, which met the necessary selection criteria, have been recruited to the National MNDA DNA Bank since commencing the PhD. If the cohort used in the analysis of Chapter 6 could be expanded in some way then the statistical power of the study could be greatly improved. Numbers depending, we could also consider widening the thresholds to examine, for example, cases with less than twelve months survival versus those with greater than five years survival. Failing that, an alternative approach may be to compare GEP's generated from biosamples collected at the point of symptom onset to those taken later on in the disease course (e.g. after 0-3, 3-6, 6-9, 9-12 and >12 months progression).

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Zu, T., et al. 2013. RAN Proteins and RNA Foci from Antisense Transcripts in C9ORF72 ALS and Frontotemporal Dementia. *Proc Natl Acad Sci USA* 110: E4968-77

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APPENDIX A: WHOLE BLOOD STUDY

List of Figures

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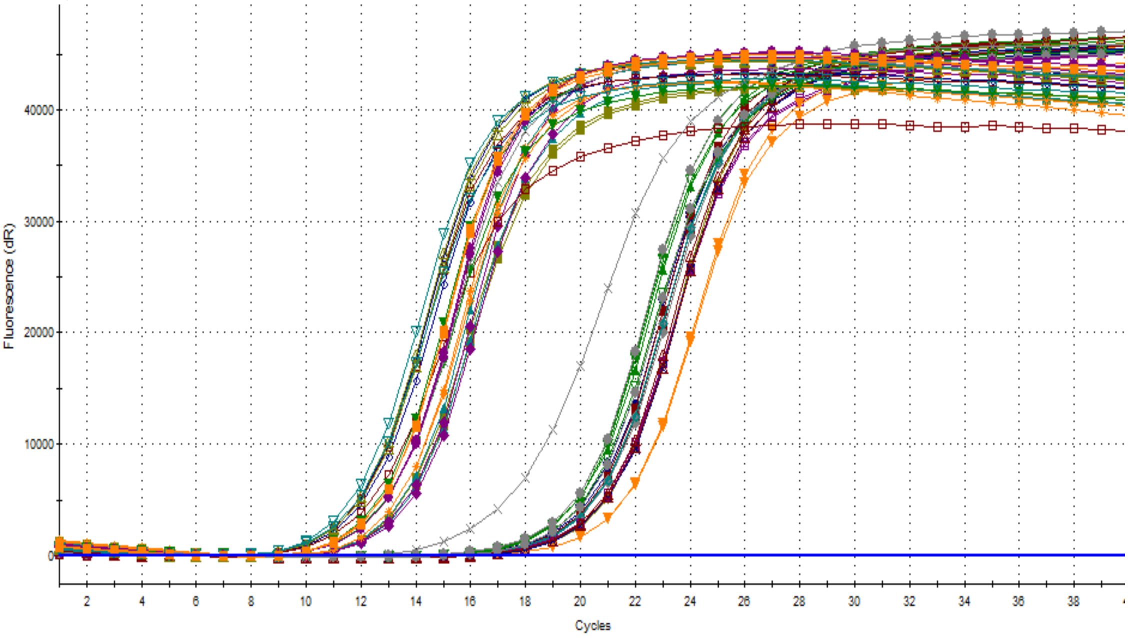
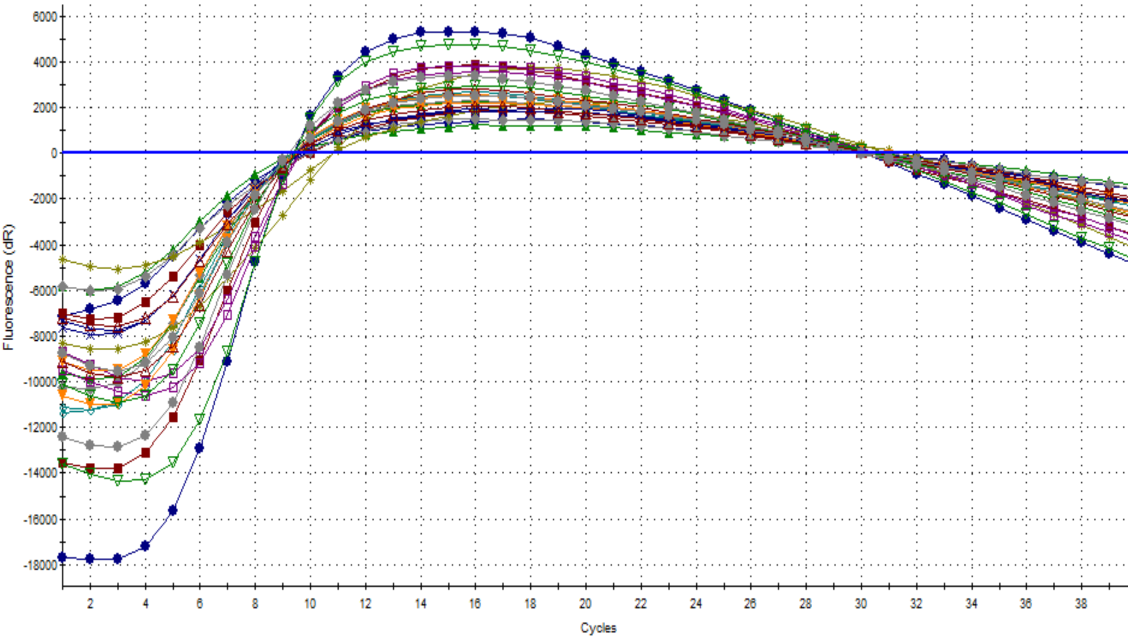
Figure A1: Representative Pre- and Post-SPIA™ qRT-PCR Profile Plots for *HBA2* and *ACTB* Measurements Using the Stratagene Brilliant II SYBR® Green Master Mix

a) Pre-SPIA™ Amplification Plots

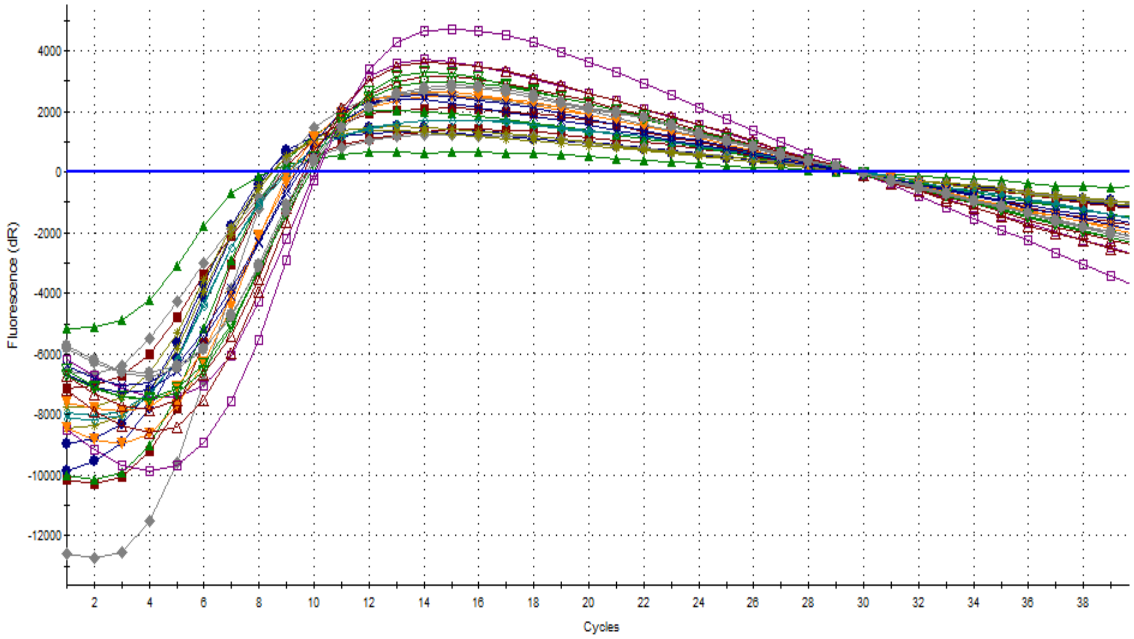


b) Post-SPIA™ Amplification Plots



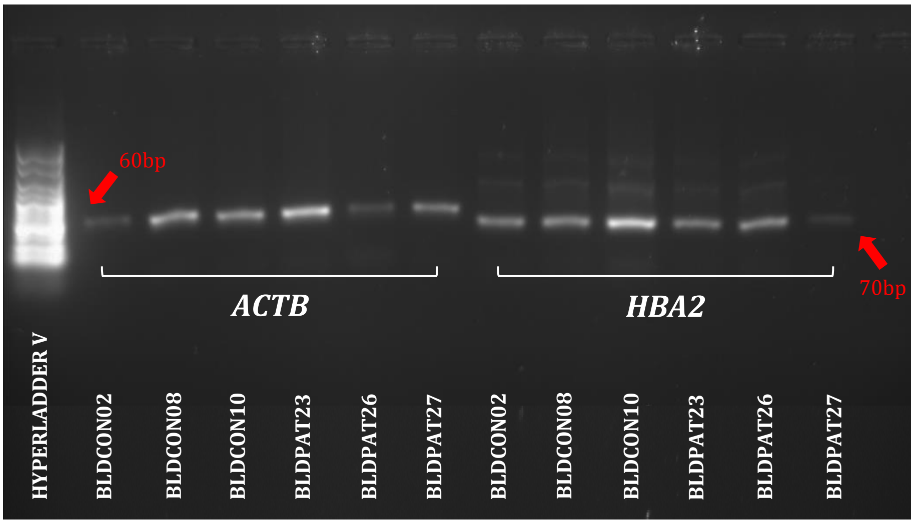
Abbreviations: *ACTB* - actin, beta, *HBA2* - haemoglobin alpha 2, qRT-PCR - quantitative real-time polymerase chain reaction and SPIA™ - single primer isothermal amplification

Figure A2: Representative Post-SPIA™ qRT-PCR Profile Plots for *HBA2* and *ACTB* Measurements Using the Roche FastStart Universal SYBR® Green Master Mix



Abbreviations: *ACTB* - actin, beta, *HBA2* - haemoglobin alpha 2, qRT-PCR - quantitative real-time polymerase chain reaction and SPIA™ - single primer isothermal amplification

Figure A3: Agarose Gel Image of *HBA2* and *ACTB* qRT-PCR Products



Abbreviations: *ACTB* - actin, beta, BLDCON - blood control, BLDPAT - blood patient, *HBA2* - haemoglobin alpha 2 and qRT-PCR - quantitative real-time polymerase chain reaction.

Table A1: JB NuGEN Ovation® Gene List (n=706) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

Probeset ID	Symbol		Fold	p-value	Probeset ID	Symbol		Fold	p-value	Probeset ID	Symbol		Fold	p-value
1556970_at	---	⇧	5.97	2.96E-06	209081_s_at	COL18A1	⇧	2.14	7.70E-03	223763_at	DTNBP1	⇧	1.95	1.07E-03
1570357_at	STX8	⇧	3.26	5.54E-05	222399_s_at	TM9SF3	⇩	2.13	0.012	212418_at	ELF1	⇩	1.94	0.025
201151_s_at	MBNL1	⇩	3.16	3.68E-03	229067_at	ODF3B	⇧	2.12	0.036	238706_at	PAPD4	⇩	1.93	0.042
231484_at	---	⇩	2.84	0.046	238327_at	SRGAP2P1	⇩	2.12	1.84E-03	222467_s_at	IRF7	⇧	1.93	0.039
216951_at	FCGR1A	⇧	2.74	0.040	219845_at	BARX1	⇧	2.12	1.79E-04	208436_s_at	SAPS3	⇩	1.93	0.025
212671_s_at	HLA-DQA1/2	⇧	2.74	0.017	219359_at	ATHL1	⇧	2.09	4.06E-03	218040_at	---	⇩	1.92	0.043
1555687_a_at	CLEC4C	⇩	2.73	0.015	210371_s_at	RBBP4	⇩	2.08	0.043	227428_at	TAZ	⇧	1.92	0.028
202118_s_at	CPNE3	⇩	2.54	0.040	220000_at	SIGLEC5	⇧	2.07	0.040	1560047_s_at	GABPA	⇩	1.92	0.022
231982_at	LOC284422	⇧	2.53	0.030	228471_at	---	⇩	2.06	0.033	203977_at	PRPF38B	⇩	1.92	0.018
206196_s_at	RUNDC3A	⇧	2.47	0.035	226792_s_at	HP	⇧	2.05	0.031	220404_at	---	⇧	1.91	0.037
206697_s_at	HP	⇧	2.40	0.021	208470_s_at	KIFC2	⇧	2.05	0.016	213439_x_at	RUNDC3A	⇧	1.91	0.029
224797_at	ARRDC3	⇩	2.37	9.47E-03	207117_at	AASDHPPT	⇩	2.04	0.014	211065_x_at	GPR97	⇧	1.91	0.027
210756_s_at	NOTCH2	⇩	2.37	2.94E-03	222633_at	ZNF117	⇩	2.04	0.010	1565777_at	PFKL	⇧	1.91	7.95E-03
201237_at	CAPZA2	⇩	2.36	0.031	202169_s_at	TBL1XR1	⇩	2.04	1.22E-04	204285_s_at	FOXH1	⇧	1.90	0.019
200605_s_at	PRKAR1A	⇩	2.34	0.043	207500_at	CASP5	⇧	2.03	0.021	200785_s_at	LRP1	⇧	1.90	8.08E-03
211781_x_at	---	⇧	2.34	0.033	239012_at	RNF144B	⇩	2.02	0.046	231407_s_at	PMAIP1	⇩	1.90	8.20E-04
231828_at	LOC253039	⇧	2.34	0.017	229198_at	METRNL	⇧	2.02	0.030	212530_at	---	⇧	1.89	0.044
243495_s_at	---	⇩	2.31	6.01E-03	225955_at	USP35	⇧	2.02	3.62E-04	213805_at	FGFR1OP2	⇩	1.89	0.036
212720_at	PAPOLA	⇩	2.29	0.019	32502_at	GDPD5	⇧	2.01	0.045	233898_s_at	CUL4A	⇧	1.89	0.027
1552552_s_at	CLEC4C	⇩	2.28	2.31E-03	222839_s_at	PAPOLG	⇩	2.00	9.16E-03	225290_at	ETNK1	⇩	1.89	0.020
223578_x_at	MALAT1	⇩	2.26	0.012	215635_at	---	⇩	1.99	0.037	244889_at	NEK7	⇩	1.89	0.016
228222_at	---	⇩	2.25	0.030	230180_at	FCHO2	⇩	1.99	0.019	229373_at	ABHD5	⇩	1.89	0.013
212368_at	C16orf7	⇧	2.23	0.038	202859_x_at	---	⇩	1.99	0.017	227757_at	LOC388210	⇧	1.89	9.07E-03
219978_s_at	ZNF292	⇩	2.23	0.015	228220_at	IL8	⇩	1.99	5.14E-03	1558747_at	---	⇩	1.88	0.038
205781_at	NUSAP1	⇩	2.23	3.82E-03	222409_at	---	⇩	1.98	0.041	207172_s_at	SMCHD1	⇩	1.88	0.036
222562_s_at	TNKS2	⇩	2.22	0.024	224778_s_at	DNPEP	⇧	1.98	9.65E-03	212943_at	MYO1G	⇧	1.88	0.016
235645_at	PTPRC	⇩	2.19	0.035	241403_at	CORO1C	⇩	1.98	7.03E-03	227953_at	CDH11	⇩	1.88	7.89E-03
1552480_s_at	ESCO1	⇩	2.19	9.17E-03	215135_at	CLK4	⇩	1.98	4.19E-03	227799_at	KIAA0528	⇩	1.88	7.55E-03
229327_s_at	---	⇩	2.16	0.017	242312_x_at	---	⇩	1.97	0.043	225178_at	DAPK1	⇩	1.87	0.033
207605_x_at	ZNF117	⇩	2.16	9.16E-03	223940_x_at	MALAT1	⇩	1.96	0.022	210116_at	PREPL	⇩	1.87	0.030
239957_at	---	⇩	2.14	0.026	1557970_s_at	RPS6KA2	⇧	1.96	2.69E-04	203139_at	SH2D1A	⇩	1.87	0.028

Table A1: JB NuGEN Ovation® Gene List (n=706) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

212215_at	PHF10	⇩	1.87	0.026
225048_at	TTC14	⇩	1.87	0.011
212887_at	PPP1CB	⇩	1.86	0.044
218733_at	---	⇩	1.86	0.039
210057_at	ANO9	⇧	1.86	0.036
227364_at	RPS6KA5	⇩	1.86	0.032
201407_s_at	SEC23A	⇩	1.86	0.022
204633_s_at	MSL2	⇩	1.86	0.015
227393_at	REC8	⇧	1.86	8.29E-03
218599_at	SMG1	⇩	1.86	4.96E-03
226010_at	SLC25A23	⇧	1.86	8.19E-05
219132_at	LAG3	⇧	1.85	0.040
214352_s_at	NSUN5C	⇧	1.85	0.031
212515_s_at	NFIX	⇧	1.85	0.025
237461_at	DDX3X	⇩	1.85	0.022
243435_at	NLRP7	⇩	1.85	0.020
227400_at	KRAS	⇩	1.85	8.23E-03
213842_x_at	PELI2	⇩	1.85	6.58E-03
206486_at	KCNQ1OT1	⇩	1.85	5.93E-04
222040_at	CENPT	⇧	1.84	0.038
216241_s_at	TCEA1	⇩	1.84	0.029
206543_at	HNRNPA1	⇩	1.84	9.92E-03
235461_at	SMARCA2	⇩	1.84	8.12E-03
218148_at	TET2	⇩	1.84	4.83E-03
218528_s_at	RNF38	⇩	1.83	0.044
223138_s_at	MVP	⇧	1.83	0.038
210313_at	LILRA4	⇩	1.83	0.032
200728_at	---	⇧	1.83	0.028
228730_s_at	DHX36	⇩	1.83	0.026
238591_at	SCRN2	⇧	1.83	0.010
202180_s_at	ACTR2	⇩	1.83	5.50E-03
229413_s_at	TRIB2	⇩	1.82	0.045
208944_at	---	⇩	1.82	0.026
202478_at	TGFBR2	⇩	1.82	9.24E-03
223964_x_at	RGS18	⇩	1.81	0.045
213875_x_at	---	⇩	1.81	0.031
223809_at	CDV3	⇩	1.81	0.026
228746_s_at	SFRS4	⇩	1.81	0.021
239512_at	C6orf62	⇩	1.81	0.020
218738_s_at	RNF138	⇩	1.81	0.018
209785_s_at	ESPN	⇧	1.81	0.016
223549_s_at	PLA2G4C	⇧	1.81	9.30E-03
211575_s_at	---	⇧	1.80	0.042
239339_at	C4orf48	⇧	1.80	0.028
238506_at	UBE3A	⇩	1.80	5.44E-03
229607_at	LRRC58	⇩	1.80	5.36E-03
229860_x_at	---	⇩	1.80	1.32E-03
222453_at	RAB14	⇩	1.79	0.041
223263_s_at	DOM3Z	⇧	1.79	0.026
210281_s_at	SIRT1	⇩	1.79	0.011
218878_s_at	FGFR1OP2	⇩	1.79	8.69E-03
200927_s_at	CYBRD1	⇩	1.79	6.05E-03
204522_at	ZMYM2	⇩	1.79	3.41E-03
225243_s_at	SLC11A1	⇧	1.78	0.045
226464_at	GLCCI1	⇩	1.78	0.037
227525_at	ZNF518A	⇩	1.78	0.034
216511_s_at	TCF7L2	⇩	1.78	0.031
204291_at	TAZ	⇧	1.78	0.028
212408_at	C3orf58	⇩	1.78	0.023
235721_at	GSTT1	⇧	1.78	0.019
210423_s_at	SLMAP	⇩	1.78	0.013
37278_at	DTX3	⇧	1.78	8.17E-03
236430_at	TOR1AIP1	⇩	1.78	5.70E-03
203815_at	TMED6	⇧	1.78	3.13E-05
216555_at	STAT6	⇧	1.77	0.050
201408_at	PPP1CB	⇩	1.77	0.021
214499_s_at	C22orf30	⇩	1.77	0.017
242844_at	MTG1	⇧	1.77	0.016
204088_at	P2RX4	⇧	1.77	0.011
201332_s_at	BCLAF1	⇩	1.77	8.57E-03
238333_s_at	PGGT1B	⇩	1.77	2.46E-03
220832_at	SFRS12	⇩	1.76	0.037
1563975_at	NSUN5C	⇧	1.76	0.034
227259_at	NUDT14	⇧	1.76	0.029
212721_at	TLR8	⇩	1.76	0.018
228631_s_at	PLA2G6	⇧	1.76	0.017
213460_x_at	ZNF688	⇧	1.76	9.61E-03
204691_x_at	CD47	⇩	1.76	6.15E-03
231914_at	RNF130	⇩	1.76	5.12E-04
225362_at	NUPL1	⇩	1.75	0.045
238317_x_at	MOBKL1B	⇩	1.75	0.037
201299_s_at	---	⇩	1.75	0.027
223984_s_at	TRIOBP	⇩	1.75	0.012
1552334_at	FLYWCH1	⇧	1.75	8.50E-03
223950_s_at	FAM122B	⇩	1.75	1.99E-03
226251_at	ASXL2	⇩	1.74	0.045
229951_x_at	---	⇩	1.74	7.81E-03
216899_s_at	AGPAT3	⇧	1.74	1.98E-03
223182_s_at	SKAP2	⇩	1.74	1.02E-03
200751_s_at	HNRNPA1	⇩	1.73	0.044
218294_s_at	HMGB1	⇩	1.73	0.043
200731_s_at	CARD8	⇩	1.73	0.043
230775_s_at	SLC30A7	⇩	1.73	0.039
221919_at	LRRC1	⇩	1.73	0.037
201493_s_at	NCOA3	⇩	1.73	0.032
218319_at	PUM2	⇩	1.73	0.031

Table A1: JB NuGEN Ovation® Gene List (n=706) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

201133_s_at	BCL6	⇧	1.73	0.028
211352_s_at	PJA2	⇩	1.73	0.025
224734_at	DOM3Z	⇧	1.73	0.024
218816_at	PTP4A1	⇩	1.73	0.023
226601_at	NUP50	⇩	1.73	0.016
1554479_a_at	---	⇧	1.73	0.015
222235_s_at	RP11	⇩	1.73	0.014
228758_at	PELI1	⇩	1.73	0.013
38157_at	CSGALNACT2	⇩	1.73	6.88E-03
238717_at	HNRNPC	⇩	1.73	5.38E-03
244679_at	COCH	⇩	1.72	0.048
220369_at	KLHL15	⇩	1.72	0.038
242576_x_at	---	⇩	1.72	0.025
244103_at	SMEK1	⇩	1.72	0.024
1554241_at	---	⇩	1.72	0.021
226370_at	C1orf55	⇩	1.72	0.017
243233_at	LOC692247	⇧	1.72	9.80E-03
224041_at	N4BP2L2	⇩	1.72	5.97E-03
1569453_a_at	TTTY6	⇧	1.72	2.07E-03
222111_at	VARS2	⇧	1.71	0.050
225997_at	GPAA1	⇧	1.71	0.049
201901_s_at	---	⇧	1.71	0.034
220515_at	YY1	⇩	1.71	0.033
203253_s_at	C8orf73	⇧	1.71	0.032
1559957_a_at	HISPPD1	⇩	1.71	0.019
226200_at	DUSP21	⇩	1.71	0.016
201618_x_at	---	⇩	1.71	0.013
227672_at	HSDL2	⇧	1.71	9.18E-03
1559128_at	MOBKL1A	⇩	1.71	3.77E-03
233369_at	LOC642852	⇧	1.71	1.54E-03
226249_at	CMTM6	⇩	1.70	0.046
232382_s_at	MAN1A1	⇩	1.70	0.046
223047_at	ZNF24	⇩	1.70	0.046
214786_at	---	⇩	1.70	0.043
221760_at	LOC650392	⇧	1.70	0.029
226441_at	CNOT8	⇩	1.70	0.026
241245_at	MAP3K2	⇩	1.70	0.021
202164_s_at	SFRS4	⇩	1.70	0.020
203247_s_at	PCMTD1	⇩	1.70	0.018
206875_s_at	HEXDC	⇧	1.70	9.56E-03
235385_at	SLK	⇩	1.70	8.45E-03
1569872_a_at	MAP3K1	⇩	1.70	3.03E-03
1555866_a_at	SNX30	⇩	1.70	2.79E-03
203397_s_at	---	⇧	1.69	0.048
216037_x_at	C11orf58	⇩	1.69	0.040
201020_at	GALNT3	⇩	1.69	0.029
213494_s_at	DENND1C	⇧	1.69	0.028
200084_at	TMTC1	⇧	1.69	0.026
202006_at	TMEM41B	⇩	1.69	0.025
212623_at	LOC440731	⇧	1.69	0.025
212306_at	CLASP2	⇩	1.69	0.021
221080_s_at	PTPN12	⇩	1.69	0.020
226322_at	YY1	⇩	1.69	0.019
202452_at	TCF7L2	⇩	1.69	0.014
238973_s_at	ZER1	⇧	1.69	0.013
201770_at	SNRPA	⇧	1.69	4.43E-03
238376_at	YWHAH	⇩	1.69	8.71E-04
203338_at	WDR43	⇩	1.68	0.042
213872_at	SLC26A8	⇧	1.68	0.040
235060_at	PARP10	⇧	1.68	0.037
1561015_at	RBM25	⇩	1.68	0.034
225174_at	LOC100190986	⇩	1.68	0.029
214662_at	DOT1L	⇧	1.68	0.029
212030_at	FCGBP	⇧	1.68	0.024
212140_at	LRCH4	⇧	1.68	0.022
209586_s_at	PDS5A	⇩	1.68	0.019
229350_x_at	C6orf62	⇩	1.68	0.018
37796_at	PRUNE	⇩	1.68	0.015
1555874_x_at	PPP2R5E	⇩	1.68	0.014
237340_at	---	⇩	1.68	0.014
204954_s_at	DNAJC10	⇩	1.68	9.18E-03
203240_at	DYRK1B	⇧	1.68	9.10E-03
226201_at	MGC21881	⇧	1.68	5.37E-03
213518_at	PRKCI	⇩	1.67	0.047
202890_at	GP1BB/SEPT5	⇧	1.67	0.047
221918_at	SMAD4	⇩	1.67	0.045
216035_x_at	HMGCR	⇩	1.67	0.045
202527_s_at	PCTK2	⇩	1.67	0.044
233329_s_at	BMP2K	⇩	1.67	0.038
238619_at	---	⇧	1.67	0.038
202540_s_at	MAP7	⇩	1.67	0.034
226853_at	---	⇩	1.67	0.030
212479_s_at	TCF7L2	⇩	1.67	0.028
219303_at	KRCC1	⇩	1.67	0.028
232311_at	RASA4/4B	⇧	1.67	0.024
231647_s_at	RMND5A	⇩	1.67	0.023
212707_s_at	RNF219	⇩	1.67	0.021
239944_at	B2M	⇩	1.67	0.019
206655_s_at	FCRL5	⇩	1.67	3.10E-03
201599_at	RSBN1	⇩	1.66	0.050
224046_s_at	NSUN5	⇧	1.66	0.050
225565_at	C16orf35	⇧	1.66	0.048
208783_s_at	MED28	⇩	1.66	0.037
220038_at	OAT	⇩	1.66	0.034
223336_s_at	FUK	⇧	1.66	0.029
225845_at	ZBTB44	⇩	1.66	0.027

Table A1: JB NuGEN Ovation® Gene List (n=706) [GeneSpring unpaired student’s t-test p<0.05, FC ≥ ±1.50]

240592_at	LCORL	⇩	1.66	0.024	211671_s_at	SLC38A2	⇩	1.64	0.045	208810_at	SAMD9	⇩	1.63	0.031
222789_at	CPSF3L	⇧	1.66	0.021	223925_s_at	RBM7	⇩	1.64	0.045	225032_at	CEP170	⇩	1.63	0.027
217544_at	SGK3	⇩	1.66	0.019	225133_at	BACH1	⇩	1.64	0.045	204057_at	FBXL4	⇩	1.63	0.025
206015_s_at	CD46	⇩	1.66	0.018	1555948_s_at	STK16	⇧	1.64	0.045	213090_s_at	LMF1	⇧	1.63	0.025
209170_s_at	RAB18	⇩	1.66	0.017	202694_at	KDM4C	⇩	1.64	0.042	221423_s_at	YIPF5	⇩	1.63	0.017
236752_at	GPM6B	⇩	1.66	0.015	202228_s_at	LOC100130332	⇩	1.64	0.040	232225_at	FNDC3B	⇩	1.63	0.012
224416_s_at	LOC729806	⇩	1.66	0.012	241610_x_at	CHKB/CPT1B	⇧	1.64	0.038	46142_at	SMARCA5	⇩	1.63	0.011
226072_at	FOXJ3	⇩	1.66	6.73E-03	227368_at	KIAA1731	⇩	1.64	0.033	1553993_s_at	---	⇧	1.63	0.011
217994_x_at	CREB1	⇩	1.66	3.45E-03	220924_s_at	STK17A	⇩	1.64	0.032	33736_at	MIER1	⇩	1.63	8.33E-03
205614_x_at	MST1	⇧	1.66	2.49E-03	218379_at	FAM120A	⇩	1.64	0.030	225980_at	LEMD3	⇩	1.62	0.050
203802_x_at	PDE7A	⇩	1.66	1.82E-03	210233_at	---	⇩	1.64	0.028	204742_s_at	PRKD3	⇩	1.62	0.050
210672_s_at	---	⇩	1.66	1.12E-03	208859_s_at	KLF3	⇩	1.64	0.019	218604_at	TMEM63C	⇧	1.62	0.050
213016_at	SPAG9	⇩	1.65	0.043	209984_at	ZMIZ2	⇧	1.64	0.017	218191_s_at	PKN2	⇩	1.62	0.041
1555762_s_at	PUM1	⇩	1.65	0.043	218318_s_at	NLK	⇩	1.64	0.016	241294_at	SBNO2	⇧	1.62	0.040
224866_at	DGKZ	⇧	1.65	0.042	204194_at	IL1RAP	⇩	1.64	0.015	222656_at	MED21	⇩	1.62	0.039
217843_s_at	BBX	⇩	1.65	0.041	210070_s_at	NPTN	⇩	1.64	0.013	225697_at	TRPT1	⇧	1.62	0.039
212468_at	FAR1	⇩	1.65	0.038	221924_at	ATRX	⇩	1.64	0.011	209362_at	EML3	⇧	1.62	0.036
229322_at	PPP2R5E	⇩	1.65	0.037	238572_at	---	⇩	1.64	3.51E-03	1562836_at	CPSF3L	⇧	1.62	0.029
203491_s_at	USP15	⇩	1.65	0.035	214532_x_at	POU5F1B	⇧	1.64	3.28E-03	218236_s_at	---	⇧	1.62	0.028
223888_s_at	---	⇩	1.65	0.035	240666_at	---	⇧	1.64	1.82E-03	225904_at	C14orf43	⇩	1.62	0.027
222473_s_at	IQGAP2	⇩	1.65	0.029	1558720_at	STOML1	⇧	1.63	0.050	212628_at	GPN2	⇧	1.62	0.026
209475_at	PNN	⇩	1.65	0.029	201152_s_at	MBNL1	⇩	1.63	0.049	218552_at	---	⇩	1.62	0.023
203011_at	NUCKS1	⇩	1.65	0.027	202769_at	DNAJB14	⇩	1.63	0.047	204166_at	ZNF444	⇧	1.62	0.022
201165_s_at	PLA2G6	⇧	1.65	0.025	235450_at	MED25	⇧	1.63	0.047	218799_at	---	⇩	1.62	0.021
238100_at	RBM15	⇩	1.65	0.020	222850_s_at	LDLR	⇩	1.63	0.045	227733_at	UBE2W	⇩	1.62	0.019
203474_at	IMPA1	⇩	1.65	0.017	202303_x_at	IRF8	⇩	1.63	0.043	229066_at	C1orf96	⇩	1.62	0.017
229353_s_at	LARS	⇩	1.65	0.012	219691_at	---	⇩	1.63	0.041	50376_at	PDS5B	⇩	1.62	0.012
231035_s_at	MED4	⇩	1.65	0.012	202068_s_at	DNAJB6	⇩	1.63	0.040	223436_s_at	CRKRS	⇩	1.62	0.010
212037_at	ERBB2IP	⇩	1.65	8.84E-03	225475_at	---	⇩	1.63	0.039	224312_x_at	ECHDC2	⇧	1.62	9.48E-03
210647_x_at	AAK1	⇩	1.65	7.54E-03	212746_s_at	RP6	⇩	1.63	0.038	212969_x_at	LOC338799	⇧	1.62	2.48E-03
207556_s_at	CEP57	⇩	1.65	6.12E-03	229212_at	TAF4	⇩	1.63	0.036	226369_at	LMBRD1	⇩	1.62	1.06E-03
1569302_at	NR3C1	⇩	1.64	0.049	218499_at	CCNG2	⇩	1.63	0.035	202514_at	DLG1	⇩	1.61	0.049

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242628_at	UNKL	⇩	1.61	0.047	1552386_at	SPTBN5	⇧	1.60	0.020	211174_s_at	RASSF5	⇩	1.59	2.57E-03
209034_at	GTF3C3	⇩	1.61	0.043	202014_at	ACAP3	⇧	1.60	0.019	220178_at	ZC3H15	⇩	1.59	2.30E-03
221064_s_at	MAP3K7	⇩	1.61	0.042	37462_i_at	PIAS1	⇩	1.60	0.017	203901_at	CCKAR	⇧	1.59	1.76E-03
201951_at	PLCD1	⇧	1.61	0.042	226470_at	BOD1L	⇩	1.60	0.014	221049_s_at	C19orf28	⇧	1.59	2.22E-04
237001_at	ARHGAP4	⇧	1.61	0.033	1556839_s_at	---	⇩	1.60	0.013	206989_s_at	LNX1	⇩	1.58	0.048
236368_at	RFNG	⇧	1.61	0.033	206402_s_at	GAPT	⇩	1.60	0.012	225885_at	AP1G2	⇧	1.58	0.048
206853_s_at	---	⇩	1.61	0.032	204375_at	HBP1	⇩	1.60	0.011	223611_s_at	ERAP2	⇩	1.58	0.046
1555439_at	ALCAM	⇩	1.61	0.030	236541_at	TMEM167B	⇩	1.60	6.99E-03	200889_s_at	MED24	⇧	1.58	0.046
205819_at	WDTC1	⇧	1.61	0.027	233625_x_at	ZEB1	⇩	1.60	6.88E-03	227462_at	IREB2	⇩	1.58	0.045
216036_x_at	---	⇩	1.61	0.025	235383_at	PAK2	⇩	1.60	6.43E-03	225892_at	HEMK1	⇧	1.58	0.042
204425_at	KIAA0368	⇩	1.61	0.021	228198_s_at	ACTR2	⇩	1.60	2.68E-03	203689_s_at	CR1	⇩	1.58	0.041
205125_at	MARCO	⇧	1.61	0.015	225529_at	G2E3	⇩	1.60	1.07E-03	206244_at	POLRMT	⇧	1.58	0.039
212968_at	PNRC1	⇩	1.61	4.23E-03	208276_at	IGFBP3	⇧	1.59	0.049	204286_s_at	SMOX	⇧	1.58	0.035
210966_x_at	LARP1	⇧	1.61	8.77E-05	243280_at	SPOPL	⇩	1.59	0.046	217608_at	EEA1	⇩	1.58	0.027
218196_at	TMTC3	⇩	1.60	0.049	201593_s_at	CXXC1	⇧	1.59	0.044	235216_at	PMAIP1	⇩	1.58	0.027
236645_at	PPP1CC	⇩	1.60	0.047	225658_at	MAP3K7IP1	⇧	1.59	0.037	218128_at	TMEM63A	⇧	1.58	0.024
217862_at	SOAT1	⇩	1.60	0.046	223650_s_at	RAB21	⇩	1.59	0.034	210357_s_at	GPR162	⇧	1.58	0.023
208876_s_at	---	⇩	1.60	0.040	228153_at	SF3A2	⇧	1.59	0.031	203782_s_at	FMR1	⇩	1.58	0.019
222495_at	MYO7B	⇧	1.60	0.038	209701_at	CRK	⇩	1.59	0.030	213043_s_at	ESCO1	⇩	1.58	0.017
1560017_at	SF3A2	⇧	1.60	0.034	202226_s_at	RRAGD	⇩	1.59	0.029	218620_s_at	SFRS12IP1	⇩	1.58	0.015
222980_at	CPSF3L	⇧	1.60	0.030	203885_at	CACNB3	⇧	1.59	0.027	203326_x_at	---	⇧	1.58	0.014
200726_at	NPFF	⇧	1.60	0.029	1558093_s_at	POLL	⇧	1.59	0.023	201613_s_at	SCYE1	⇧	1.58	0.012
225039_at	---	⇩	1.60	0.028	1554834_a_at	ERAP1	⇩	1.59	0.022	235594_at	SFRS2IP	⇩	1.58	8.48E-03
227293_at	ARSA	⇧	1.60	0.027	217955_at	OGFOD2	⇧	1.59	0.022	229559_at	FLJ40125	⇧	1.58	7.76E-03
223255_at	TMEM33	⇩	1.60	0.024	221523_s_at	---	⇩	1.59	0.019	224821_at	ABHD14B	⇧	1.58	5.11E-03
242388_x_at	GGT7	⇧	1.60	0.024	209344_at	RNF144B	⇩	1.59	0.019	205056_s_at	NFYB	⇩	1.58	8.36E-04
212758_s_at	RPE	⇩	1.60	0.023	48580_at	MATR3	⇩	1.59	0.017	202700_s_at	SSR1	⇩	1.58	5.27E-04
235009_at	RAB10	⇩	1.60	0.022	210095_s_at	GPSN2	⇧	1.59	0.015	241866_at	HDAC2	⇩	1.57	0.049
238831_at	PPP1R15A	⇧	1.60	0.022	34726_at	---	⇩	1.59	0.014	202539_s_at	EWSR1	⇩	1.57	0.048
212867_at	LOC729234	⇧	1.60	0.022	208336_s_at	TPM4	⇩	1.59	0.013	212461_at	PPP1CB	⇩	1.57	0.048
1558015_s_at	OSTM1	⇩	1.60	0.021	209381_x_at	BCL2L13	⇩	1.59	6.95E-03	201833_at	ZAP70	⇧	1.57	0.047
221561_at	CLSTN3	⇧	1.60	0.021	219246_s_at	NRBF2	⇩	1.59	2.84E-03	202412_s_at	---	⇩	1.57	0.045

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200641_s_at	LRCH4	⇧	1.57	0.044
217845_x_at	RNF207	⇧	1.57	0.041
204156_at	FBXL3	⇩	1.57	0.030
223943_s_at	ZNF862	⇧	1.57	0.030
218313_s_at	LOC731424	⇧	1.57	0.028
225132_at	DNHD1	⇧	1.57	0.027
229966_at	HIGD1A	⇩	1.57	0.025
236207_at	FBXL18	⇧	1.57	0.024
240099_at	FHIT	⇧	1.57	0.024
240789_at	GALNT7	⇩	1.57	0.022
201409_s_at	HMGCR	⇩	1.57	0.018
240248_at	---	⇩	1.57	0.018
230500_at	GMCL1	⇩	1.57	0.018
218458_at	KIAA0999	⇩	1.57	0.015
37586_at	YWHAZ	⇩	1.57	0.012
244759_x_at	ZNF142	⇧	1.57	0.010
213444_at	CLTB	⇧	1.57	8.79E-03
229631_at	PDE7A	⇩	1.57	7.60E-03
205104_at	SNPH	⇧	1.57	7.14E-03
1569095_at	SSFA2	⇩	1.57	3.59E-03
1556645_s_at	---	⇧	1.57	3.28E-03
221996_s_at	USP1	⇩	1.57	2.42E-03
204692_at	---	⇩	1.57	2.28E-03
227500_at	GNG2	⇩	1.57	2.10E-03
206492_at	SLC16A7	⇩	1.57	1.50E-03
214032_at	AZIN1	⇩	1.57	1.19E-03
202691_at	MAP4K5	⇩	1.56	0.046
236166_at	CASP8AP2	⇩	1.56	0.045
222201_s_at	USP32	⇩	1.56	0.043
202579_x_at	NUP160	⇩	1.56	0.039
202457_s_at	MICA/B	⇧	1.56	0.035
239104_at	MAP2K1	⇩	1.56	0.034
244177_at	SGK1	⇩	1.56	0.034
212709_at	LPGAT1	⇩	1.56	0.033
214753_at	IFRD1	⇩	1.56	0.032
202832_at	MGC42157	⇩	1.56	0.030
226505_x_at	GCC2	⇩	1.56	0.028
231090_s_at	C16orf58	⇧	1.56	0.028
202670_at	HMGN4	⇩	1.56	0.027
202651_at	ARID2	⇩	1.56	0.027
235072_s_at	SNRPD1	⇩	1.56	0.021
201739_at	---	⇩	1.56	0.020
202147_s_at	---	⇩	1.56	0.018
204872_at	LMF1	⇧	1.56	0.018
203552_at	---	⇩	1.56	0.017
225716_at	CLCN7	⇧	1.56	0.014
205905_s_at	N4BP2L2	⇩	1.56	0.013
38069_at	PPP3CA	⇩	1.56	9.88E-03
219135_s_at	MFHAS1	⇧	1.56	8.95E-03
213457_at	LOC285147	⇩	1.56	8.78E-03
222190_s_at	TLE4	⇩	1.56	8.68E-03
205655_at	RFFL	⇩	1.55	0.049
225219_at	LOC389834	⇩	1.55	0.048
237919_at	C1orf103	⇩	1.55	0.047
235493_at	IL1RAP	⇩	1.55	0.047
201753_s_at	PDE4DIP	⇧	1.55	0.047
205842_s_at	SH3GLB1	⇩	1.55	0.043
200777_s_at	---	⇩	1.55	0.043
225519_at	TLE4	⇩	1.55	0.042
1565544_at	RNPEPL1	⇧	1.55	0.042
220235_s_at	---	⇩	1.55	0.039
204496_at	CDKN2AIP	⇩	1.55	0.039
217951_s_at	ROCK1	⇩	1.55	0.039
209090_s_at	JAK2	⇩	1.55	0.037
205227_at	CCNG2	⇩	1.55	0.036
225509_at	SMAD5	⇩	1.55	0.035
202304_at	MDM4	⇩	1.55	0.033
209525_at	MBD3	⇧	1.55	0.032
224863_at	ARSD	⇧	1.55	0.031
238490_at	ADD3	⇩	1.55	0.029
216072_at	STRN3	⇩	1.55	0.028
216915_s_at	SAP30L	⇩	1.55	0.028
1555977_at	PIGB	⇩	1.55	0.026
212441_at	G2E3	⇩	1.55	0.026
218929_at	RASGRP2	⇧	1.55	0.022
201916_s_at	BZW1	⇩	1.55	0.021
202770_s_at	KPNA4	⇩	1.55	0.021
242760_x_at	FNDC3A	⇩	1.55	0.020
214578_s_at	WDR74	⇧	1.55	0.020
225267_at	PPP4R2	⇩	1.55	0.019
235765_at	GNAQ	⇩	1.55	0.019
226683_at	CENPB	⇧	1.55	0.018
223254_s_at	---	⇩	1.55	0.016
226558_at	SNX18	⇩	1.55	0.016
202463_s_at	HDGFRP3	⇩	1.55	0.014
212390_at	TMC4	⇧	1.55	0.014
214368_at	MST1	⇧	1.55	0.013
212437_at	SEC63	⇩	1.55	8.71E-03
226403_at	KIAA0232	⇩	1.55	7.96E-03
216320_x_at	PHF3	⇩	1.55	5.98E-03
218301_at	PTPN12	⇩	1.55	3.29E-03
220616_at	KIAA2026	⇩	1.55	1.51E-03
225280_x_at	ZNF384	⇧	1.55	5.36E-04
221712_s_at	RNF141	⇩	1.55	2.69E-05
219289_at	FBXO3	⇩	1.54	0.045
209595_at	COPB1	⇩	1.54	0.042

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227013_at	ZAP70	⇧	1.54	0.038
222145_at	AP3D1	⇧	1.54	0.037
212686_at	CPSF3L	⇧	1.54	0.037
218637_at	TIGIT	⇧	1.54	0.037
208737_at	---	⇩	1.54	0.034
239923_at	HEATR3	⇩	1.54	0.033
233308_at	IMPACT	⇩	1.54	0.024
218432_at	---	⇩	1.54	0.022
218614_at	MAF1	⇧	1.54	0.021
229392_s_at	MBD3	⇧	1.54	0.020
222998_at	C7orf38	⇧	1.54	0.016
238965_at	LATS2	⇩	1.54	0.013
210974_s_at	PABPC1L	⇧	1.54	0.013
1555613_a_at	C12orf35	⇩	1.54	7.71E-03
233563_s_at	C21orf2	⇧	1.54	7.13E-03
41160_at	PIK3R2	⇧	1.54	6.70E-03
240070_at	ATP6V1G1	⇩	1.54	5.46E-03
229762_at	SBF1	⇧	1.54	3.93E-03
226670_s_at	PPM1H	⇩	1.54	3.82E-03
212393_at	GTF2F2	⇩	1.54	2.21E-03
200806_s_at	CHMP2B	⇩	1.53	0.046
202536_at	RBM15	⇩	1.53	0.045
219286_s_at	COPS8	⇩	1.53	0.043
244662_at	ERAP2	⇩	1.53	0.042
1554915_a_at	---	⇧	1.53	0.042
202142_at	PDE12	⇩	1.53	0.041
235104_at	KIAA0240	⇩	1.53	0.041
213118_at	ITPR1	⇧	1.53	0.040
213208_at	---	⇧	1.53	0.039
226543_at	---	⇧	1.53	0.038
204689_at	DDX51	⇧	1.53	0.036
202673_at	MUTED	⇩	1.53	0.034
1555199_at	API5	⇩	1.53	0.034
214959_s_at	FMR1	⇩	1.53	0.031
215245_x_at	MMP24	⇧	1.53	0.028
236723_at	HHEX	⇩	1.53	0.026
220789_s_at	LOC728903	⇧	1.53	0.024
211323_s_at	TBRG4	⇧	1.53	0.023
203233_at	---	⇩	1.53	0.021
208534_s_at	IL4R	⇧	1.53	0.021
1560957_at	DPM1	⇩	1.53	0.017
1555872_a_at	HSPD1	⇩	1.53	0.015
213171_s_at	---	⇩	1.53	0.012
1558836_at	UHRF1BP1L	⇩	1.53	0.011
211849_s_at	GOSR1	⇩	1.53	0.011
1558739_at	RNGTT	⇧	1.53	0.011
1554085_at	RASA4	⇧	1.53	1.11E-03
213549_at	---	⇩	1.52	0.049
211963_s_at	NFYB	⇩	1.52	0.049
225222_at	SLC2A9	⇧	1.52	0.049
224823_at	C21orf91	⇩	1.52	0.048
202777_at	MAFB	⇩	1.52	0.045
1560854_s_at	ARSD	⇧	1.52	0.044
212099_at	MYLK	⇩	1.52	0.044
222313_at	PRR5	⇧	1.52	0.044
242471_at	ACSF3	⇧	1.52	0.043
242273_at	RHOB	⇩	1.52	0.040
213355_at	CNOT6	⇩	1.52	0.040
223079_s_at	SHOC2	⇩	1.52	0.039
212872_s_at	MRPL43	⇧	1.52	0.039
212289_at	---	⇩	1.52	0.038
238435_at	TNK2	⇧	1.52	0.036
222156_x_at	RDH11	⇩	1.52	0.035
209535_s_at	GLS	⇩	1.52	0.034
201775_s_at	ARPC5	⇩	1.52	0.033
226109_at	MED20	⇩	1.52	0.033
218559_s_at	---	⇩	1.52	0.032
200679_x_at	CCDC137	⇧	1.52	0.032
217970_s_at	RAP2C	⇩	1.52	0.030
217776_at	CLTB	⇧	1.52	0.029
218669_at	ZNF107	⇩	1.52	0.028
211749_s_at	---	⇧	1.52	0.022
218127_at	HIP1R	⇧	1.52	0.021
47069_at	FREM3	⇧	1.52	0.018
238893_at	ST3GAL6	⇩	1.52	0.015
203839_s_at	MPI	⇧	1.52	0.014
227464_at	CCPG1	⇩	1.52	0.012
243337_at	HMGB1	⇩	1.52	0.010
210106_at	---	⇩	1.52	9.63E-03
1556308_at	ANKRD12	⇩	1.52	9.16E-03
209558_s_at	ITPA	⇧	1.52	9.12E-03
240223_at	KIAA0494	⇩	1.52	9.03E-03
202472_at	LOC338758	⇧	1.52	6.34E-03
225933_at	VAMP3	⇩	1.52	5.53E-03
218985_at	RDH5	⇧	1.52	3.84E-03
244429_at	CA5BP	⇩	1.52	2.05E-03
223695_s_at	PRRT3	⇧	1.52	1.32E-03
230026_at	HIAT1	⇩	1.52	1.14E-03
209171_at	---	⇩	1.52	5.99E-04
205172_x_at	SLC2A8	⇧	1.52	3.50E-04
208883_at	PTPN23	⇧	1.51	0.048
238687_x_at	FAM20B	⇩	1.51	0.047
241242_at	SLC25A37	⇧	1.51	0.046
231747_at	NRG1	⇧	1.51	0.041
225350_s_at	MSRB3	⇩	1.51	0.040
225782_at	LOC100129006	⇧	1.51	0.040

Table A1: JB NuGEN Ovation® Gene List (n=706) [GeneSpring unpaired student's t-test $p<0.05$, FC ≥ ±1.50]

225693_s_at	CCHCR1	⇧	1.51	0.040
202915_s_at	UBTD2	⇩	1.51	0.039
210621_s_at	TM2D1	⇩	1.51	0.035
232964_at	KCTD9	⇩	1.51	0.035
224827_at	ZNF770	⇩	1.51	0.032
221579_s_at	ZYG11B	⇩	1.51	0.027
213882_at	RASA1	⇩	1.51	0.025
207198_s_at	CAMTA1	⇩	1.51	0.021
226810_at	OGFRL1	⇩	1.51	0.017
218823_s_at	COASY	⇧	1.51	0.017
55065_at	CYSLTR1	⇩	1.51	0.016
201913_s_at	NUDT3	⇩	1.51	0.013
212596_s_at	---	⇧	1.51	0.012
238568_s_at	MARK4	⇧	1.51	5.65E-03
206237_s_at	LIMS1	⇩	1.51	5.48E-03
243757_at	---	⇧	1.51	4.49E-03
218978_s_at	---	⇩	1.51	3.96E-03
212193_s_at	SPDYE1	⇩	1.51	1.77E-03
223150_s_at	UBR5	⇩	1.51	1.72E-03
230095_at	HMGXB4	⇧	1.51	4.65E-04
209698_at	LARP1	⇧	1.51	1.52E-05
241642_x_at	C5orf44	⇩	1.50	0.048
226128_at	TLK1	⇩	1.50	0.043
202056_at	ACER3	⇩	1.50	0.043
206544_x_at	BTF3L4	⇩	1.50	0.042
205215_at	SMARCA2	⇩	1.50	0.042
1559369_at	CES2	⇧	1.50	0.042
200767_s_at	FAM159A	⇧	1.50	0.040
225976_at	FCHO2	⇩	1.50	0.032
206542_s_at	FAM120A	⇩	1.50	0.030
222688_at	TRADD	⇧	1.50	0.029
1555153_s_at	RNF2	⇩	1.50	0.027
231927_at	ATF6	⇩	1.50	0.027
222206_s_at	NCLN	⇧	1.50	0.026
1729_at	SMARCA2	⇩	1.50	0.025
209667_at	---	⇩	1.50	0.013
237033_at	KPNA1	⇩	1.50	5.32E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test $p<0.05$, FC ≥ ±1.50]

Probeset ID	Symbol		Fold	p-value	Probeset ID	Symbol		Fold	p-value	Probeset ID	Symbol		Fold	p-value
224559_at	MALAT1	⇧	13.2	8.30E-07	215599_at	LOC653188	⇧	4.25	4.90E-04	242431_at	---	⇧	3.86	3.20E-06
228582_x_at	MALAT1	⇧	12.2	4.60E-05	239014_at	CCAR1	⇩	4.24	2.10E-04	230206_at	DOCK5	⇧	3.85	1.60E-05
217414_x_at	HBA1/2	⇩	9.12	0.030	213757_at	---	⇧	4.23	2.40E-03	1555745_a_at	LYZ	⇩	3.84	0.020
221491_x_at	HLA-DRB1/3-5	⇩	9.11	0.025	228251_at	LOC100130930	⇧	4.21	4.50E-04	1559142_at	MYST3	⇧	3.83	1.40E-05
228697_at	HINT3	⇧	8.34	1.80E-05	222179_at	CDC5L	⇩	4.19	2.20E-04	231484_at	---	⇧	3.82	0.028
1559500_at	VPS8	⇧	7.45	1.40E-04	1569706_at	MYSM1	⇧	4.17	4.40E-05	226762_at	PURB	⇧	3.81	6.50E-04
241879_at	LPP	⇧	7.17	2.20E-06	1565743_at	---	⇧	4.16	1.70E-05	235999_at	---	⇧	3.81	2.10E-04
232535_at	---	⇧	6.68	9.60E-07	232958_at	---	⇧	4.14	1.10E-03	241702_at	---	⇧	3.79	8.10E-04
211699_x_at	HBA1/2	⇩	6.46	0.046	233706_at	---	⇧	4.12	2.10E-04	237590_at	---	⇧	3.79	4.30E-05
235008_at	---	⇩	6.17	5.50E-06	1560662_s_at	WHAMML1/2	⇧	4.11	7.10E-05	1562467_at	---	⇧	3.75	4.70E-05
204270_at	SKI	⇩	5.95	7.10E-05	243559_at	---	⇧	4.10	1.80E-03	239453_at	---	⇧	3.75	1.50E-05
213998_s_at	DDX17	⇩	5.93	8.10E-05	208442_s_at	ATM	⇧	4.10	4.20E-04	242975_s_at	---	⇧	3.71	9.90E-05
236201_at	---	⇧	5.83	6.20E-03	238185_at	---	⇧	4.08	9.90E-06	228248_at	RICTOR	⇧	3.69	8.50E-05
1570361_a_at	---	⇧	5.75	6.00E-05	222787_s_at	TMEM106B	⇧	4.07	1.30E-04	239393_at	---	⇧	3.66	2.90E-05
229982_at	QSER1	⇧	5.32	1.20E-04	243089_at	---	⇧	4.04	4.00E-04	218400_at	OAS3	⇩	3.65	0.016
215175_at	PCNX	⇧	5.26	2.40E-03	1556277_a_at	PAPD4	⇧	4.02	1.90E-04	236930_at	NUMB	⇧	3.64	2.50E-04
204018_x_at	HBA1/2	⇩	5.23	0.045	236808_at	FGFR1OP2	⇧	3.99	7.20E-04	235613_at	---	⇧	3.62	7.10E-04
226931_at	TMTC1	⇧	5.15	3.60E-04	241041_at	---	⇧	3.99	4.40E-04	236000_s_at	---	⇧	3.61	1.10E-03
241610_x_at	---	⇧	4.94	1.00E-04	240652_at	---	⇧	3.97	1.60E-04	211310_at	EZH1	⇧	3.61	1.00E-04
207604_s_at	SLC4A7	⇧	4.88	1.20E-06	1567045_at	---	⇧	3.97	2.70E-05	221745_at	WDR68	⇧	3.60	2.00E-04
242974_at	CD47	⇧	4.78	3.50E-06	1562283_at	---	⇧	3.96	1.10E-03	1565788_at	---	⇧	3.60	1.30E-04
205654_at	C4BPA	⇧	4.75	0.029	224829_at	CPEB4	⇧	3.96	2.20E-04	208523_x_at	HIST1H2BI	⇩	3.60	4.30E-06
239751_at	LOC100506860	⇧	4.74	4.60E-06	208930_s_at	ILF3	⇧	3.94	2.30E-04	201340_s_at	ENC1	⇧	3.58	5.20E-06
242029_at	FNDC3B	⇧	4.67	5.10E-05	208268_at	ADAM28	⇧	3.90	2.40E-03	234044_at	---	⇧	3.57	2.30E-03
220900_at	---	⇧	4.48	7.50E-06	235643_at	SAMD9L	⇧	3.89	1.60E-03	214690_at	TAF1B	⇧	3.57	2.00E-04
226322_at	TMTC1	⇧	4.47	4.50E-03	242903_at	IFNGR1	⇧	3.89	8.00E-05	231173_at	PYROXD1	⇧	3.56	2.80E-03
232365_at	SIAH1	⇧	4.40	4.60E-04	1560776_at	---	⇧	3.89	3.70E-05	241860_at	---	⇧	3.55	1.90E-03
212182_at	NUDT4	⇧	4.39	5.60E-05	233724_at	ARNT	⇧	3.89	5.10E-07	1557244_a_at	---	⇩	3.55	1.60E-04
242659_at	---	⇧	4.36	3.40E-06	232386_at	VPS13C	⇧	3.88	3.30E-05	1566002_at	---	⇧	3.55	1.50E-04
1565868_at	CD44	⇧	4.30	3.40E-05	231097_at	---	⇧	3.87	4.20E-04	208579_x_at	H2BFS	⇩	3.54	6.80E-05
236439_at	---	⇧	4.25	5.90E-04	236293_at	RHOH	⇧	3.86	1.30E-04	210858_x_at	ATM	⇧	3.54	7.00E-06

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

211734_s_at	FCER1A	⇩	3.53	0.020
234210_x_at	ACTR2	⇧	3.52	4.50E-04
226999_at	RNPC3	⇧	3.52	2.30E-05
1569408_at	EIF2C4	⇧	3.51	2.60E-04
217160_at	TSPY1	⇧	3.51	1.40E-04
236435_at	---	⇧	3.49	7.10E-04
212172_at	AK2	⇧	3.49	1.10E-04
1560926_at	---	⇧	3.48	6.30E-04
225720_at	SYNPO2	⇩	3.47	6.50E-03
215483_at	AKAP9	⇧	3.47	1.90E-03
210867_at	CNOT4	⇧	3.47	2.70E-04
1557036_at	ZBTB1	⇧	3.46	5.40E-03
1556462_a_at	---	⇧	3.46	5.30E-04
1556158_at	FAM154B	⇧	3.45	0.012
233964_at	---	⇧	3.45	2.00E-04
206088_at	LRRC37A2/3	⇧	3.44	1.30E-03
236043_at	LOC100130175	⇧	3.43	7.40E-05
209458_x_at	HBA1/2	⇩	3.42	0.024
238611_at	---	⇧	3.42	3.80E-05
1565620_at	AGAP4	⇧	3.41	7.30E-04
243490_at	---	⇧	3.40	1.00E-03
236432_at	---	⇧	3.38	4.20E-03
242467_at	---	⇧	3.38	4.80E-05
205118_at	FPR1	⇧	3.37	2.50E-03
234326_at	---	⇧	3.36	2.90E-03
1556461_at	---	⇧	3.36	7.70E-04
1564164_at	DENND1B	⇧	3.36	1.10E-04
240544_at	---	⇧	3.36	1.30E-06
220338_at	RALGPS2	⇧	3.35	2.40E-03
215986_at	---	⇧	3.35	1.70E-04
216765_at	MAP2K5	⇧	3.35	9.60E-05
215043_s_at	SMA4/5	⇧	3.34	5.20E-03
238787_at	DENND1B	⇧	3.34	5.00E-03
228222_at	PPP1CB	⇧	3.34	1.30E-03
242693_at	---	⇧	3.34	7.90E-04
203496_s_at	MED1	⇧	3.34	1.10E-04
239167_at	---	⇧	3.34	8.10E-05
203290_at	HLA-DQA1	⇩	3.33	0.023
232311_at	B2M	⇧	3.33	3.10E-04
211745_x_at	HBA1/2	⇩	3.31	0.027
228498_at	B4GALT1	⇧	3.30	2.00E-03
1559201_a_at	OSTF1	⇧	3.30	6.10E-04
240103_at	---	⇧	3.30	4.90E-04
242622_x_at	PTEN	⇧	3.29	2.00E-03
1558080_s_at	DNAJC3	⇧	3.29	1.60E-03
241824_at	---	⇧	3.28	9.80E-04
224230_at	IL1F8	⇧	3.28	1.20E-05
240593_x_at	---	⇧	3.27	3.20E-04
203749_s_at	RARA	⇧	3.26	3.50E-03
1554676_at	SRGN	⇧	3.26	2.80E-03
214405_at	---	⇧	3.26	1.70E-03
1557707_at	---	⇧	3.26	8.20E-04
235879_at	MBNL1	⇧	3.26	9.70E-05
1558710_at	---	⇧	3.26	6.10E-06
1565915_at	---	⇧	3.26	1.20E-06
222341_x_at	---	⇧	3.23	0.019
1554306_at	ITPKB	⇧	3.23	1.90E-04
216300_x_at	RARA	⇧	3.21	2.60E-03
231829_at	MAVS	⇧	3.19	7.30E-04
1570021_at	---	⇧	3.19	3.20E-04
243496_at	RAB18	⇧	3.19	3.20E-04
1558842_at	---	⇧	3.18	3.00E-03
238931_at	METT10D	⇧	3.18	6.70E-04
1552787_at	HELB	⇧	3.17	1.20E-03
241843_at	SNORA28	⇧	3.16	1.20E-03
238761_at	ELK4	⇧	3.16	2.50E-04
234059_at	---	⇧	3.16	4.60E-06
243458_at	---	⇧	3.15	1.50E-03
237963_x_at	---	⇧	3.15	5.10E-04
222319_at	---	⇧	3.15	1.90E-04
1557811_a_at	---	⇧	3.14	3.10E-04
1555194_at	---	⇧	3.14	1.50E-04
209398_at	HIST1H1C	⇩	3.13	3.50E-03
243876_at	---	⇧	3.13	6.90E-05
236794_at	---	⇧	3.13	5.10E-05
1554241_at	COCH	⇧	3.13	4.30E-05
228471_at	ANKRD44	⇧	3.12	1.60E-05
222728_s_at	TAF1D	⇧	3.11	4.00E-04
229353_s_at	NUCKS1	⇧	3.10	2.90E-03
236354_at	---	⇧	3.09	1.20E-03
228638_at	FAM76A	⇧	3.09	3.50E-04
230270_at	PRPF38B	⇧	3.09	2.50E-04
222826_at	PLDN	⇧	3.09	4.30E-05
1558315_s_at	HOOK3	⇧	3.09	2.00E-05
215659_at	GSDMB	⇧	3.07	2.70E-04
1555423_at	SSH2	⇧	3.06	7.20E-04
206544_x_at	SMARCA2	⇩	3.06	5.40E-04
212081_x_at	BAT2	⇧	3.05	0.018
242859_at	---	⇧	3.05	9.30E-04
242299_at	---	⇧	3.05	5.00E-04
239861_at	---	⇧	3.04	6.30E-04
219186_at	ZBTB7A	⇧	3.04	1.00E-04
1555167_s_at	NAMPT	⇩	3.03	0.037
1565811_at	---	⇧	3.03	3.30E-03
220494_s_at	---	⇧	3.03	7.40E-04
231999_at	ANKRD11	⇧	3.02	1.40E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

238769_at	---	⇧	3.01	3.90E-03	232179_at	LOC158863	⇧	2.93	4.10E-04	242261_at	IREB2	⇧	2.84	1.10E-03
234112_at	---	⇧	3.01	2.10E-03	229422_at	NRD1	⇧	2.92	2.40E-04	233314_at	PTEN	⇩	2.84	6.70E-04
237067_at	---	⇧	3.00	2.10E-03	238193_at	---	⇧	2.92	7.70E-05	1568866_at	---	⇧	2.84	5.90E-04
1555920_at	CBX3	⇧	3.00	9.30E-04	1558802_at	---	⇧	2.91	9.30E-04	243964_at	---	⇧	2.84	3.30E-04
236254_at	VPS13B	⇧	3.00	5.30E-04	1561340_at	---	⇧	2.91	5.40E-06	217534_at	FAM49B	⇧	2.84	5.80E-05
1565913_at	---	⇧	3.00	1.80E-04	226736_at	CHURC1	⇧	2.90	0.035	230621_at	IAH1	⇧	2.83	3.80E-05
236237_at	---	⇧	2.99	7.20E-03	236975_at	---	⇧	2.90	0.018	235172_at	---	⇧	2.82	5.60E-03
243134_at	---	⇧	2.99	4.60E-04	236659_x_at	---	⇧	2.90	1.80E-03	211644_x_at	IGK	⇩	2.82	3.30E-04
208629_s_at	HADHA	⇧	2.99	4.10E-04	224563_at	WASF2	⇩	2.89	6.00E-03	231252_at	C2orf67	⇧	2.82	2.00E-04
1561654_at	---	⇧	2.99	7.50E-05	1569262_x_at	UBE2CBP	⇧	2.89	5.10E-03	220655_at	TNIP3	⇧	2.82	2.50E-05
1560058_at	LOC399900	⇧	2.98	6.90E-03	237322_at	MIAT	⇧	2.89	2.90E-03	204192_at	CD37	⇩	2.81	0.018
208764_s_at	ATP5G2	⇩	2.98	3.50E-04	242576_x_at	N4BP2L2	⇧	2.89	2.10E-03	235851_s_at	GNAS	⇧	2.81	6.10E-03
237387_at	---	⇧	2.98	6.20E-05	232418_at	LZTFL1	⇧	2.89	9.40E-04	243182_at	---	⇧	2.81	5.80E-03
204863_s_at	IL6ST	⇧	2.97	9.50E-03	238902_at	PCMTD1	⇧	2.89	8.70E-04	236533_at	ASAP1	⇧	2.81	1.90E-04
223487_x_at	GNB4	⇧	2.97	3.10E-03	1559039_at	DHX36	⇧	2.89	1.60E-05	1560048_at	---	⇧	2.81	1.30E-04
212417_at	SCAMP1	⇧	2.97	1.10E-03	217811_at	SELT	⇩	2.88	9.30E-03	227897_at	---	⇧	2.81	1.90E-05
237197_at	---	⇩	2.97	9.30E-04	1567044_s_at	---	⇧	2.88	2.40E-03	222067_x_at	HIST1H2BD	⇩	2.81	1.50E-05
243149_at	---	⇧	2.97	7.00E-04	222929_at	FAM160B2	⇧	2.88	5.70E-05	1563226_at	SLC38A10	⇧	2.80	6.60E-03
1555392_at	LOC100128868	⇧	2.97	6.20E-04	233995_at	---	⇧	2.87	4.20E-03	1554084_a_at	NOL9	⇧	2.80	3.00E-04
219980_at	C4orf29	⇧	2.97	1.70E-04	200806_s_at	HSPD1	⇩	2.87	5.50E-04	243454_at	---	⇧	2.80	8.30E-05
1564767_at	---	⇧	2.97	4.10E-05	206454_s_at	RHO	⇩	2.86	0.014	208546_x_at	HIST1H2BH	⇩	2.80	2.40E-05
230392_at	---	⇧	2.96	4.00E-03	226663_at	ANKRD10	⇧	2.86	1.60E-03	1562255_at	SYTL3	⇧	2.79	0.011
217363_x_at	---	⇩	2.96	2.40E-03	205310_at	FBXO46	⇧	2.86	2.70E-04	1555116_s_at	SLC11A1	⇧	2.79	1.70E-03
1565810_at	---	⇧	2.96	1.40E-03	238672_at	---	⇧	2.86	7.70E-05	215874_at	---	⇧	2.79	1.10E-03
203533_s_at	CUL5	⇧	2.96	3.50E-04	210666_at	IDS	⇧	2.86	5.70E-05	1552302_at	TMEM106A	⇧	2.79	4.40E-05
238363_at	---	⇧	2.95	8.30E-05	207631_at	NBR2	⇧	2.86	3.70E-05	241497_at	---	⇧	2.78	0.013
1556323_at	CUGBP2	⇧	2.94	5.40E-04	244508_at	SEPT7	⇧	2.85	8.10E-03	1566608_at	---	⇧	2.78	2.00E-03
238610_s_at	---	⇧	2.94	2.70E-05	1560349_at	---	⇧	2.85	2.80E-04	235220_at	YIPF4	⇧	2.78	1.30E-03
213954_at	FAM169A	⇧	2.93	7.80E-03	1559347_at	---	⇧	2.85	1.50E-04	233872_x_at	ARHGAP5	⇧	2.78	9.90E-04
244473_at	---	⇧	2.93	7.20E-03	1564776_at	---	⇧	2.84	5.40E-03	233239_at	---	⇧	2.78	2.20E-04
221688_s_at	IMP3	⇩	2.93	4.00E-03	222850_s_at	DNAJB14	⇧	2.84	4.40E-03	237459_at	---	⇧	2.78	9.40E-05
244773_at	---	⇧	2.93	1.40E-03	234621_at	---	⇩	2.84	2.70E-03	244165_at	C10orf18	⇧	2.77	3.80E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

215392_at	---	⇧	2.77	1.50E-03	231507_at	---	⇧	2.70	2.80E-03	206965_at	KLF12	⇧	2.66	3.10E-03
233400_at	---	⇧	2.77	1.50E-03	238013_at	PLEKHA2	⇧	2.70	1.40E-03	240105_at	---	⇧	2.66	2.70E-03
232392_at	SFRS3	⇧	2.76	2.10E-03	224697_at	WDR22	⇩	2.70	6.00E-04	227062_at	NCRNA00084	⇧	2.65	9.60E-03
233204_at	LOC728153	⇧	2.76	9.30E-04	230407_at	SBNO1	⇧	2.70	4.40E-04	1559747_at	SPG11	⇧	2.65	1.40E-03
232412_at	FBXL20	⇧	2.76	7.00E-04	236985_at	---	⇧	2.70	3.90E-04	230128_at	IGL	⇧	2.65	0.017
209060_x_at	NCOA3	⇧	2.76	4.40E-04	244539_at	---	⇧	2.70	2.80E-04	203415_at	PDCD6	⇩	2.65	0.017
243031_at	---	⇧	2.75	8.30E-03	221829_s_at	TNPO1	⇧	2.70	3.20E-05	242712_x_at	RGPD1-8	⇧	2.64	1.60E-03
215434_x_at	NBPF1/10	⇧	2.75	7.30E-03	216735_x_at	---	⇧	2.70	8.90E-06	AFFX-r2-Bs-lys-5_at	---	⇩	2.63	0.022
232622_at	---	⇧	2.75	1.20E-03	1557543_at	---	⇧	2.69	2.60E-03	1558569_at	UNQ6228	⇧	2.63	0.017
235926_at	ANAPC5	⇧	2.75	8.00E-04	206697_s_at	HP	⇧	2.69	2.50E-03	219158_s_at	NARG1	⇧	2.63	4.80E-03
239405_at	---	⇧	2.75	6.10E-04	208490_x_at	HIST1H2BF	⇩	2.69	1.60E-03	1558922_at	---	⇧	2.63	3.00E-03
1566003_x_at	---	⇧	2.75	4.00E-04	228545_at	ZNF148	⇧	2.69	1.20E-03	238271_x_at	---	⇧	2.63	7.10E-04
1558515_at	FTX	⇧	2.75	2.60E-04	243178_at	---	⇧	2.69	5.30E-04	1559391_s_at	---	⇧	2.63	5.90E-04
216198_at	ATF7IP	⇧	2.75	1.50E-04	227145_at	LOXL4	⇧	2.69	2.20E-04	203482_at	FAM178A	⇧	2.63	5.60E-04
231005_at	---	⇧	2.75	1.10E-04	214777_at	IGKV4-1	⇩	2.68	3.80E-03	230543_at	---	⇧	2.63	2.60E-04
232637_at	SEPT2	⇧	2.75	6.80E-06	228834_at	TOB1	⇧	2.68	2.60E-03	216767_at	---	⇧	2.63	9.10E-05
243469_at	---	⇧	2.74	2.20E-03	201868_s_at	TBL1X	⇧	2.68	1.80E-03	241259_at	GAB3	⇧	2.63	2.30E-05
1557797_a_at	---	⇧	2.74	9.90E-04	233009_at	---	⇧	2.68	1.60E-03	211424_x_at	METTL7A	⇧	2.63	2.30E-05
234009_at	---	⇧	2.74	7.90E-04	235957_at	GRIP1	⇧	2.68	8.80E-04	207067_s_at	HDC	⇩	2.62	0.031
242117_at	---	⇧	2.74	5.50E-04	1566426_at	---	⇧	2.68	8.10E-04	209750_at	NR1D2	⇧	2.62	0.011
214693_x_at	NBPF10	⇧	2.73	4.30E-03	230629_s_at	EP400	⇧	2.68	4.90E-04	238851_at	ANKRD13A	⇧	2.62	2.20E-03
238982_at	DENR	⇧	2.73	3.30E-03	240482_at	---	⇧	2.68	9.90E-07	239661_at	---	⇧	2.62	1.40E-03
233824_at	---	⇧	2.73	1.20E-03	1555091_at	PPM1F	⇧	2.67	4.80E-03	238317_x_at	---	⇧	2.62	1.00E-03
207492_at	NGLY1	⇧	2.72	5.40E-04	1557305_at	TACC1	⇧	2.67	8.30E-04	239364_at	---	⇧	2.62	3.30E-04
203007_x_at	LYPLA1	⇧	2.72	1.70E-04	238430_x_at	SLFN5	⇧	2.67	4.10E-04	231281_at	---	⇧	2.62	2.80E-05
220572_at	---	⇧	2.72	1.20E-04	208527_x_at	HIST1H2BE	⇩	2.67	1.10E-04	AFFX-LysX-5_at	---	⇩	2.62	0.013
215524_x_at	TRAC	⇩	2.72	1.00E-05	230461_s_at	---	⇧	2.67	6.50E-05	1566113_at	---	⇧	2.61	4.40E-03
217753_s_at	RPS26	⇧	2.71	4.30E-03	230466_s_at	RASSF3	⇧	2.67	5.40E-05	1558747_at	SMCHD1	⇧	2.61	3.40E-03
238563_at	---	⇧	2.71	5.80E-04	1558698_at	ZNF264	⇧	2.66	0.019	236907_at	---	⇧	2.61	2.10E-03
239533_at	GPR155	⇧	2.71	1.30E-04	1566485_at	---	⇧	2.66	3.10E-03	232440_at	ZDHHC13	⇧	2.61	7.80E-04

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

205594_at	ZNF652	⇧	2.61	1.50E-04
241692_at	---	⇧	2.61	3.00E-05
232537_x_at	MARK3	⇧	2.60	8.00E-03
210384_at	PRMT2	⇧	2.60	5.10E-03
220710_at	C15orf28	⇧	2.60	1.20E-03
243667_at	---	⇧	2.60	7.50E-04
1555945_s_at	FAM120A	⇧	2.60	3.30E-04
236327_at	---	⇧	2.60	2.60E-04
240036_at	SEC14L1	⇧	2.59	9.20E-03
235567_at	RORA	⇧	2.59	6.80E-03
234474_x_at	IL6ST	⇧	2.59	6.60E-03
208200_at	IL1A	⇧	2.59	1.40E-03
239629_at	CFLAR	⇧	2.59	6.10E-04
229398_at	RAB18	⇧	2.59	5.00E-04
1564021_at	---	⇧	2.59	3.80E-04
225304_s_at	NDUFA11	⇩	2.59	1.70E-04
224726_at	MIB1	⇧	2.59	1.10E-04
210517_s_at	AKAP12	⇩	2.58	0.041
229187_at	LOC283788	⇧	2.58	5.70E-03
232978_at	---	⇧	2.58	3.90E-03
1558028_x_at	LOC647979	⇧	2.58	2.90E-03
242343_x_at	---	⇧	2.58	1.90E-03
227851_s_at	---	⇧	2.58	1.10E-04
229010_at	CBL	⇧	2.57	0.019
201369_s_at	ZFP36L2	⇧	2.57	0.012
1557238_s_at	---	⇧	2.57	3.70E-03
239978_at	---	⇧	2.57	1.20E-03
242480_at	---	⇧	2.57	9.30E-04
235660_at	---	⇧	2.57	4.50E-05
235271_s_at	ZNF397	⇧	2.57	4.30E-05
206408_at	LRRTM2	⇧	2.57	1.20E-05
202379_s_at	NKTR	⇧	2.56	1.60E-03
219125_s_at	RAG1AP1	⇧	2.56	2.90E-06
234288_at	---	⇧	2.55	0.027
209127_s_at	SART3	⇧	2.55	0.010
242384_at	---	⇧	2.55	7.90E-03
215464_s_at	TAX1BP3	⇩	2.55	4.10E-03
1565566_a_at	---	⇧	2.55	1.30E-03
236841_at	---	⇧	2.55	6.50E-04
210484_s_at	TNFRSF10C	⇩	2.55	4.70E-04
215385_at	---	⇧	2.55	2.90E-04
217368_at	ATP5G2	⇩	2.55	4.60E-05
216373_at	TAPT1	⇧	2.55	1.50E-05
201237_at	CAPZA2	⇧	2.53	0.019
236223_s_at	RIT1	⇧	2.53	4.80E-03
216401_x_at	LOC652493	⇩	2.53	3.90E-03
229858_at	---	⇧	2.53	3.70E-03
1555814_a_at	RHOA	⇩	2.53	3.30E-03
205727_at	TEP1	⇧	2.53	2.70E-03
1560486_at	STXBP3	⇧	2.53	4.40E-04
236356_at	NDUFS1	⇧	2.53	3.40E-04
243498_at	---	⇧	2.53	3.10E-04
214815_at	TRIM33	⇧	2.52	0.021
235811_at	---	⇧	2.52	0.015
211459_at	---	⇧	2.52	5.10E-03
215029_at	---	⇧	2.52	5.00E-03
224766_at	RPL37	⇧	2.52	2.20E-03
239605_x_at	---	⇧	2.52	1.50E-03
243910_x_at	CAND1	⇧	2.52	1.60E-04
1558699_a_at	HERPUD2	⇧	2.52	8.20E-05
226548_at	SBK1	⇧	2.51	4.90E-03
229193_at	LUC7L3	⇧	2.51	4.80E-03
240498_at	---	⇧	2.51	1.70E-03
1556849_at	---	⇧	2.51	4.10E-04
224346_at	---	⇩	2.51	2.20E-04
241050_at	---	⇩	2.50	0.020
202412_s_at	USP1	⇧	2.50	4.90E-03
208151_x_at	DDX17	⇧	2.50	4.00E-03
231848_x_at	ZNF207	⇧	2.50	3.90E-03
211395_x_at	FCGR2C	⇩	2.50	2.10E-03
1556318_s_at	CAND1	⇧	2.50	7.90E-04
214257_s_at	---	⇧	2.50	5.40E-04
230494_at	SLC20A1	⇧	2.50	4.90E-04
214768_x_at	FAM20B	⇩	2.50	2.90E-04
211411_at	---	⇧	2.50	3.70E-05
1564794_at	---	⇧	2.50	3.30E-05
229606_at	---	⇧	2.50	1.70E-05
242280_x_at	CPEB4	⇧	2.49	0.024
213328_at	NEK1	⇧	2.49	0.019
212027_at	RBM25	⇧	2.49	0.016
201670_s_at	MARCKS	⇧	2.49	0.011
1558732_at	MAP4K4	⇧	2.49	5.20E-03
239778_x_at	---	⇧	2.49	3.20E-03
230375_at	SFRS18	⇧	2.49	2.80E-03
237216_at	---	⇧	2.49	1.70E-03
213517_at	PCBP2	⇧	2.49	1.50E-03
219382_at	SERTAD3	⇧	2.49	3.90E-04
63825_at	ABHD2	⇧	2.48	0.024
233261_at	EBF1	⇧	2.48	0.013
236429_at	ZNF83	⇧	2.48	5.40E-03
1564378_a_at	---	⇧	2.48	2.30E-03
211941_s_at	PEBP1	⇩	2.48	2.20E-03
1557810_at	---	⇧	2.48	1.80E-03
1552664_at	FLCN	⇧	2.48	1.30E-03
239392_s_at	POGK	⇧	2.48	8.40E-04
243046_at	---	⇧	2.48	6.40E-04

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

240706_at	---	⇧	2.48	3.80E-05	210992_x_at	FCGR2C	⇩	2.44	3.90E-03	235009_at	BOD1L	⇧	2.41	2.80E-03
216252_x_at	FAS	⇩	2.47	0.025	1555425_x_at	SSH2	⇧	2.44	1.30E-03	1553727_at	B4GALNT3	⇧	2.41	2.20E-03
222330_at	---	⇧	2.47	4.00E-03	1555303_at	---	⇧	2.44	1.00E-03	217378_x_at	---	⇩	2.41	1.90E-03
242646_at	---	⇧	2.47	3.60E-03	1557737_s_at	NKTR	⇧	2.44	9.20E-04	1558173_a_at	LUZP1	⇧	2.41	1.80E-03
216380_x_at	RPS28P6	⇩	2.47	3.60E-03	1556060_a_at	ZNF451	⇧	2.44	8.70E-04	1556007_s_at	CSNK1A1	⇧	2.41	1.10E-03
215176_x_at	---	⇩	2.47	2.90E-03	1563473_at	---	⇧	2.44	6.30E-04	1554178_a_at	FAM126B	⇧	2.40	0.012
212384_at	BAT1	⇧	2.47	2.50E-03	232312_at	SAPS3	⇧	2.44	1.30E-04	213742_at	SFRS11	⇧	2.40	1.70E-03
216813_at	---	⇧	2.47	1.40E-03	209225_x_at	TNPO1	⇧	2.44	3.50E-05	232775_at	---	⇧	2.40	9.50E-05
215252_at	---	⇧	2.47	1.00E-03	218866_s_at	POLR3K	⇩	2.44	3.10E-06	234149_at	---	⇧	2.40	4.10E-06
205462_s_at	HPCAL1	⇩	2.47	7.10E-04	221205_at	---	⇧	2.43	7.90E-03	221563_at	DUSP10	⇧	2.40	2.40E-06
230000_at	RNF213	⇧	2.47	4.80E-04	240478_at	---	⇧	2.43	1.30E-03	206371_at	FOLR3	⇩	2.39	0.027
234488_s_at	GMCL1	⇧	2.47	4.60E-04	223380_s_at	LATS2	⇧	2.43	1.30E-03	230014_at	---	⇧	2.39	0.015
232188_at	AKAP13	⇧	2.46	5.10E-03	211643_x_at	IGK	⇩	2.43	9.90E-04	239274_at	---	⇧	2.39	9.60E-03
233819_s_at	RNF160	⇧	2.46	5.10E-03	214305_s_at	SF3B1	⇧	2.43	7.30E-04	243789_at	---	⇧	2.39	7.00E-03
242024_at	---	⇧	2.46	3.10E-03	242248_at	PHKB	⇧	2.43	4.70E-04	233309_at	---	⇧	2.39	3.40E-03
236224_at	RIT1	⇧	2.46	1.90E-03	1562611_at	---	⇧	2.43	4.10E-04	236266_at	RORA	⇧	2.39	1.10E-03
237588_at	---	⇧	2.46	7.20E-04	230892_at	---	⇧	2.43	2.60E-04	241413_at	---	⇧	2.39	9.60E-04
208819_at	RAB8A	⇧	2.46	3.70E-04	217591_at	SKIL	⇧	2.43	1.80E-04	222529_at	SLC25A37	⇧	2.39	9.60E-04
1566848_x_at	---	⇧	2.46	3.40E-04	208132_x_at	BAT2	⇧	2.42	0.029	243981_at	STK4	⇧	2.39	7.20E-04
233816_at	---	⇧	2.46	2.90E-04	204174_at	ALOX5AP	⇩	2.42	0.025	243908_at	---	⇧	2.39	4.60E-04
215719_x_at	FAS	⇩	2.45	0.033	234000_s_at	PTPLAD1	⇧	2.42	9.20E-03	227039_at	AKAP13	⇧	2.39	3.80E-04
236862_at	GOPC	⇧	2.45	8.70E-03	1559479_at	PI4K2B	⇧	2.42	4.70E-03	229257_at	TNRC18	⇧	2.39	1.20E-04
214352_s_at	KRAS	⇧	2.45	2.60E-03	227931_at	INO80D	⇧	2.42	1.30E-03	240044_x_at	TNRC6B	⇧	2.39	1.50E-05
230970_at	---	⇧	2.45	2.00E-03	1555339_at	RAP1A	⇩	2.42	1.10E-03	240772_at	---	⇧	2.38	0.011
229293_at	---	⇧	2.45	5.60E-04	208627_s_at	YBX1	⇩	2.42	3.50E-04	239742_at	TULP4	⇧	2.38	3.70E-03
232885_at	---	⇧	2.45	1.60E-04	205221_at	HGD	⇩	2.42	3.30E-04	242498_x_at	---	⇧	2.38	3.40E-03
215956_at	---	⇧	2.45	1.40E-04	1558830_at	---	⇧	2.42	1.70E-04	230833_at	ACRBP	⇩	2.38	2.90E-03
227697_at	SOCS3	⇧	2.45	1.10E-04	240080_at	---	⇧	2.42	1.70E-04	1556821_x_at	DLEU2	⇧	2.38	2.20E-03
227419_x_at	PLAC9	⇧	2.45	9.20E-06	221483_s_at	ARPP19	⇧	2.42	1.60E-06	215398_at	---	⇧	2.38	2.10E-03
239486_at	---	⇧	2.44	0.017	240016_at	---	⇧	2.41	0.012	235526_at	SOX6	⇩	2.38	1.30E-03
239487_at	FAM98A	⇧	2.44	0.013	234151_at	---	⇧	2.41	9.40E-03	212641_at	HIVEP2	⇩	2.38	9.60E-04
1562677_at	HMMR	⇧	2.44	0.011	243233_at	---	⇧	2.41	6.00E-03	213229_at	DICER1	⇧	2.38	5.90E-04

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

215620_at	RREB1	⇧	2.38	4.10E-04	239948_at	NUP153	⇧	2.35	1.70E-03	204180_s_at	ZBTB43	⇧	2.31	1.90E-03
1562849_at	---	⇧	2.38	1.80E-04	217653_x_at	---	⇧	2.35	6.20E-04	242144_at	---	⇧	2.31	1.80E-03
227639_at	PIGK	⇧	2.38	4.50E-05	217445_s_at	GART	⇧	2.35	3.00E-04	1561963_at	MIR4296	⇧	2.31	1.70E-03
215894_at	PTGDR	⇧	2.37	0.026	1553047_at	PIP4K2B	⇧	2.35	1.80E-04	244753_at	---	⇧	2.31	1.10E-03
1563621_at	---	⇧	2.37	0.024	214246_x_at	MINK1	⇧	2.35	6.70E-05	207038_at	SLC16A6	⇧	2.31	1.10E-03
1569142_at	TRIM13	⇧	2.37	0.016	1568867_x_at	---	⇧	2.34	1.50E-03	238536_at	---	⇧	2.31	7.20E-04
243561_at	---	⇧	2.37	5.30E-03	235668_at	PRDM1	⇧	2.34	6.30E-04	233099_at	---	⇧	2.31	4.10E-04
1559044_at	EXOSC1	⇧	2.37	3.20E-03	216844_at	ZC3H7B	⇧	2.34	4.20E-05	206681_x_at	GP2	⇧	2.31	3.00E-04
240254_at	---	⇧	2.37	2.70E-03	221211_s_at	C21orf7	⇩	2.33	0.021	243997_x_at	---	⇧	2.30	0.011
240146_at	---	⇧	2.37	1.80E-03	201294_s_at	WSB1	⇧	2.33	0.011	1555058_a_at	LPGAT1	⇧	2.30	0.010
239545_at	---	⇧	2.37	1.80E-03	1558924_s_at	CLIP1	⇧	2.33	9.60E-03	243005_at	---	⇧	2.30	9.90E-03
222582_at	PRKAG2	⇧	2.37	1.60E-03	238303_at	STT3B	⇧	2.33	6.10E-03	237018_at	---	⇧	2.30	7.70E-03
216983_s_at	ZNF224	⇧	2.37	6.70E-04	1559895_x_at	---	⇧	2.33	4.50E-03	242558_at	---	⇧	2.30	6.60E-03
224974_at	SUDS3	⇧	2.37	5.70E-04	1570248_at	---	⇧	2.33	3.10E-03	242877_at	---	⇧	2.30	6.20E-03
230779_at	TNRC6B	⇧	2.37	5.40E-04	241631_at	---	⇧	2.33	3.00E-03	233007_at	---	⇧	2.30	5.90E-03
240554_at	AKAP8L	⇧	2.37	4.20E-04	238722_x_at	NAPEPLD	⇧	2.33	2.90E-03	1556820_a_at	DLEU2	⇧	2.30	3.40E-03
244818_at	LOC390933	⇧	2.37	2.10E-04	237586_at	---	⇧	2.33	2.30E-04	241508_at	---	⇧	2.30	2.20E-03
236419_at	---	⇧	2.36	0.037	240691_at	---	⇧	2.33	6.10E-05	1569368_at	LOC283693	⇩	2.30	1.90E-03
236495_at	---	⇧	2.36	0.011	213120_at	UHRF1BP1L	⇧	2.33	1.40E-05	242755_at	---	⇧	2.30	1.70E-03
1559331_x_at	---	⇧	2.36	6.10E-03	206565_x_at	SMA4	⇧	2.32	0.012	241501_at	---	⇧	2.30	1.60E-03
238040_at	---	⇧	2.36	6.00E-03	204713_s_at	F5	⇧	2.32	0.011	232931_at	SNRNP200	⇧	2.30	1.30E-03
216947_at	DES	⇩	2.36	3.40E-03	231793_s_at	CAMK2D	⇧	2.32	5.20E-03	232858_at	---	⇧	2.30	8.70E-04
241838_at	---	⇧	2.36	2.90E-03	201918_at	SLC25A36	⇧	2.32	4.90E-03	238534_at	LRRFIP1	⇧	2.30	8.70E-04
235469_at	FAM133B	⇧	2.36	1.40E-03	228030_at	---	⇧	2.32	4.70E-03	226085_at	CBX5	⇧	2.30	6.80E-04
231878_at	C16orf53	⇧	2.36	7.80E-04	221905_at	CYLD	⇧	2.32	2.70E-03	240210_at	ATAD3C	⇧	2.30	3.50E-04
213518_at	PRKCI	⇧	2.36	6.90E-04	225265_at	RBMS1	⇧	2.32	1.00E-03	214488_at	RAP2B	⇧	2.30	3.40E-04
223217_s_at	NFKBIZ	⇧	2.36	2.60E-04	214871_x_at	---	⇧	2.32	7.10E-04	215070_x_at	RABGAP1	⇧	2.30	2.90E-04
242146_at	SNRPA1	⇧	2.36	9.70E-05	221540_x_at	GTF2H2B-D	⇧	2.32	2.40E-04	242691_at	---	⇧	2.30	2.70E-04
240248_at	---	⇧	2.35	0.036	204119_s_at	ADK	⇩	2.32	1.50E-04	1553625_at	FAM98B	⇧	2.30	1.20E-04
214918_at	HNRNPM	⇧	2.35	0.025	243512_x_at	---	⇧	2.31	0.012	1559964_at	FLJ38717	⇧	2.29	0.033
238970_at	---	⇧	2.35	0.019	216022_at	---	⇧	2.31	4.70E-03	203939_at	NT5E	⇩	2.29	0.019
230702_at	C8orf16	⇧	2.35	0.013	208960_s_at	KLF6	⇩	2.31	3.40E-03	222679_s_at	DCUN1D1	⇧	2.29	0.012

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

225414_at	RNF149	⇧	2.29	8.40E-03
236941_at	C22orf30	⇧	2.29	6.80E-03
230703_at	---	⇧	2.29	5.70E-03
242110_at	---	⇧	2.29	5.40E-03
235409_at	MGA	⇧	2.29	3.60E-03
223934_at	SP140L	⇧	2.29	3.40E-03
207470_at	---	⇧	2.29	1.70E-03
215058_at	DENND5B	⇧	2.29	7.00E-04
216112_at	---	⇧	2.29	2.20E-04
1562071_at	---	⇧	2.29	1.30E-04
213553_x_at	APOC1	⇧	2.29	4.70E-05
206354_at	SLCO1B3	⇩	2.28	0.033
1559496_at	PPA2	⇧	2.28	0.013
211192_s_at	CD84	⇩	2.28	0.012
216147_at	---	⇧	2.28	8.40E-04
1569380_a_at	HERPUD1	⇧	2.28	7.80E-04
200796_s_at	MCL1	⇩	2.28	3.70E-04
209024_s_at	SYNCRIP	⇧	2.27	0.035
1558154_at	---	⇧	2.27	0.020
1552552_s_at	CLEC4C	⇩	2.27	0.018
233302_at	---	⇧	2.27	0.014
241837_at	---	⇧	2.27	0.013
1561276_at	DOCK5	⇧	2.27	0.013
1562307_at	---	⇧	2.27	0.012
226880_at	NUCKS1	⇧	2.27	0.012
236552_at	---	⇧	2.27	0.011
236966_at	ARMC8	⇧	2.27	6.20E-03
236484_at	---	⇧	2.27	4.90E-03
1559612_at	---	⇧	2.27	3.20E-03
230808_at	FNTA	⇧	2.27	3.00E-03
224275_at	GPR98	⇧	2.27	1.60E-03
215859_at	NCLN	⇧	2.27	1.20E-03
218008_at	C7orf42	⇧	2.27	6.40E-04
211902_x_at	TRA	⇩	2.27	6.00E-04
234395_at	---	⇧	2.27	5.10E-05
222196_at	LOC286434	⇧	2.26	0.048
241620_at	SMCHD1	⇧	2.26	0.040
211430_s_at	IGH	⇩	2.26	0.037
242163_at	THRAP3	⇧	2.26	0.019
1566809_a_at	---	⇧	2.26	0.018
231495_at	---	⇧	2.26	8.70E-03
228603_at	ACTR3	⇧	2.26	5.60E-03
1552486_s_at	LACTB	⇩	2.26	4.60E-03
1559949_at	---	⇧	2.26	4.40E-03
213650_at	GOLGA8A/B	⇧	2.26	3.80E-03
217610_at	SPDYE2	⇧	2.26	3.40E-03
201883_s_at	B4GALT1	⇩	2.26	2.60E-03
200914_x_at	KTN1	⇧	2.26	2.10E-03
235028_at	---	⇧	2.26	2.00E-03
239905_at	YTHDC1	⇧	2.26	1.80E-03
1559600_at	---	⇧	2.26	1.60E-03
214522_x_at	HIST1H3D	⇩	2.26	1.40E-03
226533_at	HINT3	⇧	2.26	9.50E-04
230179_at	LOC285812	⇧	2.26	5.40E-04
244614_at	TFG	⇧	2.26	4.20E-04
1566043_at	---	⇧	2.26	1.20E-04
235713_at	ALKBH8	⇧	2.26	1.10E-06
236140_at	GCLM	⇧	2.25	6.40E-03
1562443_at	RLBP1L2	⇩	2.25	6.10E-03
231152_at	INO80D	⇧	2.25	5.60E-03
228147_at	SEPT7P2	⇧	2.25	4.90E-03
244447_at	---	⇧	2.25	3.70E-03
232441_at	KRR1	⇧	2.25	2.70E-03
236139_at	---	⇧	2.25	1.90E-03
228496_s_at	CRIM1	⇧	2.25	1.50E-03
1552536_at	VTI1A	⇧	2.25	8.30E-04
205069_s_at	ARHGAP26	⇧	2.25	7.60E-04
232216_at	YME1L1	⇧	2.25	7.40E-04
215587_x_at	---	⇧	2.25	1.80E-04
231235_at	NKTR	⇧	2.24	0.036
215314_at	---	⇧	2.24	0.017
1569512_at	---	⇧	2.24	0.017
207057_at	SLC16A7	⇧	2.24	0.017
232584_at	---	⇧	2.24	0.014
211645_x_at	---	⇩	2.24	7.50E-03
215996_at	---	⇧	2.24	7.20E-03
241940_at	---	⇧	2.24	6.40E-03
1553973_a_at	SPINK6	⇩	2.24	3.90E-03
238595_at	---	⇧	2.24	2.90E-03
242279_at	---	⇧	2.24	2.50E-03
1570571_at	CCDC91	⇧	2.24	2.30E-03
1553515_at	MYEOV2	⇩	2.24	5.50E-04
204318_s_at	GTSE1	⇧	2.24	1.50E-04
241346_at	ARHGAP30	⇧	2.23	0.018
244679_at	---	⇧	2.23	0.017
202323_s_at	ACBD3	⇧	2.23	0.014
237456_at	---	⇧	2.23	0.013
243263_at	C17orf55	⇧	2.23	9.00E-03
221496_s_at	TOB2	⇧	2.23	6.40E-03
216351_x_at	DAZ1-4	⇧	2.23	2.90E-03
229091_s_at	CCNJ	⇧	2.23	2.10E-03
205127_at	PTGS1	⇩	2.23	1.10E-03
232951_at	---	⇧	2.23	8.70E-04
1569004_at	---	⇧	2.23	7.70E-04
239296_at	---	⇧	2.23	5.90E-04
233716_at	---	⇧	2.23	5.80E-04

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

200892_s_at	TRA2B	⇩	2.23	5.70E-04	236310_at	ZNF37BP	⇧	2.21	1.00E-05	242983_at	---	⇧	2.18	2.20E-03
235380_at	---	⇧	2.23	4.00E-04	1566040_at	---	⇧	2.20	0.031	205209_at	ACVR1B	⇧	2.18	4.70E-04
243013_at	---	⇧	2.23	3.10E-04	212634_at	KIAA0776	⇧	2.20	0.022	237878_at	---	⇧	2.18	4.60E-04
207238_s_at	PTPRC	⇩	2.22	0.044	228907_at	---	⇧	2.20	0.011	1566598_at	---	⇧	2.18	1.80E-04
223134_at	BBX	⇧	2.22	0.010	232094_at	C15orf29	⇧	2.20	8.50E-03	244187_at	---	⇧	2.18	7.20E-05
238159_at	---	⇧	2.22	7.90E-03	215567_at	FCF1	⇧	2.20	5.10E-03	200947_s_at	GLUD1	⇧	2.18	9.60E-06
1566191_at	SUZ12	⇧	2.22	7.70E-03	210792_x_at	SIVA1	⇩	2.20	5.10E-03	244349_at	---	⇧	2.17	0.048
224185_at	WRAP53	⇧	2.22	6.40E-03	243229_at	---	⇧	2.20	4.60E-03	222895_s_at	BCL11B	⇧	2.17	0.012
234148_at	---	⇧	2.22	3.90E-03	216576_x_at	IGKC	⇩	2.20	4.40E-03	232521_at	PCSK7	⇧	2.17	0.010
244270_at	---	⇧	2.22	2.10E-03	238530_at	NNT	⇧	2.20	2.10E-03	205798_at	IL7R	⇧	2.17	8.30E-03
225191_at	CIRBP	⇧	2.22	2.00E-03	233915_at	C5orf36	⇧	2.20	5.20E-04	232356_at	---	⇧	2.17	5.50E-03
220477_s_at	C20orf30	⇩	2.22	3.50E-04	209947_at	UBAP2L	⇧	2.20	2.60E-05	217602_at	PPIA	⇧	2.17	4.80E-03
229355_at	UBE2D3	⇧	2.22	8.40E-05	201120_s_at	PGRMC1	⇩	2.19	0.039	1555759_a_at	CCL5	⇩	2.17	4.20E-03
1558882_at	LOC401233	⇧	2.21	0.047	1569346_a_at	---	⇧	2.19	0.024	207130_at	ZMYND8	⇧	2.17	3.00E-03
244035_at	---	⇧	2.21	0.038	241913_at	---	⇧	2.19	0.020	207445_s_at	CCR9	⇩	2.17	2.40E-03
236558_at	---	⇧	2.21	0.017	213281_at	JUN	⇧	2.19	0.018	241203_at	---	⇧	2.17	2.00E-03
224943_at	BTBD7	⇧	2.21	0.014	1565627_a_at	---	⇧	2.19	0.015	241717_at	LOC285281	⇩	2.17	1.60E-03
222266_at	C19orf2	⇧	2.21	0.014	215338_s_at	NKTR	⇧	2.19	0.011	213015_at	BBX	⇧	2.17	9.30E-04
1562317_at	FAM186A	⇩	2.21	0.013	220072_at	CSPP1	⇧	2.19	8.00E-03	232629_at	PROK2	⇧	2.17	6.70E-04
212890_at	SLC38A10	⇩	2.21	6.70E-03	213922_at	TTBK2	⇧	2.19	2.60E-03	1559355_at	NXPH2	⇧	2.17	1.60E-04
244105_at	WHAMML1	⇧	2.21	5.80E-03	1566607_at	---	⇧	2.19	1.80E-04	212926_at	SMC5	⇧	2.17	1.70E-05
226167_at	SYT7	⇧	2.21	5.30E-03	224535_s_at	MRP63	⇩	2.19	1.30E-04	202971_s_at	DYRK2	⇧	2.16	0.023
239601_at	---	⇧	2.21	3.70E-03	216166_at	---	⇧	2.19	6.50E-05	209911_x_at	HIST1H2BD	⇩	2.16	0.012
239421_at	FLJ35776	⇧	2.21	3.30E-03	203094_at	MAD2L1BP	⇩	2.19	2.70E-05	202166_s_at	PPP1R2	⇩	2.16	0.012
217565_at	GRIA3	⇧	2.21	2.20E-03	1555780_a_at	RHEB	⇩	2.18	0.041	238146_at	---	⇧	2.16	8.40E-03
1566209_at	---	⇩	2.21	1.70E-03	240971_x_at	---	⇧	2.18	0.012	226404_at	RBM39	⇧	2.16	7.90E-03
1558831_x_at	---	⇧	2.21	6.10E-04	243395_at	---	⇧	2.18	0.012	227364_at	---	⇧	2.16	6.60E-03
229733_s_at	---	⇧	2.21	5.30E-04	243739_at	---	⇧	2.18	0.011	240238_at	---	⇧	2.16	3.60E-03
213026_at	ATG12	⇧	2.21	5.10E-04	202124_s_at	TRAK2	⇧	2.18	8.60E-03	232952_at	---	⇧	2.16	2.50E-03
217649_at	ZFAND5	⇧	2.21	4.60E-04	230580_at	---	⇧	2.18	7.40E-03	237333_at	RBBP4	⇧	2.16	2.20E-03
210972_x_at	TRAC	⇩	2.21	3.00E-04	216207_x_at	IGKC	⇩	2.18	3.90E-03	1559038_at	SEPT2	⇧	2.16	1.60E-03
230946_at	FMN2	⇧	2.21	1.70E-04	242239_at	---	⇧	2.18	3.60E-03	213850_s_at	SFRS2IP	⇧	2.16	9.20E-04

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

225647_s_at	CTSC	⇩	2.16	1.70E-04
1565862_a_at	---	⇩	2.15	0.026
1555687_a_at	CLEC4C	⇩	2.15	0.018
224480_s_at	AGPAT9	⇧	2.15	0.012
1557895_at	FLJ35934	⇧	2.15	0.011
222024_s_at	AKAP13	⇧	2.15	8.60E-03
214678_x_at	ZFX	⇧	2.15	7.40E-03
218859_s_at	ESF1	⇧	2.15	7.10E-03
227741_at	PTPLB	⇧	2.15	6.60E-03
228315_at	ZMAT3	⇧	2.15	6.50E-03
232410_at	---	⇧	2.15	5.60E-03
203934_at	KDR	⇧	2.15	5.30E-03
243341_at	---	⇧	2.15	1.90E-03
209671_x_at	TRAC	⇩	2.15	1.00E-03
242672_at	---	⇧	2.15	9.80E-04
1559249_at	ATXN1	⇧	2.15	6.20E-04
218848_at	THOC6	⇧	2.15	3.70E-04
223432_at	OSBP2	⇧	2.14	0.032
225954_s_at	MIDN	⇧	2.14	0.020
233248_at	---	⇧	2.14	0.013
243748_at	---	⇧	2.14	7.30E-03
232338_at	---	⇧	2.14	5.30E-03
230999_at	FLJ39051	⇧	2.14	4.60E-03
1563130_a_at	---	⇧	2.14	3.80E-03
225507_at	SFRS18	⇧	2.14	2.70E-03
207643_s_at	TNFRSF1A	⇧	2.14	2.70E-03
1560741_at	SNRPN	⇧	2.14	2.60E-03
213812_s_at	CAMKK2	⇧	2.14	2.10E-03
219606_at	PHF20L1	⇧	2.14	1.10E-03
210501_x_at	EIF3K	⇩	2.14	1.00E-03
1560119_at	LOC389634	⇧	2.14	7.10E-04
216174_at	HCRP1	⇧	2.14	5.30E-04
1570249_x_at	---	⇧	2.14	2.50E-04
224651_at	CCNY	⇧	2.14	1.70E-04
242617_at	TMED8	⇧	2.14	4.80E-05
204774_at	EVI2A	⇧	2.13	0.047
244267_at	SATB1	⇧	2.13	0.039
230324_at	---	⇧	2.13	0.018
240601_at	---	⇧	2.13	0.015
1552622_s_at	POLR2J2/4	⇧	2.13	7.40E-03
235429_at	EIF3E	⇧	2.13	5.80E-03
229905_at	RAP1GDS1	⇧	2.13	5.60E-03
218050_at	UFM1	⇧	2.13	5.40E-03
225294_s_at	TRAPPC1	⇩	2.13	5.20E-03
216984_x_at	IGLV2-11	⇩	2.13	5.10E-03
243660_at	CHD9	⇧	2.13	4.80E-03
229966_at	EWSR1	⇧	2.13	2.90E-03
243868_at	RFX3	⇧	2.13	1.40E-03
240813_at	---	⇧	2.13	1.10E-03
1560445_x_at	ARHGEF1	⇧	2.13	8.20E-04
234890_at	LOC100288175	⇧	2.13	7.50E-05
204506_at	PPP3R1	⇧	2.13	2.80E-05
229943_at	TRIM13	⇧	2.12	0.031
222731_at	ZDHHC2	⇧	2.12	0.018
243807_at	NCOA7	⇧	2.12	7.20E-03
240282_at	WDR1	⇧	2.12	6.00E-03
229694_at	BRWD2	⇧	2.12	2.30E-03
210693_at	SPPL2B	⇧	2.12	1.30E-03
219617_at	C2orf34	⇧	2.12	6.40E-04
216274_s_at	SEC11A	⇩	2.12	3.70E-04
210334_x_at	BIRC5	⇧	2.12	2.70E-04
216769_x_at	---	⇧	2.12	1.50E-04
241688_at	---	⇧	2.12	8.80E-05
207548_at	GRM7	⇧	2.12	8.40E-05
233599_at	hCG_2003663	⇧	2.12	8.30E-05
1554281_at	---	⇩	2.11	0.036
221830_at	RAP2A	⇧	2.11	0.030
240265_at	TRAF3IP3	⇧	2.11	0.025
220674_at	CD22	⇧	2.11	0.019
233700_at	---	⇧	2.11	0.017
241627_x_at	FLJ10357	⇧	2.11	0.012
218280_x_at	HIST2H2AA3	⇩	2.11	0.012
242260_at	MATR3	⇧	2.11	9.40E-03
224140_at	NPCDR1	⇧	2.11	7.90E-03
242347_at	---	⇧	2.11	7.30E-03
1557360_at	LRPPRC	⇧	2.11	7.10E-03
232890_at	---	⇧	2.11	6.00E-03
226267_at	JDP2	⇧	2.11	3.50E-03
221222_s_at	C1orf56	⇧	2.11	2.90E-03
241904_at	---	⇧	2.11	2.00E-03
217157_x_at	IGK	⇩	2.11	1.90E-03
232724_at	MS4A6A	⇧	2.11	1.80E-03
239021_at	TLR6	⇧	2.11	8.60E-04
217643_x_at	---	⇧	2.11	8.40E-04
1560827_at	---	⇧	2.11	6.00E-04
214656_x_at	MYO1C	⇧	2.11	3.20E-04
238277_at	---	⇧	2.11	3.00E-04
233014_at	---	⇧	2.11	2.20E-04
225210_s_at	FAM103A1	⇧	2.11	1.80E-04
235540_at	GNRH1	⇧	2.11	1.60E-04
237152_at	hCG_17324	⇧	2.11	1.60E-04
1561855_x_at	---	⇧	2.11	6.20E-05
1566966_at	---	⇧	2.11	4.10E-05
205234_at	SLC16A4	⇧	2.11	2.40E-05
222154_s_at	LOC26010	⇩	2.10	0.046
222366_at	---	⇧	2.10	0.017

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

218294_s_at	NUP50	⇧	2.10	0.013	235374_at	MDH1	⇧	2.09	5.10E-03	228726_at	SERPINB1	⇧	2.08	6.70E-06
234430_at	ANTXR1	⇧	2.10	0.012	232556_at	---	⇧	2.09	4.60E-03	206176_at	BMP6	⇩	2.07	0.025
1557953_at	ZKSCAN1	⇧	2.10	0.012	224851_at	CDK6	⇧	2.09	4.50E-03	235376_at	---	⇧	2.07	0.020
236524_at	---	⇧	2.10	0.011	203028_s_at	CYBA	⇩	2.09	4.00E-03	236088_at	NTNG1	⇩	2.07	0.018
241619_at	CALM1	⇧	2.10	6.10E-03	243904_at	STXBP5	⇧	2.09	3.40E-03	54970_at	ZMIZ2	⇧	2.07	0.016
1552621_at	POLR2J2	⇧	2.10	5.30E-03	234594_at	C14orf85	⇧	2.09	2.90E-03	216585_at	---	⇩	2.07	0.013
225046_at	LOC100132181	⇩	2.10	4.50E-03	233061_at	FITM2	⇧	2.09	2.70E-03	204982_at	GIT2	⇧	2.07	9.00E-03
208662_s_at	TTC3	⇧	2.10	3.80E-03	1569841_x_at	---	⇧	2.09	1.60E-03	219024_at	PLEKHA1	⇧	2.07	8.80E-03
215429_s_at	ZNF428	⇧	2.10	2.50E-03	214843_s_at	USP33	⇧	2.09	4.60E-04	1562338_at	MARCH1	⇧	2.07	8.70E-03
1557100_s_at	HECTD1	⇧	2.10	1.90E-03	242430_at	CCDC69	⇧	2.09	3.20E-04	225034_at	ST3GAL1	⇧	2.07	8.10E-03
200745_s_at	GNB1	⇧	2.10	1.50E-03	237267_at	LOC100506675	⇧	2.09	1.50E-04	220943_s_at	C2orf56	⇧	2.07	4.80E-03
212220_at	PSME4	⇧	2.10	9.20E-04	231453_at	LOC284067	⇧	2.09	8.10E-05	242403_at	---	⇧	2.07	4.40E-03
1568858_at	---	⇧	2.10	5.30E-04	204331_s_at	MRPS12	⇩	2.09	2.50E-05	219831_at	CDKL3	⇧	2.07	4.10E-03
1564242_at	---	⇩	2.10	5.10E-04	216580_at	RPL7	⇩	2.08	0.037	227480_at	SUSD2	⇧	2.07	2.40E-03
207185_at	SLC10A1	⇧	2.10	3.70E-04	1557252_at	---	⇧	2.08	0.032	236107_at	UBE2Z	⇧	2.07	1.60E-03
226052_at	BRD4	⇧	2.10	4.60E-05	214850_at	LOC100170939	⇧	2.08	0.031	243895_x_at	---	⇧	2.07	1.30E-03
215652_at	SDHD	⇧	2.09	0.045	240307_at	---	⇧	2.08	0.025	229704_at	PDS5B	⇧	2.07	9.90E-04
217022_s_at	IGH	⇩	2.09	0.042	207674_at	FCAR	⇩	2.08	0.018	229334_at	RUFY3	⇧	2.07	6.90E-04
236610_at	---	⇧	2.09	0.025	230980_x_at	---	⇧	2.08	0.016	1553265_at	SLC23A3	⇧	2.07	1.60E-04
208694_at	PRKDC	⇧	2.09	0.024	239557_at	---	⇧	2.08	0.013	216216_at	SLIT3	⇧	2.07	1.40E-04
203387_s_at	TBC1D4	⇩	2.09	0.014	232030_at	KIAA1632	⇧	2.08	0.012	237650_at	---	⇧	2.07	8.70E-05
233867_at	---	⇧	2.09	0.013	222620_s_at	DNAJC1	⇧	2.08	8.00E-03	233622_x_at	---	⇧	2.07	4.20E-05
243646_at	---	⇧	2.09	0.011	217671_at	DSERG1	⇧	2.08	7.80E-03	203756_at	ARHGEF17	⇧	2.07	9.90E-06
232879_at	CRTC3	⇧	2.09	0.010	221761_at	ADSS	⇩	2.08	6.50E-03	214128_at	DAGLA	⇧	2.07	8.80E-06
243356_at	FAM7A3	⇧	2.09	0.010	1565821_at	---	⇧	2.08	4.30E-03	211000_s_at	IL6ST	⇧	2.06	0.028
203628_at	IGF1R	⇧	2.09	9.60E-03	219622_at	RAB20	⇩	2.08	2.70E-03	237009_at	---	⇧	2.06	0.022
1557581_x_at	---	⇧	2.09	7.80E-03	241520_x_at	---	⇧	2.08	8.80E-04	240339_at	---	⇧	2.06	0.014
202905_x_at	NBN	⇧	2.09	7.40E-03	243578_at	---	⇧	2.08	6.10E-04	229765_at	ZNF207	⇧	2.06	0.014
1569601_at	---	⇧	2.09	6.80E-03	237104_at	---	⇧	2.08	3.10E-04	200612_s_at	AP2B1	⇧	2.06	0.012
244226_s_at	---	⇧	2.09	5.70E-03	238395_at	---	⇧	2.08	1.60E-04	200951_s_at	CCND2	⇩	2.06	0.011
239464_at	---	⇧	2.09	5.60E-03	214798_at	ATP2C2	⇧	2.08	1.20E-04	1558766_at	---	⇧	2.06	7.90E-03
242287_at	CLIP1	⇧	2.09	5.30E-03	220084_at	C14orf105	⇧	2.08	2.50E-05	209059_s_at	EDF1	⇩	2.06	7.60E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

242572_at	---	⇧	2.06	6.40E-03
209579_s_at	MBD4	⇧	2.06	4.60E-03
222320_at	---	⇧	2.06	4.10E-03
216922_x_at	DAZ1-4	⇧	2.06	2.70E-03
207735_at	RNF125	⇧	2.06	2.20E-03
240737_at	---	⇧	2.06	2.00E-03
244607_at	---	⇧	2.06	1.80E-03
204000_at	GNB5	⇧	2.06	1.80E-03
243587_x_at	---	⇧	2.06	1.20E-03
243870_at	---	⇧	2.06	7.80E-04
241722_x_at	---	⇧	2.06	7.50E-04
241716_at	HSPD1	⇧	2.06	7.10E-04
222443_s_at	RBM8A	⇩	2.06	1.40E-04
243771_at	---	⇧	2.06	9.20E-06
1554690_a_at	TACC1	⇧	2.05	0.032
237113_at	---	⇩	2.05	0.025
215635_at	---	⇧	2.05	0.021
228483_s_at	TAF9B	⇧	2.05	0.020
227747_at	MPZL3	⇧	2.05	0.018
1557580_at	---	⇧	2.05	0.016
214469_at	HIST1H2AE	⇩	2.05	0.015
237803_x_at	---	⇧	2.05	0.012
236346_at	---	⇧	2.05	0.012
229897_at	ZNF641	⇧	2.05	0.012
208601_s_at	TUBB1	⇩	2.05	0.011
238869_at	---	⇧	2.05	7.10E-03
217304_at	SHMT1	⇧	2.05	6.90E-03
220845_at	ACOXL	⇧	2.05	5.20E-03
242040_at	GCNT7	⇧	2.05	5.10E-03
243037_at	---	⇧	2.05	3.60E-03
1553703_at	ZNF791	⇧	2.05	2.00E-03
1562454_at	---	⇧	2.05	1.60E-03
1557169_x_at	HCG11	⇧	2.05	8.90E-04
229593_at	H2AFY	⇧	2.05	4.70E-04
204094_s_at	TSC22D2	⇧	2.05	3.90E-04
242780_at	VAPA	⇧	2.05	3.20E-04
1552628_a_at	HERPUD2	⇧	2.05	1.40E-04
220252_x_at	CXorf21	⇧	2.05	6.60E-05
AFFX-HUMRGE /M10098_5_at	---	⇩	2.04	0.012
243528_at	---	⇧	2.04	0.025
243109_at	MCTP2	⇧	2.04	0.024
231866_at	LNPEP	⇧	2.04	0.019
242068_at	---	⇧	2.04	0.015
222313_at	---	⇧	2.04	0.014
1557145_at	STK38	⇧	2.04	0.014
203299_s_at	AP1S2	⇧	2.04	0.013
222404_x_at	PTPLAD1	⇧	2.04	0.010
228594_at	C5orf33	⇧	2.04	8.60E-03
215474_at	---	⇧	2.04	6.90E-03
242803_at	---	⇧	2.04	6.70E-03
238660_at	WDFY3	⇧	2.04	6.60E-03
217087_at	C1orf68	⇧	2.04	4.60E-03
222027_at	NUCKS1	⇧	2.04	3.90E-03
233815_at	NAALAD2	⇧	2.04	1.80E-03
1556209_at	CLEC2B	⇧	2.04	1.50E-03
213574_s_at	---	⇧	2.04	1.10E-03
229392_s_at	PIK3R2	⇧	2.04	8.80E-04
237954_x_at	---	⇧	2.04	6.80E-04
1563482_at	---	⇧	2.04	5.50E-04
233693_at	C1orf201	⇧	2.04	3.20E-04
233109_at	COL12A1	⇧	2.04	2.70E-04
1561718_at	---	⇧	2.04	1.80E-04
208077_at	C9orf38	⇧	2.04	1.60E-04
239115_at	---	⇧	2.04	2.40E-05
209703_x_at	METTL7A	⇧	2.04	1.10E-05
1566541_at	---	⇧	2.04	2.90E-06
1566446_at	---	⇧	2.03	0.030
224531_at	GPR61	⇩	2.03	0.027
208661_s_at	TTC3	⇧	2.03	0.025
227223_at	RBM39	⇧	2.03	0.022
214911_s_at	BRD2	⇧	2.03	0.020
227962_at	ACOX1	⇧	2.03	0.012
243683_at	MORF4L2	⇧	2.03	0.011
1552867_at	---	⇧	2.03	0.010
239957_at	---	⇧	2.03	8.30E-03
220216_at	C8orf44	⇧	2.03	7.60E-03
238651_at	---	⇧	2.03	6.40E-03
240141_at	---	⇧	2.03	6.30E-03
211048_s_at	PDIA4	⇧	2.03	6.10E-03
214291_at	RPL17	⇧	2.03	4.80E-03
222667_s_at	ASH1L	⇧	2.03	4.20E-03
237798_at	---	⇧	2.03	3.60E-03
208987_s_at	KDM2A	⇧	2.03	3.50E-03
226266_at	PGS1	⇧	2.03	3.50E-03
243381_at	---	⇧	2.03	2.60E-03
212917_x_at	RECQL	⇧	2.03	2.10E-03
240957_at	---	⇧	2.03	1.80E-03
216645_at	---	⇧	2.03	1.50E-03
222395_s_at	UBE2Z	⇧	2.03	1.40E-03
1557589_a_at	---	⇧	2.03	9.60E-04
230027_s_at	MRPL43	⇩	2.03	7.90E-04
1568801_at	C15orf44	⇧	2.03	3.30E-04
214650_x_at	MOG	⇧	2.03	3.30E-04

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

213818_x_at	TMEM223	⇧	2.03	2.80E-04
215656_at	LMAN2	⇩	2.03	1.50E-04
201296_s_at	WSB1	⇧	2.03	5.90E-05
AFFX-M27830_5_at	---	⇩	2.03	0.013
204750_s_at	DSC2	⇧	2.02	0.045
205961_s_at	PSIP1	⇩	2.02	0.021
211467_s_at	NFIB	⇩	2.02	0.019
1560443_at	---	⇧	2.02	8.00E-03
241930_x_at	LOC442113	⇧	2.02	6.30E-03
230379_x_at	C2orf56	⇧	2.02	5.20E-03
242728_at	---	⇧	2.02	5.10E-03
207474_at	SNRK	⇧	2.02	4.00E-03
216783_at	---	⇧	2.02	3.90E-03
236149_at	---	⇧	2.02	3.10E-03
207648_at	DRP2	⇧	2.02	3.10E-03
228088_at	SESTD1	⇧	2.02	2.50E-03
215648_at	---	⇧	2.02	1.90E-03
1569450_at	CAPZA2	⇧	2.02	1.90E-03
237062_at	---	⇧	2.02	1.70E-03
215468_at	LOC647070	⇧	2.02	1.70E-03
209499_x_at	TNFSF13	⇩	2.02	1.20E-03
243992_at	---	⇧	2.02	1.00E-03
217704_x_at	SUZ12P	⇧	2.02	7.20E-04
236715_x_at	UACA	⇧	2.02	5.20E-04
220374_at	KLHL28	⇧	2.02	1.80E-04
237232_at	---	⇧	2.02	1.60E-04
AFFX-r2-Bs-dap-5_at	---	⇧	2.02	0.032
209583_s_at	CD200	⇩	2.01	0.031
204908_s_at	BCL3	⇧	2.01	0.024
215121_x_at	IGL	⇩	2.01	0.023
239504_at	---	⇧	2.01	0.018
229272_at	FNBP4	⇧	2.01	0.017
238949_at	RNF145	⇩	2.01	0.015
219978_s_at	NUSAP1	⇧	2.01	0.014
244341_at	---	⇧	2.01	0.011
222357_at	ZBTB20	⇧	2.01	9.70E-03
1557236_at	APOL6	⇧	2.01	9.50E-03
235970_at	LCORL	⇧	2.01	8.90E-03
1555273_at	GALNTL6	⇧	2.01	8.50E-03
204643_s_at	ENOX2	⇩	2.01	8.20E-03
213803_at	---	⇧	2.01	7.70E-03
1559663_at	---	⇧	2.01	7.20E-03
235954_at	---	⇧	2.01	7.00E-03
236613_at	RBM25	⇧	2.01	6.10E-03
243514_at	---	⇧	2.01	4.80E-03
240221_at	CSNK1A1	⇧	2.01	2.90E-03
224778_s_at	TAOK1	⇧	2.01	2.70E-03
201070_x_at	SF3B1	⇧	2.01	2.60E-03
227396_at	PTPRJ	⇧	2.01	2.40E-03
243509_at	---	⇧	2.01	2.30E-03
232141_at	U2AF1	⇧	2.01	2.20E-03
216621_at	---	⇧	2.01	2.10E-03
239937_at	ZNF207	⇧	2.01	1.90E-03
243724_at	---	⇧	2.01	1.40E-03
1556655_s_at	---	⇧	2.01	1.30E-03
243709_at	SLC38A9	⇧	2.01	1.20E-03
218314_s_at	C11orf57	⇧	2.01	1.10E-03
201407_s_at	PPP1CB	⇧	2.01	1.10E-03
230868_at	---	⇧	2.01	7.70E-04
232294_at	LOC219347	⇧	2.01	6.30E-04
226035_at	USP31	⇧	2.01	1.40E-04
214802_at	EXOC7	⇧	2.00	0.024
1569159_at	LZTS1	⇩	2.00	0.023
242916_at	CEP110	⇧	2.00	0.019
209138_x_at	IGL	⇩	2.00	0.019
201996_s_at	SPEN	⇧	2.00	0.018
239171_at	---	⇧	2.00	0.013
230733_at	---	⇧	2.00	0.013
1554638_at	ZFYVE16	⇧	2.00	0.013
1556493_a_at	KDM4C	⇧	2.00	0.011
1570200_at	HELB	⇧	2.00	8.60E-03
239724_at	---	⇧	2.00	6.60E-03
208549_x_at	PTMAP7	⇧	2.00	6.40E-03
215231_at	PRKAG2	⇧	2.00	6.20E-03
237943_at	---	⇧	2.00	5.70E-03
233274_at	---	⇧	2.00	5.00E-03
236953_s_at	NHLRC3	⇧	2.00	5.00E-03
1565762_at	---	⇧	2.00	4.70E-03
222023_at	AKAP13	⇧	2.00	4.20E-03
237118_at	---	⇧	2.00	3.90E-03
208180_s_at	HIST1H4B	⇩	2.00	3.40E-03
234737_at	NT5DC3	⇧	2.00	3.20E-03
200622_x_at	CALM3	⇩	2.00	3.10E-03
237555_at	CARS2	⇧	2.00	3.10E-03
220612_at	---	⇧	2.00	2.70E-03
1555977_at	MYL12A	⇧	2.00	2.00E-03
226874_at	KLHL8	⇧	2.00	1.90E-03
226400_at	CDC42	⇧	2.00	1.60E-03
230123_at	NECAP2	⇧	2.00	1.60E-03
225628_s_at	MLLT6	⇧	2.00	1.40E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

1560204_at	NT5DC4	⇧	2.00	1.20E-03
230681_at	TBRG1	⇧	2.00	4.50E-04
220864_s_at	NDUFA13	⇩	2.00	3.80E-04
220791_x_at	SCN11A	⇧	2.00	3.70E-04
234479_at	PCDHB18	⇧	2.00	2.40E-04
218000_s_at	PHLDA1	⇧	2.00	2.40E-04
215604_x_at	---	⇧	2.00	2.20E-04
239967_at	---	⇧	2.00	5.20E-05
235894_at	---	⇧	2.00	3.70E-05
215548_s_at	SCFD1	⇩	1.99	0.037
231370_at	---	⇧	1.99	0.028
1552480_s_at	PTPRC	⇧	1.99	0.026
202955_s_at	ARFGEF1	⇩	1.99	0.020
239651_at	ANAPC5	⇧	1.99	0.015
217814_at	CCDC47	⇩	1.99	9.00E-03
223080_at	GLS	⇧	1.99	8.30E-03
1554543_at	SPAG9	⇧	1.99	7.50E-03
238295_at	C17orf42	⇧	1.99	6.20E-03
243072_at	---	⇧	1.99	5.70E-03
224345_x_at	FAM162A	⇩	1.99	5.50E-03
1559060_a_at	FNIP1	⇧	1.99	5.50E-03
213718_at	RBM4	⇧	1.99	5.50E-03
237310_at	---	⇧	1.99	5.40E-03
223209_s_at	SELS	⇩	1.99	4.80E-03
1557270_at	---	⇧	1.99	3.70E-03
225551_at	C1orf71	⇧	1.99	3.50E-03
232363_at	---	⇧	1.99	2.90E-03
242423_x_at	---	⇧	1.99	1.90E-03
215908_at	---	⇧	1.99	1.30E-03
243852_at	LUC7L2	⇧	1.99	1.30E-03
1553020_at	SMCR5	⇧	1.99	1.20E-03
224602_at	C4orf3	⇩	1.99	8.40E-04
224438_at	---	⇧	1.99	4.70E-04
220113_x_at	POLR1B	⇧	1.99	4.30E-04
214594_x_at	ATP8B1	⇧	1.99	4.10E-04
208470_s_at	HP	⇧	1.98	0.046
219529_at	CLIC3	⇩	1.98	0.031
202131_s_at	RIOK3	⇧	1.98	0.029
227668_at	C17orf56	⇩	1.98	0.028
223802_s_at	RBBP6	⇩	1.98	0.025
243450_at	---	⇧	1.98	0.020
201666_at	TIMP1	⇩	1.98	0.018
1561644_x_at	---	⇧	1.98	5.00E-03
217966_s_at	FAM129A	⇧	1.98	2.70E-03
209796_s_at	CNPY2	⇩	1.98	2.60E-03
203392_s_at	CTBP1	⇧	1.98	2.40E-03
243296_at	NAMPT	⇧	1.98	2.40E-03
36711_at	MAFF	⇧	1.98	2.30E-03
215012_at	ZNF451	⇧	1.98	2.30E-03
226080_at	SSH2	⇧	1.98	2.10E-03
1567251_at	OR10A3	⇧	1.98	1.40E-03
1570134_at	---	⇧	1.98	1.30E-03
1559597_at	---	⇧	1.98	6.30E-04
227948_at	FGD4	⇧	1.98	5.60E-04
1566778_at	---	⇧	1.98	5.10E-04
217481_x_at	---	⇩	1.98	3.00E-04
1559616_x_at	ZNF626	⇧	1.98	2.50E-04
1558740_s_at	---	⇧	1.98	2.10E-04
1562645_at	LOC401176	⇩	1.97	0.047
236934_at	---	⇧	1.97	0.046
209287_s_at	CDC42EP3	⇩	1.97	0.032
226686_at	CISD2	⇧	1.97	0.026
242214_at	RPS27A	⇧	1.97	0.023
211781_x_at	---	⇧	1.97	0.020
236752_at	---	⇧	1.97	0.011
208811_s_at	DNAJB6	⇩	1.97	0.011
209686_at	S100B	⇩	1.97	0.011
223193_x_at	FAM162A	⇩	1.97	9.90E-03
239571_at	---	⇧	1.97	9.30E-03
233105_at	---	⇧	1.97	9.30E-03
229713_at	PIP4K2A	⇧	1.97	7.40E-03
242819_at	---	⇧	1.97	7.10E-03
220942_x_at	FAM162A	⇩	1.97	6.90E-03
215946_x_at	IGLL3	⇩	1.97	6.60E-03
244801_at	PSMB7	⇧	1.97	5.40E-03
238449_at	LOC595101	⇧	1.97	4.70E-03
225640_at	LOC401504	⇧	1.97	3.90E-03
220901_at	GPR157	⇧	1.97	3.60E-03
220342_x_at	EDEM3	⇧	1.97	3.40E-03
221939_at	YIPF2	⇧	1.97	3.30E-03
242121_at	---	⇧	1.97	2.40E-03
233585_at	SDK2	⇩	1.97	1.80E-03
239614_x_at	---	⇧	1.97	1.50E-03
208900_s_at	TOP1	⇧	1.97	1.50E-03
229467_at	PCBP2	⇧	1.97	1.40E-03
218924_s_at	CTBS	⇧	1.97	1.30E-03
201726_at	ELAVL1	⇧	1.97	1.20E-03
1563488_at	TMEM132B	⇧	1.97	9.20E-04
1560540_x_at	---	⇧	1.97	5.30E-04
203326_x_at	---	⇧	1.97	4.60E-04
221176_x_at	WBSCR23	⇧	1.97	2.80E-04
238863_x_at	COG8	⇧	1.97	2.20E-04
239029_at	LOC100129701	⇧	1.97	7.10E-05
215086_at	IBTK	⇧	1.97	1.80E-05
219533_at	CDKN1C	⇧	1.97	1.60E-05
1568764_x_at	PDCD6	⇧	1.96	0.046

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

238150_at	---	⇩	1.96	0.044
243350_at	---	⇧	1.96	0.031
242695_at	---	⇧	1.96	0.031
1558011_at	---	⇧	1.96	0.024
232980_at	LMBRD1	⇧	1.96	0.024
226184_at	FMNL2	⇩	1.96	0.018
242482_at	PRKAR1A	⇧	1.96	0.017
228195_at	C2orf88	⇩	1.96	0.013
215206_at	---	⇧	1.96	0.011
235956_at	KIAA1377	⇧	1.96	0.011
239954_at	ZNF160	⇧	1.96	0.011
213879_at	---	⇧	1.96	8.70E-03
210802_s_at	DIMT1L	⇩	1.96	7.90E-03
1569041_at	---	⇧	1.96	7.10E-03
210285_x_at	WTAP	⇩	1.96	6.30E-03
202065_s_at	PPFIA1	⇧	1.96	5.00E-03
221986_s_at	KLHL24	⇧	1.96	4.30E-03
219675_s_at	UXS1	⇩	1.96	3.50E-03
243201_at	HNRNPH2	⇧	1.96	3.20E-03
222286_at	SNAPC3	⇧	1.96	3.20E-03
225814_at	XRN1	⇧	1.96	3.00E-03
219031_s_at	NIP7	⇧	1.96	2.60E-03
222387_s_at	VPS35	⇧	1.96	2.50E-03
236235_at	ITCH	⇧	1.96	2.40E-03
226667_x_at	EPN1	⇧	1.96	1.90E-03
237825_x_at	---	⇧	1.96	1.70E-03
1557302_at	ZNF585B	⇧	1.96	1.20E-03
205683_x_at	TPSAB1	⇧	1.96	7.40E-04
222033_s_at	FLT1	⇧	1.96	2.90E-04
1570020_at	AACSL	⇧	1.96	1.90E-04
1566597_at	---	⇧	1.96	1.70E-04
220483_s_at	RNF19A	⇧	1.96	1.70E-04
216679_at	TIGD1L	⇧	1.96	1.20E-04
239335_at	ZNF710	⇧	1.96	1.10E-04
1559821_at	---	⇧	1.96	9.80E-05
209463_s_at	TAF12	⇩	1.96	7.80E-05
1558890_at	---	⇩	1.96	3.60E-06
218978_s_at	SLC25A37	⇧	1.95	0.047
209581_at	PLA2G16	⇩	1.95	0.038
244659_at	LOC100131015	⇩	1.95	0.030
240326_at	---	⇧	1.95	0.024
223955_at	EFCAB4B	⇩	1.95	0.015
237239_at	---	⇧	1.95	0.014
240271_at	---	⇧	1.95	0.014
212386_at	TCF4	⇧	1.95	0.014
230425_at	EPHB1	⇩	1.95	0.011
241106_at	---	⇧	1.95	8.50E-03
244023_at	SYK	⇧	1.95	7.00E-03
240148_at	MSH6	⇧	1.95	6.70E-03
215457_at	---	⇧	1.95	6.20E-03
231042_s_at	---	⇧	1.95	5.80E-03
232575_at	PCA3	⇧	1.95	4.50E-03
212040_at	TGOLN2	⇧	1.95	4.30E-03
236666_s_at	LOC390205	⇧	1.95	3.50E-03
1558418_at	---	⇧	1.95	3.40E-03
1553704_x_at	ZNF791	⇧	1.95	2.80E-03
215375_x_at	LRRFIP1	⇧	1.95	2.70E-03
1559270_at	ZFHX4	⇩	1.95	2.40E-03
214754_at	TET3	⇩	1.95	2.20E-03
222214_at	---	⇧	1.95	2.00E-03
203590_at	DYNC1LI2	⇧	1.95	1.70E-03
1563321_s_at	MLLT10	⇧	1.95	1.70E-03
219267_at	GLTP	⇧	1.95	1.30E-03
206169_x_at	ZC3H7B	⇧	1.95	1.30E-03
214805_at	EIF4A1	⇧	1.95	1.20E-03
223519_at	ZAK	⇧	1.95	1.20E-03
205642_at	CEP110	⇩	1.95	1.00E-03
222439_s_at	THRAP3	⇧	1.95	4.30E-04
1564148_at	---	⇧	1.95	3.20E-04
1559530_at	---	⇧	1.95	2.10E-04
203210_s_at	RFC5	⇩	1.95	1.70E-04
1556831_at	DYNC1H1	⇧	1.95	1.50E-04
1559971_at	BSDC1	⇧	1.95	1.40E-04
233075_at	HERC2P7	⇩	1.95	1.30E-04
228068_at	GOLGA7B	⇧	1.95	4.90E-05
243827_at	---	⇧	1.94	0.046
237452_at	---	⇧	1.94	0.045
233869_x_at	---	⇧	1.94	0.042
223952_x_at	DHRS9	⇩	1.94	0.042
218521_s_at	UBE2W	⇧	1.94	0.040
240442_at	---	⇧	1.94	0.035
215379_x_at	IGL	⇩	1.94	0.027
222409_at	CORO1C	⇧	1.94	0.025
215342_s_at	RABGAP1L	⇧	1.94	0.024
243768_at	---	⇧	1.94	0.023
208496_x_at	HIST1H3G	⇩	1.94	0.020
207507_s_at	ATP5G3	⇩	1.94	0.018
231316_at	---	⇧	1.94	0.013
212451_at	SECISBP2L	⇧	1.94	0.013
241036_at	---	⇧	1.94	0.012
1560474_at	---	⇧	1.94	0.011
222507_s_at	TMEM9B	⇩	1.94	7.30E-03
1558678_s_at	MALAT1	⇧	1.94	6.80E-03
241242_at	---	⇧	1.94	5.60E-03
243630_at	NDUFB1	⇧	1.94	5.30E-03
225937_at	CUX1	⇧	1.94	4.40E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

212852_s_at	TROVE2	⇧	1.94	4.10E-03	205215_at	RNF2	⇧	1.93	6.60E-03	242167_at	---	⇧	1.92	0.018
201212_at	LGMN	⇩	1.94	3.90E-03	212536_at	ATP11B	⇧	1.93	6.40E-03	207322_at	ITSN1	⇩	1.92	0.016
1565604_at	PWP2	⇧	1.94	2.80E-03	244010_at	---	⇧	1.93	4.80E-03	236944_at	---	⇧	1.92	0.013
207728_at	ATF7IP	⇧	1.94	2.40E-03	1563502_at	ZDHHC2	⇧	1.93	4.50E-03	244412_at	---	⇧	1.92	9.80E-03
1554641_a_at	TET3	⇧	1.94	1.70E-03	204616_at	UCHL3	⇩	1.93	3.70E-03	200952_s_at	CCND2	⇧	1.92	9.70E-03
234084_x_at	---	⇧	1.94	1.60E-03	235551_at	WDR4	⇧	1.93	3.50E-03	234459_at	PPHLN1	⇧	1.92	9.60E-03
241882_at	CAMTA1	⇧	1.94	1.50E-03	240521_at	---	⇧	1.93	3.10E-03	212420_at	ELF1	⇧	1.92	8.60E-03
1556894_at	NT5DC2	⇧	1.94	1.50E-03	216290_x_at	---	⇧	1.93	2.90E-03	206756_at	CHST7	⇩	1.92	8.40E-03
1560209_at	---	⇧	1.94	1.40E-03	203489_at	SIVA1	⇩	1.93	2.50E-03	231366_at	FDPSL2A	⇧	1.92	8.40E-03
233263_at	---	⇧	1.94	1.20E-03	235240_at	ATXN3	⇧	1.93	2.10E-03	242958_x_at	---	⇧	1.92	6.90E-03
207133_x_at	ALPK1	⇧	1.94	8.30E-04	232096_x_at	FOXP1-IT1	⇧	1.93	2.10E-03	218775_s_at	WWC2	⇧	1.92	6.60E-03
217793_at	RAB11B	⇧	1.94	6.10E-04	1553252_a_at	BRWD3	⇧	1.93	1.90E-03	1559979_at	SYF2	⇧	1.92	6.10E-03
232636_at	SLITRK4	⇩	1.94	4.80E-04	1560422_at	---	⇧	1.93	1.30E-03	236251_at	---	⇧	1.92	5.10E-03
231597_x_at	---	⇧	1.94	4.60E-04	208759_at	NCSTN	⇧	1.93	7.70E-04	204786_s_at	IFNAR2	⇧	1.92	3.40E-03
220352_x_at	FLJ42627	⇧	1.94	2.50E-04	241223_x_at	---	⇧	1.93	6.70E-04	224074_at	VSX1	⇩	1.92	2.80E-03
225668_at	FAM173B	⇧	1.94	2.40E-04	234656_x_at	---	⇧	1.93	5.60E-04	226975_at	RNPC3	⇧	1.92	2.70E-03
232894_at	---	⇧	1.94	2.10E-04	1558142_at	TNRC6B	⇧	1.93	5.50E-04	200889_s_at	SSR1	⇩	1.92	2.70E-03
216151_at	---	⇧	1.94	2.00E-04	242578_x_at	SLC22A3	⇧	1.93	4.20E-04	214130_s_at	PDE4DIP	⇩	1.92	2.40E-03
214308_s_at	HGD	⇩	1.94	1.50E-04	242182_x_at	---	⇧	1.93	4.10E-04	221276_s_at	SYNC	⇧	1.92	2.00E-03
242277_at	---	⇧	1.94	2.10E-05	233321_x_at	LOC90834	⇧	1.93	3.90E-04	239692_at	---	⇧	1.92	1.60E-03
1564236_at	---	⇧	1.93	0.039	218525_s_at	HIF1AN	⇧	1.93	2.20E-04	1565603_at	PWP2	⇧	1.92	1.40E-03
223210_at	CHURC1	⇧	1.93	0.039	1561471_at	LOC441009	⇧	1.93	2.00E-04	238083_at	PARP10	⇧	1.92	1.30E-03
1560259_at	---	⇧	1.93	0.038	233757_x_at	---	⇧	1.93	1.70E-04	225234_at	CBL	⇧	1.92	1.20E-03
226189_at	ITGB8	⇩	1.93	0.031	209619_at	CD74	⇩	1.92	0.047	1552274_at	PXK	⇧	1.92	1.00E-03
242911_at	MED13L	⇧	1.93	0.029	244026_at	---	⇧	1.92	0.045	220875_at	---	⇧	1.92	6.50E-04
212249_at	PIK3R1	⇧	1.93	0.027	207291_at	PRRG4	⇧	1.92	0.035	222363_at	---	⇧	1.92	4.40E-04
1569647_at	LOC643623	⇧	1.93	0.023	239833_at	---	⇧	1.92	0.022	225197_at	LOC100505487	⇧	1.92	3.80E-04
1570566_at	---	⇧	1.93	0.019	238468_at	TNRC6B	⇧	1.92	0.022	1553531_at	PCSK6	⇧	1.92	3.60E-04
243316_x_at	VPS26A	⇧	1.93	0.012	222875_at	DHX33	⇧	1.92	0.021	218155_x_at	TSR1	⇧	1.92	1.70E-04
243640_x_at	---	⇧	1.93	0.011	205767_at	EREG	⇧	1.92	0.021	204373_s_at	CEP350	⇧	1.92	1.50E-04
1567997_x_at	---	⇧	1.93	9.20E-03	232627_at	HGS	⇧	1.92	0.020	235709_at	GAS2L3	⇧	1.92	1.30E-04
201730_s_at	TPR	⇧	1.93	7.80E-03	232595_at	---	⇧	1.92	0.019	212096_s_at	MTUS1	⇩	1.91	0.046

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

215555_at	---	⇧	1.91	0.043
227958_s_at	GSN	⇩	1.91	0.043
214814_at	YTHDC1	⇧	1.91	0.041
1555730_a_at	CFL1	⇩	1.91	0.037
209255_at	KLHDC10	⇩	1.91	0.036
239023_at	---	⇧	1.91	0.024
241776_at	---	⇧	1.91	0.023
218026_at	CCDC56	⇩	1.91	0.022
217148_x_at	IGL	⇩	1.91	0.020
237383_at	---	⇧	1.91	0.015
232912_at	GPR180	⇧	1.91	0.015
240948_at	---	⇧	1.91	0.014
236685_at	---	⇧	1.91	0.010
240383_at	UBE2D3	⇧	1.91	0.010
228337_at	PWWP2A	⇧	1.91	9.70E-03
236846_at	LOC284757	⇧	1.91	9.50E-03
232145_at	C2orf68	⇩	1.91	7.60E-03
210943_s_at	LYST	⇧	1.91	7.40E-03
200081_s_at	RPS6	⇩	1.91	7.10E-03
234949_at	LOC283788	⇧	1.91	6.50E-03
236590_at	---	⇧	1.91	6.20E-03
202697_at	NUDT21	⇩	1.91	6.10E-03
210895_s_at	CD86	⇩	1.91	5.90E-03
202233_s_at	UQCRH	⇩	1.91	5.50E-03
233730_at	FAM135A	⇧	1.91	3.00E-03
215863_at	TFR2	⇧	1.91	2.90E-03
233473_x_at	---	⇧	1.91	2.10E-03
214103_s_at	RAP2A	⇧	1.91	2.00E-03
1558652_at	KIAA1310	⇧	1.91	1.90E-03
233056_x_at	DLGAP4	⇧	1.91	1.80E-03
1556359_at	C6orf89	⇧	1.91	1.70E-03
237868_x_at	---	⇧	1.91	1.30E-03
217385_at	---	⇧	1.91	1.30E-03
1555317_at	POLK	⇧	1.91	1.30E-03
215439_x_at	---	⇧	1.91	1.10E-03
1553600_at	TMIE	⇧	1.91	1.10E-03
203090_at	SDF2	⇩	1.91	7.80E-04
221996_s_at	CLTB	⇧	1.91	5.90E-04
233090_at	---	⇧	1.91	4.90E-04
210417_s_at	PI4KB	⇧	1.91	4.50E-04
216229_x_at	HCG2P7	⇧	1.91	4.40E-04
217554_at	---	⇧	1.91	4.30E-04
232644_x_at	OCIAD1	⇧	1.91	2.60E-04
1569417_at	---	⇧	1.91	1.80E-04
233495_at	EXOSC3	⇧	1.91	1.80E-04
234724_x_at	PCDHB18	⇧	1.91	1.10E-04
1563012_x_at	---	⇧	1.91	1.00E-04
202464_s_at	PFKFB3	⇧	1.91	9.30E-05
1552975_x_at	---	⇧	1.91	6.00E-05
242740_at	---	⇧	1.91	2.70E-05
1559025_at	SEPT9	⇧	1.90	0.044
218136_s_at	SLC25A37	⇩	1.90	0.023
240866_at	---	⇧	1.90	0.022
231578_at	GBP1	⇧	1.90	0.021
242563_at	---	⇧	1.90	0.018
227529_s_at	AKAP12	⇩	1.90	0.017
209421_at	MSH2	⇩	1.90	0.016
215069_at	NMT2	⇧	1.90	0.014
225156_at	ELOF1	⇧	1.90	0.012
208615_s_at	PTP4A2	⇧	1.90	0.012
212007_at	UBXN4	⇧	1.90	0.012
215440_s_at	BEX4	⇩	1.90	0.011
1555086_at	STAT5B	⇧	1.90	0.011
244433_at	---	⇧	1.90	9.90E-03
230058_at	SDCCAG3	⇧	1.90	8.40E-03
235698_at	ZFP90	⇧	1.90	7.10E-03
203189_s_at	NDUFS8	⇩	1.90	6.80E-03
209187_at	DR1	⇧	1.90	5.60E-03
209321_s_at	ADCY3	⇩	1.90	4.80E-03
1566111_at	PIEZO1	⇧	1.90	4.30E-03
233216_at	ZDHHC21	⇧	1.90	4.10E-03
210240_s_at	CDKN2D	⇩	1.90	3.20E-03
208514_at	KCNE1	⇩	1.90	2.90E-03
203542_s_at	KLF9	⇧	1.90	2.80E-03
232929_at	---	⇧	1.90	2.20E-03
239251_at	---	⇧	1.90	2.10E-03
1559725_at	---	⇧	1.90	1.90E-03
203398_s_at	GALNT3	⇧	1.90	1.90E-03
244716_x_at	TMIGD2	⇧	1.90	1.70E-03
242438_at	ASXL1	⇧	1.90	1.60E-03
234346_x_at	---	⇧	1.90	1.30E-03
200751_s_at	HNRNPC	⇩	1.90	1.30E-03
232915_at	DDX49	⇧	1.90	1.10E-03
235654_at	TMEM218	⇧	1.90	1.10E-03
232169_x_at	NDUFS8	⇧	1.90	1.00E-03
203276_at	LMNB1	⇧	1.90	9.00E-04
239830_at	---	⇧	1.90	8.60E-04
210368_at	PCDHGA8	⇧	1.90	6.70E-04
232266_x_at	CDC2L5	⇧	1.90	5.50E-04
241617_x_at	---	⇩	1.90	3.80E-04
242171_at	---	⇧	1.90	2.60E-04
203735_x_at	PPFIBP1	⇩	1.90	2.40E-04
241743_at	---	⇧	1.90	1.90E-04
224548_at	HES7	⇩	1.90	1.40E-04
1556003_a_at	---	⇧	1.90	1.10E-04
210916_s_at	CD44	⇩	1.90	3.90E-05

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

220068_at	VPREB3	⇩	1.89	0.048
231038_s_at	---	⇧	1.89	0.044
223254_s_at	G2E3	⇧	1.89	0.041
235049_at	ADCY1	⇧	1.89	0.032
237181_at	---	⇧	1.89	0.029
205861_at	SPIB	⇩	1.89	0.023
213361_at	TDRD7	⇩	1.89	0.022
39313_at	WNK1	⇧	1.89	0.021
235222_x_at	XIAP	⇧	1.89	0.018
215221_at	---	⇧	1.89	0.016
240673_at	---	⇧	1.89	0.014
238199_x_at	LOC440552	⇧	1.89	0.012
232315_at	LOC400713	⇩	1.89	7.90E-03
1569080_at	RNF165	⇧	1.89	7.50E-03
1569331_at	---	⇧	1.89	7.20E-03
220586_at	CHD9	⇧	1.89	7.10E-03
212517_at	ATRN	⇩	1.89	6.30E-03
211930_at	HNRNPA3	⇧	1.89	5.90E-03
208872_s_at	REEP5	⇩	1.89	5.80E-03
215866_at	---	⇧	1.89	4.90E-03
204347_at	AK3L1	⇧	1.89	4.20E-03
1557131_at	LOC254100	⇧	1.89	3.80E-03
1560042_at	FAM82A1	⇧	1.89	3.10E-03
222796_at	PTCD1	⇧	1.89	2.40E-03
1559119_at	---	⇧	1.89	2.00E-03
204618_s_at	GABPB1	⇧	1.89	1.70E-03
242531_at	RRAGC	⇧	1.89	5.70E-04
238050_at	ANTXR2	⇧	1.89	4.80E-04
1570198_x_at	---	⇧	1.89	3.10E-04
1565769_at	---	⇧	1.89	2.20E-04
205153_s_at	CD40	⇩	1.89	1.90E-04
AFFX-r2-Ec-bioB-3_at	---	⇩	1.88	2.54E-05
224009_x_at	DHRS9	⇩	1.88	0.046
1558220_at	MUC20	⇧	1.88	0.037
1560271_at	---	⇧	1.88	0.036
214677_x_at	IGL	⇩	1.88	0.036
232796_at	---	⇧	1.88	0.033
1569180_at	---	⇧	1.88	0.026
1562280_at	---	⇧	1.88	0.021
230698_at	CALN1	⇧	1.88	0.018
226386_at	C7orf30	⇩	1.88	0.017
211868_x_at	IGH	⇩	1.88	0.016
242853_at	---	⇧	1.88	0.015
219293_s_at	OLA1	⇧	1.88	0.012
240723_at	---	⇧	1.88	9.00E-03
242878_at	---	⇧	1.88	8.90E-03
222906_at	FLVCR1	⇧	1.88	7.70E-03
232264_at	---	⇧	1.88	7.60E-03
215224_at	SNORA21	⇧	1.88	6.70E-03
242609_x_at	---	⇧	1.88	5.90E-03
242946_at	CD53	⇧	1.88	5.80E-03
224281_s_at	NGRN	⇩	1.88	5.80E-03
224853_at	SLAIN2	⇩	1.88	5.40E-03
200983_x_at	CD59	⇩	1.88	2.90E-03
241616_at	---	⇧	1.88	2.60E-03
201106_at	GPX4	⇩	1.88	1.70E-03
238279_x_at	---	⇧	1.88	1.60E-03
1562352_at	---	⇧	1.88	8.00E-04
1558826_at	ZNF831	⇩	1.88	6.50E-04
215846_at	---	⇧	1.88	6.40E-04
222649_at	XPO4	⇧	1.88	5.30E-04
238980_x_at	C17orf56	⇧	1.88	5.00E-04
233046_at	---	⇧	1.88	2.60E-04
241594_at	LOC643449	⇧	1.88	2.40E-04
207657_x_at	TNPO1	⇧	1.88	2.40E-04
233605_x_at	HNRNPM	⇧	1.88	1.80E-04
207756_at	---	⇧	1.88	1.70E-04
232719_at	BRUNOL4	⇩	1.88	3.30E-05
229841_at	---	⇧	1.87	0.050
235369_at	C14orf28	⇧	1.87	0.048
202708_s_at	HIST2H2BE	⇩	1.87	0.047
232614_at	---	⇧	1.87	0.046
214201_x_at	BAT2	⇧	1.87	0.044
243473_at	---	⇧	1.87	0.028
213741_s_at	KPNA1	⇧	1.87	0.025
222600_s_at	UBA6	⇧	1.87	0.022
210100_s_at	ABCA2	⇧	1.87	0.020
239474_at	---	⇧	1.87	0.019
230341_x_at	ADAMTS10	⇧	1.87	0.019
1558877_at	---	⇧	1.87	0.018
219279_at	DOCK10	⇩	1.87	0.018
239237_at	LOC100506776	⇧	1.87	0.015
231886_at	---	⇧	1.87	0.011
1559232_a_at	---	⇧	1.87	0.011
224241_s_at	LOC100132388	⇩	1.87	0.011
1560112_at	WDFY2	⇧	1.87	0.011
235061_at	PPM1K	⇧	1.87	0.010
215036_at	IGLC1	⇧	1.87	8.20E-03
220010_at	KCNE1L	⇧	1.87	7.80E-03
218609_s_at	NUDT2	⇩	1.87	7.70E-03
213168_at	SP3	⇧	1.87	6.10E-03
214807_at	---	⇧	1.87	5.70E-03
233653_at	---	⇧	1.87	4.60E-03
1558816_at	ZNF664	⇧	1.87	3.70E-03
1565852_at	---	⇧	1.87	3.20E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

212525_s_at	H2AFX	⇧	1.87	3.10E-03
1552788_a_at	HELB	⇧	1.87	2.50E-03
203954_x_at	CLDN3	⇧	1.87	2.00E-03
211605_s_at	RARA	⇧	1.87	2.00E-03
1559882_at	SAMHD1	⇧	1.87	1.50E-03
242126_at	---	⇧	1.87	1.30E-03
239188_at	PPP2R3C	⇧	1.87	1.20E-03
212479_s_at	RMND5A	⇧	1.87	1.20E-03
220510_at	RHBG	⇧	1.87	1.10E-03
200973_s_at	TSPAN3	⇩	1.87	8.10E-04
1570205_at	---	⇧	1.87	6.30E-04
224105_x_at	---	⇧	1.87	4.80E-04
241163_at	---	⇧	1.87	3.40E-04
208224_at	HOXB1	⇧	1.87	2.50E-04
1566152_a_at	CLP1	⇧	1.87	1.20E-04
201028_s_at	CD99	⇩	1.87	9.50E-05
244869_at	---	⇧	1.86	0.041
227817_at	PRKCB	⇧	1.86	0.038
211794_at	FYB	⇧	1.86	0.037
205849_s_at	UQCRB	⇩	1.86	0.037
208685_x_at	BRD2	⇧	1.86	0.032
237377_at	---	⇧	1.86	0.028
208910_s_at	C1QBP	⇩	1.86	0.027
210948_s_at	LEF1	⇧	1.86	0.024
1557632_at	IKZF1	⇧	1.86	0.023
240397_x_at	---	⇧	1.86	0.021
240139_at	---	⇧	1.86	0.019
201757_at	RPL10	⇩	1.86	0.018
239131_at	---	⇧	1.86	0.017
214058_at	MYCL1	⇩	1.86	0.017
1562442_a_at	SSBP1	⇧	1.86	0.016
238555_at	MRPS31	⇧	1.86	0.013
219874_at	SLC12A8	⇩	1.86	0.011
242714_at	---	⇧	1.86	9.40E-03
1567458_s_at	RAC1	⇧	1.86	9.10E-03
1570108_at	---	⇧	1.86	8.80E-03
242661_x_at	ALS2CR12	⇧	1.86	7.90E-03
228106_at	C4orf30	⇧	1.86	7.20E-03
221449_s_at	ITFG1	⇩	1.86	6.80E-03
1555832_s_at	KLF6	⇧	1.86	4.80E-03
212208_at	MED13L	⇧	1.86	4.40E-03
235940_at	C9orf64	⇧	1.86	3.60E-03
243993_at	---	⇧	1.86	2.80E-03
216933_x_at	APC	⇧	1.86	2.80E-03
232445_at	SYT9	⇧	1.86	1.70E-03
237026_at	---	⇧	1.86	1.30E-03
211798_x_at	IGLJ3	⇩	1.86	1.30E-03
242633_x_at	---	⇧	1.86	1.20E-03
243067_at	---	⇧	1.86	1.10E-03
1559128_at	HSDL2	⇧	1.86	8.90E-04
232516_x_at	DAP3	⇧	1.86	7.00E-04
226062_x_at	FAM63A	⇧	1.86	6.50E-04
222925_at	DCDC2	⇩	1.86	6.30E-04
210760_x_at	TRIP11	⇧	1.86	5.40E-04
1552752_a_at	CADM2	⇧	1.86	3.30E-04
207436_x_at	KIAA0894	⇧	1.86	2.30E-04
220796_x_at	SLC35E1	⇧	1.86	2.30E-04
1555048_a_at	C21orf29	⇧	1.86	9.60E-06
220940_at	ANKRD36B	⇧	1.85	0.047
239755_at	---	⇧	1.85	0.043
231577_s_at	GBP1	⇧	1.85	0.039
201360_at	CST3	⇩	1.85	0.036
200007_at	SRP14	⇩	1.85	0.033
236490_at	NEDD4L	⇩	1.85	0.024
205442_at	MFAP3L	⇩	1.85	0.021
220467_at	---	⇧	1.85	0.015
221531_at	WDR61	⇩	1.85	0.014
222378_at	---	⇧	1.85	0.012
1570259_at	LIMS1	⇧	1.85	0.012
233228_at	---	⇧	1.85	0.011
1556432_at	---	⇧	1.85	0.011
232896_at	ERBB2IP	⇧	1.85	0.010
217973_at	DCXR	⇩	1.85	8.90E-03
1563453_at	---	⇧	1.85	8.50E-03
227259_at	CD47	⇧	1.85	7.80E-03
215018_at	KIAA1731	⇧	1.85	7.70E-03
230064_at	---	⇧	1.85	7.20E-03
208614_s_at	FLNB	⇩	1.85	6.70E-03
203321_s_at	ADNP2	⇧	1.85	6.30E-03
228284_at	TLE1	⇩	1.85	4.70E-03
236809_at	---	⇧	1.85	4.60E-03
1561451_a_at	ADAM29	⇧	1.85	4.30E-03
202113_s_at	SNX2	⇩	1.85	4.20E-03
203798_s_at	VSNL1	⇩	1.85	3.70E-03
221269_s_at	SH3BGRL3	⇩	1.85	3.60E-03
209865_at	SLC35A3	⇧	1.85	3.10E-03
241798_at	---	⇧	1.85	3.00E-03
215213_at	NUP54	⇧	1.85	2.50E-03
201225_s_at	SRRM1	⇧	1.85	2.50E-03
1562031_at	JAK2	⇧	1.85	1.90E-03
1568618_a_at	GALNT1	⇧	1.85	1.70E-03
208823_s_at	PCTK1	⇧	1.85	1.20E-03
220448_at	KCNK12	⇧	1.85	9.00E-04
237230_at	GPHA2	⇩	1.85	6.10E-04
209696_at	FBP1	⇩	1.85	3.90E-04
1553315_at	SLFNL1	⇧	1.85	3.90E-04

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

221499_s_at	STX16	⇧	1.85	3.10E-04
200046_at	DAD1	⇩	1.85	2.60E-04
202493_x_at	CSH1	⇧	1.85	2.30E-04
233783_at	---	⇧	1.85	1.20E-04
38892_at	KIAA0240	⇧	1.85	1.00E-04
1561918_at	---	⇧	1.85	3.50E-05
221844_x_at	SPCS3	⇧	1.85	1.50E-05
228304_at	RBM43	⇧	1.84	0.044
239893_at	---	⇧	1.84	0.041
243751_at	CHD2	⇧	1.84	0.041
241885_at	---	⇧	1.84	0.037
201794_s_at	SMG7	⇧	1.84	0.036
222420_s_at	UBE2H	⇧	1.84	0.035
233510_s_at	PARVG	⇩	1.84	0.030
227232_at	EVL	⇧	1.84	0.029
1569181_x_at	---	⇧	1.84	0.026
1565703_at	SMAD4	⇧	1.84	0.021
239655_at	---	⇧	1.84	0.019
222544_s_at	WHSC1L1	⇧	1.84	0.019
207089_at	NRAP	⇩	1.84	0.018
1569302_at	KIAA1731	⇧	1.84	0.017
219417_s_at	C17orf59	⇩	1.84	0.016
208054_at	HERC4	⇧	1.84	0.016
1553271_at	DIP2B	⇧	1.84	0.014
237753_at	IL21R	⇧	1.84	0.011
1570587_at	---	⇧	1.84	9.70E-03
243664_at	TXNL1	⇧	1.84	8.70E-03
235761_at	---	⇧	1.84	8.60E-03
220221_at	VPS13D	⇧	1.84	6.30E-03
214509_at	HIST1H3I	⇩	1.84	4.40E-03
1555514_a_at	PIAS2	⇧	1.84	4.30E-03
203114_at	SSSCA1	⇩	1.84	3.40E-03
239268_at	NDUFS1	⇧	1.84	3.20E-03
1560026_at	---	⇧	1.84	2.90E-03
207037_at	TNFRSF11A	⇧	1.84	2.90E-03
223350_x_at	LIN7C	⇧	1.84	2.70E-03
232342_at	MTMR14	⇧	1.84	2.50E-03
215893_x_at	---	⇧	1.84	2.20E-03
236122_at	---	⇧	1.84	2.00E-03
218119_at	TIMM23	⇩	1.84	1.70E-03
240791_at	---	⇧	1.84	1.30E-03
226377_at	NFIC	⇧	1.84	1.30E-03
232957_x_at	---	⇧	1.84	1.20E-03
241799_x_at	---	⇧	1.84	1.10E-03
234098_at	SOBP	⇧	1.84	1.10E-03
1554899_s_at	FCER1G	⇩	1.84	8.20E-04
233939_at	REXO1	⇧	1.84	8.00E-04
217253_at	SH3BP2	⇧	1.84	5.10E-04
231781_s_at	LRRC2	⇧	1.84	3.00E-04
238102_s_at	LOC149478	⇩	1.84	1.20E-04
AFFX-DapX-5_at	---	⇧	1.84	0.027
1566854_at	---	⇧	1.83	0.041
213642_at	---	⇧	1.83	0.039
226283_at	WDR51B	⇧	1.83	0.036
222306_at	---	⇧	1.83	0.033
206765_at	KCNJ2	⇧	1.83	0.032
213939_s_at	RUFY3	⇧	1.83	0.032
224605_at	C4orf3	⇧	1.83	0.027
209241_x_at	MINK1	⇧	1.83	0.027
217594_at	ZCCHC11	⇧	1.83	0.026
204513_s_at	ELMO1	⇧	1.83	0.021
1557065_at	YLPM1	⇧	1.83	0.021
201490_s_at	PPIF	⇩	1.83	0.020
238723_at	ATXN3	⇧	1.83	0.018
222316_at	---	⇧	1.83	0.017
234255_at	---	⇧	1.83	0.016
243127_x_at	DNASE1	⇧	1.83	0.013
215513_at	HYMAI	⇧	1.83	0.012
215287_at	STRN	⇧	1.83	0.010
209281_s_at	ATP2B1	⇧	1.83	9.50E-03
201606_s_at	PWP1	⇧	1.83	9.20E-03
212501_at	CEBPB	⇧	1.83	7.50E-03
1564438_at	---	⇧	1.83	7.40E-03
202874_s_at	ATP6V1C1	⇩	1.83	7.10E-03
1557562_at	GRIPAP1	⇧	1.83	6.70E-03
240205_x_at	---	⇧	1.83	5.90E-03
228067_at	C2orf55	⇩	1.83	5.60E-03
202068_s_at	LDLR	⇩	1.83	5.40E-03
1566507_a_at	FBXO9	⇧	1.83	5.30E-03
244220_at	---	⇧	1.83	3.70E-03
232767_at	CADM1	⇧	1.83	3.60E-03
207352_s_at	GABRB2	⇩	1.83	3.00E-03
231902_at	ZNF827	⇧	1.83	2.70E-03
1556778_at	---	⇧	1.83	2.10E-03
212487_at	GPATCH8	⇧	1.83	2.10E-03
243860_at	---	⇧	1.83	2.00E-03
1558792_x_at	AP2A1	⇧	1.83	2.00E-03
238713_at	---	⇧	1.83	1.50E-03
203191_at	ABCB6	⇩	1.83	9.50E-04
244024_at	ZNF182	⇧	1.83	9.10E-04
236395_at	---	⇧	1.83	8.60E-04
1557409_at	---	⇧	1.83	8.30E-04
244699_at	AHI1	⇧	1.83	6.40E-04

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

211775_x_at	MGC13053	⇧	1.83	6.40E-04	200039_s_at	PSMB2	⇩	1.82	1.40E-03	242645_at	---	⇧	1.81	0.010
215532_x_at	ZNF492	⇧	1.83	5.40E-04	234020_x_at	---	⇧	1.82	1.30E-03	203408_s_at	SATB1	⇧	1.81	9.30E-03
222356_at	---	⇧	1.83	2.60E-04	230685_at	FLJ33630	⇧	1.82	1.10E-03	237208_at	WDR61	⇧	1.81	9.30E-03
244135_at	---	⇧	1.83	2.10E-04	200824_at	GSTP1	⇩	1.82	1.10E-03	223181_at	C18orf55	⇩	1.81	9.20E-03
202190_at	CSTF1	⇩	1.83	2.00E-04	1566150_at	CALML4	⇩	1.82	9.40E-04	240659_x_at	---	⇧	1.81	8.70E-03
218381_s_at	U2AF2	⇧	1.83	9.90E-05	232064_at	FER	⇧	1.82	9.10E-04	230669_at	RASA2	⇧	1.81	8.70E-03
237072_at	---	⇧	1.83	1.50E-05	1552870_s_at	C1orf125	⇩	1.82	9.00E-04	207431_s_at	DEGS1	⇧	1.81	7.60E-03
AFFX-BioB-3_at	---	⇩	1.82	2.59E-04	202057_at	KPNA1	⇧	1.82	8.70E-04	204048_s_at	PHACTR2	⇧	1.81	7.30E-03
242879_x_at	AKT3	⇧	1.82	0.035	215909_x_at	MINK1	⇧	1.82	8.50E-04	239331_at	---	⇧	1.81	5.60E-03
240513_at	EIF3M	⇧	1.82	0.025	210679_x_at	---	⇧	1.82	6.40E-04	242190_at	SDAD1	⇧	1.81	5.10E-03
227819_at	LGR6	⇧	1.82	0.025	208137_x_at	ZNF611	⇧	1.82	6.30E-04	1558783_at	---	⇧	1.81	5.00E-03
242844_at	PGGT1B	⇧	1.82	0.022	1560543_at	GRK4	⇧	1.82	6.10E-04	221286_s_at	MGC29506	⇩	1.81	4.40E-03
233593_at	---	⇧	1.82	0.019	236181_at	LOC100132181	⇧	1.82	5.90E-04	221568_s_at	LIN7C	⇧	1.81	4.10E-03
215630_at	---	⇧	1.82	0.018	215588_x_at	RIOK3	⇧	1.82	4.90E-04	209254_at	KLHDC10	⇧	1.81	3.70E-03
225850_at	SFT2D1	⇩	1.82	8.80E-03	222223_s_at	IL1F5	⇧	1.82	3.20E-04	202475_at	TMEM147	⇩	1.81	2.80E-03
238064_at	---	⇧	1.82	8.20E-03	232455_x_at	LOC340085	⇧	1.82	1.70E-04	212361_s_at	ATP2A2	⇩	1.81	2.50E-03
1563460_at	---	⇧	1.82	7.50E-03	208817_at	COMT	⇩	1.82	9.20E-05	224806_at	TRIM25	⇧	1.81	2.20E-03
1561545_at	EPN2-AS1	⇧	1.82	5.60E-03	243878_at	---	⇧	1.81	0.045	215445_x_at	---	⇧	1.81	1.80E-03
219625_s_at	COL4A3BP	⇧	1.82	5.50E-03	206311_s_at	PLA2G1B	⇧	1.81	0.037	243221_at	FAM20A	⇩	1.81	1.80E-03
222888_at	CCNJ	⇧	1.82	4.70E-03	232426_at	SV2B	⇩	1.81	0.037	215359_x_at	ZNF44	⇧	1.81	1.70E-03
1563166_at	---	⇧	1.82	4.00E-03	204369_at	PIK3CA	⇩	1.81	0.036	222104_x_at	GTF2H3	⇧	1.81	1.50E-03
202298_at	NDUFA1	⇩	1.82	3.90E-03	239227_at	---	⇧	1.81	0.033	229749_at	ANO4	⇧	1.81	1.20E-03
220659_s_at	C7orf43	⇧	1.82	3.80E-03	236621_at	RPS27	⇧	1.81	0.027	220720_x_at	FAM128B	⇧	1.81	1.20E-03
213158_at	---	⇧	1.82	3.60E-03	1555913_at	GON4L	⇧	1.81	0.025	234224_at	---	⇧	1.81	8.70E-04
235730_at	---	⇧	1.82	3.30E-03	204069_at	MEIS1	⇩	1.81	0.020	214715_x_at	ZNF160	⇧	1.81	7.70E-04
233017_x_at	---	⇧	1.82	2.70E-03	225451_at	GRIPAP1	⇧	1.81	0.018	1557197_a_at	LGALS3	⇧	1.81	6.40E-04
234820_at	MAS1L	⇩	1.82	2.50E-03	239049_at	---	⇧	1.81	0.016	238366_at	C1orf228	⇧	1.81	6.30E-04
215639_at	SH2D3C	⇧	1.82	2.40E-03	228853_at	STYX	⇧	1.81	0.015	232814_x_at	KLC1	⇧	1.81	5.20E-04
203433_at	MTHFS	⇩	1.82	1.70E-03	222809_x_at	CCDC85C	⇩	1.81	0.014	233381_at	RUFY1	⇧	1.81	4.70E-04
234245_at	---	⇧	1.82	1.40E-03	209023_s_at	STAG2	⇧	1.81	0.012	207730_x_at	---	⇧	1.81	4.00E-04
237889_s_at	LOC553137	⇧	1.82	1.40E-03	229514_at	C14orf118	⇧	1.81	0.011	239378_at	PITRM1	⇧	1.81	2.30E-04

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

208547_at	HIST1H2BB	⇩	1.81	9.40E-05	212814_at	AHCYL2	⇧	1.80	6.00E-03	210869_s_at	MCAM	⇧	1.80	1.20E-04
243655_x_at	---	⇧	1.81	7.30E-05	217603_at	ATP6V0A2	⇧	1.80	6.00E-03	208967_s_at	AK2	⇩	1.80	1.80E-06
210637_at	TACR1	⇧	1.81	6.60E-05	1553747_at	MGC16025	⇧	1.80	5.90E-03	201998_at	ST6GAL1	⇩	1.79	0.045
AFFX-r2-Ec-bioC-5_at	---	⇩	1.80	1.08E-05	1553972_a_at	CBS	⇧	1.80	5.60E-03	1565638_at	---	⇧	1.79	0.042
206267_s_at	MATK	⇧	1.80	0.041	240839_at	---	⇧	1.80	5.20E-03	1565889_at	---	⇧	1.79	0.037
223243_s_at	EDEM3	⇧	1.80	0.039	1570441_at	NAPB	⇧	1.80	5.10E-03	233898_s_at	FGFR1OP2	⇧	1.79	0.037
212509_s_at	MXRA7	⇧	1.80	0.038	1557521_a_at	---	⇧	1.80	4.10E-03	1556914_at	---	⇧	1.79	0.032
211352_s_at	NCOA3	⇧	1.80	0.033	240510_at	NBN	⇧	1.80	3.90E-03	232486_at	LRFN1	⇧	1.79	0.030
234196_at	---	⇧	1.80	0.027	205169_at	RBBP5	⇧	1.80	3.90E-03	236839_at	---	⇧	1.79	0.028
213789_at	---	⇧	1.80	0.026	1558739_at	---	⇧	1.80	3.10E-03	232020_at	SMURF2	⇧	1.79	0.026
214388_at	---	⇧	1.80	0.024	237725_x_at	SMC5	⇧	1.80	2.90E-03	225957_at	C5orf41	⇧	1.79	0.024
209259_s_at	SMC3	⇩	1.80	0.023	222708_s_at	STX17	⇧	1.80	2.70E-03	208768_x_at	RPL22	⇩	1.79	0.024
226159_at	C5orf51	⇧	1.80	0.022	202662_s_at	ITPR2	⇩	1.80	2.20E-03	243916_x_at	UBLCP1	⇧	1.79	0.023
221775_x_at	RPL22	⇩	1.80	0.022	243934_at	ODF3B	⇧	1.80	2.20E-03	212779_at	KIAA1109	⇩	1.79	0.019
207700_s_at	NCOA3	⇧	1.80	0.019	213350_at	RPS11	⇧	1.80	1.80E-03	237461_at	NLRP7	⇩	1.79	0.019
242233_at	---	⇧	1.80	0.018	216612_x_at	---	⇧	1.80	1.60E-03	213593_s_at	TRA2A	⇧	1.79	0.019
224637_at	LOC100128731	⇩	1.80	0.016	205469_s_at	IRF5	⇩	1.80	1.10E-03	243846_x_at	---	⇧	1.79	0.018
1564029_at	USP49	⇧	1.80	0.016	241046_at	LOC100505903	⇧	1.80	1.00E-03	218495_at	UXT	⇩	1.79	0.017
206295_at	IL18	⇧	1.80	0.014	225712_at	GEMIN5	⇩	1.80	8.90E-04	204861_s_at	NAIP	⇧	1.79	0.015
203166_at	CFDP1	⇩	1.80	0.013	1557512_at	---	⇧	1.80	7.60E-04	1569201_a_at	---	⇧	1.79	0.014
212000_at	SFRS14	⇧	1.80	0.013	240046_at	---	⇧	1.80	6.60E-04	221494_x_at	EIF3K	⇩	1.79	0.012
242970_at	DIP2B	⇧	1.80	0.012	224134_at	MGC10814	⇧	1.80	6.60E-04	242059_at	---	⇧	1.79	0.011
234164_at	---	⇧	1.80	0.011	241303_x_at	---	⇧	1.80	5.70E-04	1557564_at	---	⇩	1.79	0.010
209408_at	KIF2C	⇩	1.80	0.011	231856_at	KIAA1244	⇧	1.80	5.60E-04	228019_s_at	MRPS18C	⇩	1.79	0.010
202784_s_at	NNT	⇩	1.80	0.010	1554476_x_at	ZNF808	⇧	1.80	5.30E-04	1556339_a_at	---	⇧	1.79	7.30E-03
208301_at	---	⇧	1.80	8.20E-03	213936_x_at	SFTPB	⇧	1.80	5.10E-04	237178_at	---	⇧	1.79	5.30E-03
1561036_at	---	⇩	1.80	8.10E-03	241928_at	---	⇧	1.80	4.50E-04	1553726_s_at	C6orf170	⇧	1.79	4.90E-03
224970_at	NFIA	⇧	1.80	7.10E-03	205988_at	CD84	⇧	1.80	3.70E-04	210470_x_at	NONO	⇧	1.79	4.30E-03
235780_at	PRKACB	⇧	1.80	6.60E-03	218291_at	ROBLD3	⇩	1.80	3.70E-04	220855_at	CLTC-IT1	⇧	1.79	3.70E-03
36004_at	IKBKG	⇩	1.80	6.20E-03	1556352_at	---	⇧	1.80	1.60E-04	230659_at	---	⇧	1.79	2.90E-03
204292_x_at	STK11	⇧	1.80	6.20E-03	1560101_at	SYDE2	⇧	1.80	1.50E-04	244132_x_at	ZNF518A	⇧	1.79	2.90E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student’s t-test p<0.05, FC ≥ ±1.50]

222668_at	KCTD15	⇧	1.79	2.70E-03
231818_x_at	---	⇧	1.79	2.50E-03
243866_x_at	---	⇧	1.79	2.40E-03
243482_at	---	⇧	1.79	2.20E-03
239333_x_at	---	⇧	1.79	1.90E-03
1565754_x_at	FGD2	⇧	1.79	1.70E-03
201577_at	NME1	⇩	1.79	1.40E-03
233273_at	---	⇧	1.79	1.30E-03
1569128_at	C3orf38	⇧	1.79	1.30E-03
240906_at	---	⇧	1.79	1.20E-03
211006_s_at	KCNB1	⇧	1.79	1.20E-03
211374_x_at	---	⇧	1.79	9.00E-04
216135_at	IQCK	⇧	1.79	8.30E-04
206773_at	LY6H	⇧	1.79	7.20E-04
244426_at	---	⇧	1.79	6.90E-04
216051_x_at	PRINS	⇧	1.79	5.00E-04
241099_at	---	⇧	1.79	3.70E-04
233796_at	---	⇧	1.79	3.00E-04
223928_s_at	GUCA1C	⇧	1.79	1.30E-04
230340_s_at	WASL	⇧	1.79	5.60E-05
244164_at	---	⇧	1.78	0.041
1559413_at	TCP11L2	⇧	1.78	0.038
243236_at	---	⇧	1.78	0.027
239056_at	SEC22C	⇩	1.78	0.025
242616_at	---	⇧	1.78	0.023
205516_x_at	CIZ1	⇩	1.78	0.021
232581_x_at	HIVEP3	⇩	1.78	0.021
211612_s_at	IL13RA1	⇩	1.78	0.021
239757_at	ZFAND6	⇧	1.78	0.020
204302_s_at	KIAA0427	⇧	1.78	0.017
1569311_at	LOC554203	⇧	1.78	0.017
205037_at	RABL4	⇩	1.78	0.017
239166_at	---	⇧	1.78	0.015
211921_x_at	PTMA	⇧	1.78	0.015
237336_at	ADD2	⇧	1.78	0.014
33148_at	ZFR	⇧	1.78	0.014
1564640_at	MGA	⇧	1.78	0.013
202996_at	POLD4	⇩	1.78	0.012
241294_at	---	⇧	1.78	0.011
235308_at	ZBTB20	⇧	1.78	0.010
229835_s_at	SLMO2	⇧	1.78	9.80E-03
232688_at	BMP2K	⇧	1.78	8.70E-03
1560500_at	---	⇧	1.78	8.60E-03
242562_at	DNAJC24	⇧	1.78	7.70E-03
242197_x_at	CD36	⇧	1.78	7.50E-03
217446_x_at	---	⇧	1.78	6.50E-03
233431_x_at	---	⇧	1.78	6.10E-03
238741_at	FAM83A	⇩	1.78	5.60E-03
242383_at	---	⇧	1.78	4.50E-03
232570_s_at	ADAM33	⇧	1.78	3.70E-03
32099_at	SAFB2	⇧	1.78	3.50E-03
244021_at	---	⇧	1.78	3.20E-03
218084_x_at	FXYD5	⇩	1.78	3.10E-03
1564004_at	---	⇧	1.78	3.00E-03
203665_at	HMOX1	⇩	1.78	3.00E-03
227991_x_at	ZBTB43	⇧	1.78	2.90E-03
223018_at	NOB1	⇩	1.78	2.80E-03
232303_at	ZNF608	⇧	1.78	2.60E-03
221195_at	RNFT1	⇧	1.78	2.50E-03
234650_at	---	⇧	1.78	2.20E-03
205063_at	SIP1	⇧	1.78	2.00E-03
221367_at	MOS	⇩	1.78	1.30E-03
231775_at	TNFRSF10A	⇧	1.78	1.30E-03
235650_at	FLJ23834	⇧	1.78	1.20E-03
216459_x_at	TIGD1L	⇧	1.78	1.20E-03
1560031_at	FRMD4A	⇧	1.78	1.10E-03
207109_at	POU2F3	⇧	1.78	1.00E-03
230630_at	AK3L1	⇧	1.78	5.90E-04
1557117_at	---	⇩	1.78	3.00E-04
212236_x_at	KRT17	⇧	1.78	8.20E-05
208003_s_at	NFAT5	⇧	1.77	0.049
219521_at	B3GAT1	⇧	1.77	0.046
236027_at	C10orf78	⇧	1.77	0.045
235456_at	---	⇩	1.77	0.044
207286_at	CEP135	⇧	1.77	0.041
202006_at	PTPN12	⇩	1.77	0.038
1564154_at	---	⇧	1.77	0.037
213069_at	HEG1	⇩	1.77	0.036
230987_at	---	⇧	1.77	0.034
237438_at	---	⇧	1.77	0.033
224227_s_at	BDP1	⇧	1.77	0.028
206204_at	GRB14	⇩	1.77	0.027
234576_at	ANPEP	⇩	1.77	0.025
202125_s_at	TRAK2	⇧	1.77	0.024
91816_f_at	MEX3D	⇧	1.77	0.022
239788_at	---	⇧	1.77	0.019
1558111_at	MBNL1	⇧	1.77	0.019
240758_at	---	⇧	1.77	0.017
210092_at	MAGOH	⇩	1.77	0.015
1559154_at	---	⇧	1.77	0.014
211764_s_at	UBE2D1	⇧	1.77	0.014
237448_at	---	⇧	1.77	0.013
244546_at	CYCS	⇧	1.77	0.012
221928_at	ACACB	⇧	1.77	0.011
235542_at	TET3	⇩	1.77	0.011
210561_s_at	WSB1	⇧	1.77	0.011

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

212058_at	SR140	⇩	1.77	9.60E-03	217656_at	---	⇧	1.76	0.048	225748_at	LTV1	⇩	1.76	8.00E-03
217618_x_at	HUS1	⇧	1.77	9.30E-03	243423_at	TNIP1	⇧	1.76	0.047	213649_at	SFRS7	⇧	1.76	7.90E-03
200978_at	MDH1	⇩	1.77	8.60E-03	222833_at	LPCAT2	⇧	1.76	0.041	1558504_at	---	⇧	1.76	7.30E-03
228173_at	GNAS	⇧	1.77	8.50E-03	236955_at	---	⇧	1.76	0.031	1553920_at	C9orf84	⇧	1.76	6.60E-03
230426_at	DLD	⇧	1.77	7.80E-03	226347_at	FUT11	⇧	1.76	0.030	1566609_at	---	⇩	1.76	6.40E-03
224254_x_at	---	⇧	1.77	6.80E-03	242549_at	PRKD3	⇧	1.76	0.030	225684_at	FAM33A	⇧	1.76	6.10E-03
201140_s_at	RAB5C	⇧	1.77	6.70E-03	232333_at	---	⇧	1.76	0.027	224847_at	CDK6	⇩	1.76	5.90E-03
219775_s_at	CPLX3	⇧	1.77	6.00E-03	229115_at	DYNC1H1	⇧	1.76	0.025	233709_at	---	⇧	1.76	4.20E-03
1569551_at	---	⇧	1.77	5.70E-03	1557527_at	---	⇧	1.76	0.024	224322_at	ARID4B	⇧	1.76	4.00E-03
1569538_at	---	⇧	1.77	5.10E-03	244145_at	---	⇧	1.76	0.023	235729_at	ZNF514	⇧	1.76	3.70E-03
1557522_x_at	---	⇧	1.77	4.70E-03	218920_at	FLJ10404	⇧	1.76	0.023	209376_x_at	SFRS2IP	⇧	1.76	3.20E-03
216197_at	ATF7IP	⇧	1.77	3.00E-03	214101_s_at	---	⇧	1.76	0.021	234822_at	---	⇩	1.76	2.40E-03
201280_s_at	DAB2	⇧	1.77	2.90E-03	227369_at	SERBP1	⇧	1.76	0.021	1559011_at	FLJ13773	⇧	1.76	2.30E-03
239627_at	TMED9	⇧	1.77	2.50E-03	1565895_at	---	⇧	1.76	0.018	241086_at	---	⇧	1.76	2.20E-03
227311_at	SNX25	⇧	1.77	2.00E-03	1564568_at	CRLF1	⇧	1.76	0.017	221120_at	---	⇧	1.76	2.10E-03
1553686_at	C18orf25	⇩	1.77	1.90E-03	208581_x_at	MT1X	⇩	1.76	0.017	202499_s_at	SLC2A3	⇧	1.76	1.80E-03
208803_s_at	SRP72	⇩	1.77	1.50E-03	1562945_at	---	⇩	1.76	0.016	241065_x_at	CMAS	⇧	1.76	1.20E-03
215582_x_at	MCM3AP	⇧	1.77	1.40E-03	1554177_a_at	ATP5S	⇧	1.76	0.016	1552745_at	SLCO6A1	⇧	1.76	1.10E-03
216466_at	NAV3	⇧	1.77	1.40E-03	208206_s_at	RASGRP2	⇧	1.76	0.016	203898_at	CRCP	⇧	1.76	9.40E-04
233840_at	---	⇧	1.77	1.20E-03	212794_s_at	KIAA1033	⇧	1.76	0.014	207732_s_at	DLG3	⇧	1.76	6.90E-04
208247_at	C3orf51	⇧	1.77	7.30E-04	223190_s_at	MLL5	⇧	1.76	0.014	1562905_at	---	⇧	1.76	6.40E-04
209807_s_at	NFIX	⇩	1.77	6.60E-04	209074_s_at	FAM107A	⇩	1.76	0.013	240616_at	LOC100131110	⇧	1.76	5.70E-04
236812_at	STMN4	⇧	1.77	5.10E-04	219757_s_at	C14orf101	⇧	1.76	0.012	227514_at	ITPRIPL2	⇧	1.76	5.00E-04
208286_x_at	POU5F1	⇧	1.77	4.60E-04	242837_at	SFRS4	⇧	1.76	0.012	212466_at	SPRED2	⇧	1.76	4.60E-04
222337_at	---	⇧	1.77	4.20E-04	207536_s_at	TNFRSF9	⇧	1.76	0.012	242537_at	---	⇧	1.76	2.20E-04
219975_x_at	OLAH	⇧	1.77	3.20E-04	217701_x_at	---	⇧	1.76	0.011	225700_at	GLCCI1	⇩	1.76	2.20E-04
217396_at	---	⇧	1.77	2.80E-04	238170_at	---	⇧	1.76	0.010	204468_s_at	TIE1	⇧	1.76	2.20E-04
1555014_x_at	---	⇧	1.77	2.50E-04	213002_at	MARCKS	⇧	1.76	0.010	1553575_at	ND6	⇧	1.76	1.30E-04
1568915_at	---	⇧	1.77	2.30E-04	1556434_at	---	⇧	1.76	9.90E-03	204666_s_at	RP5-1000E10.4	⇧	1.76	1.10E-04
212258_s_at	SMARCA2	⇧	1.77	1.90E-04	223178_s_at	NT5DC1	⇧	1.76	9.90E-03	220696_at	---	⇧	1.76	4.50E-05
1559820_at	---	⇧	1.77	1.70E-04	212965_at	HIC2	⇧	1.76	8.70E-03	237748_at	SCGBL	⇩	1.76	2.50E-05
225122_at	RNF31	⇧	1.77	3.40E-05	242265_at	BRD8	⇧	1.76	8.30E-03	226715_at	FOXK1	⇧	1.75	0.050

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

229168_at	COL23A1	⇧	1.75	0.046	215490_at	C1orf69	⇧	1.75	8.30E-03	209443_at	SERPINA5	⇧	1.75	4.20E-04
201904_s_at	CTDSPL	⇩	1.75	0.046	227546_x_at	AURKAIP1	⇧	1.75	8.10E-03	241680_at	---	⇧	1.75	3.10E-04
235757_at	---	⇧	1.75	0.045	1560558_at	C9orf80	⇧	1.75	7.90E-03	1569100_a_at	---	⇧	1.75	3.00E-04
229497_at	ANKDD1A	⇧	1.75	0.042	224939_at	NUFIP2	⇧	1.75	7.90E-03	219113_x_at	HSD17B14	⇧	1.75	2.90E-04
217802_s_at	NUCKS1	⇧	1.75	0.042	226024_at	COMMD1	⇩	1.75	6.70E-03	228511_s_at	ZNF219	⇧	1.75	1.90E-04
238890_at	PSMG1	⇧	1.75	0.040	212418_at	ELF1	⇩	1.75	5.40E-03	242991_at	TJP2	⇧	1.75	1.10E-04
232204_at	EBF1	⇧	1.75	0.039	223882_at	FAM172A	⇧	1.75	5.20E-03	233038_at	---	⇧	1.75	1.00E-04
243648_at	---	⇧	1.75	0.037	242175_at	---	⇧	1.75	4.90E-03	218438_s_at	MED28	⇩	1.74	0.049
240358_at	---	⇧	1.75	0.036	242560_at	FANCD2	⇧	1.75	4.30E-03	210807_s_at	SLC16A7	⇧	1.74	0.039
241779_at	MTX3	⇧	1.75	0.032	227703_s_at	SYTL4	⇩	1.75	4.20E-03	228558_at	C14orf80	⇩	1.74	0.038
239709_at	---	⇧	1.75	0.031	206247_at	MICB	⇧	1.75	3.50E-03	238513_at	PRRG4	⇧	1.74	0.038
241769_at	---	⇧	1.75	0.029	240160_x_at	---	⇧	1.75	3.30E-03	223270_at	CTDSPL2	⇧	1.74	0.034
1561763_at	---	⇧	1.75	0.028	211864_s_at	MYOF	⇩	1.75	3.00E-03	203259_s_at	HDDC2	⇩	1.74	0.033
238558_at	---	⇧	1.75	0.025	242357_x_at	---	⇧	1.75	2.90E-03	220370_s_at	USP36	⇧	1.74	0.033
227082_at	---	⇧	1.75	0.024	215250_at	TMEM111	⇧	1.75	2.80E-03	235071_at	WDR92	⇧	1.74	0.033
206116_s_at	TPM1	⇩	1.75	0.024	200655_s_at	CALM1	⇧	1.75	2.60E-03	229987_at	---	⇧	1.74	0.032
214502_at	HIST1H2BJ	⇩	1.75	0.023	210873_x_at	APOBEC3A	⇧	1.75	2.50E-03	218360_at	RAB22A	⇩	1.74	0.031
236386_at	SUZ12P	⇧	1.75	0.022	217016_x_at	FLJ23172	⇧	1.75	2.30E-03	211922_s_at	CAT	⇩	1.74	0.029
219359_at	ATHL1	⇧	1.75	0.021	215853_at	---	⇧	1.75	2.00E-03	232055_at	SFXN1	⇧	1.74	0.029
240594_at	---	⇧	1.75	0.020	1552961_at	---	⇧	1.75	1.90E-03	214182_at	LOC100132430	⇧	1.74	0.024
222035_s_at	PAPOLA	⇩	1.75	0.018	242256_x_at	---	⇧	1.75	1.90E-03	1557452_at	---	⇧	1.74	0.021
220369_at	SMEK1	⇧	1.75	0.016	1559731_x_at	MACROD1	⇧	1.75	1.90E-03	1556931_at	---	⇧	1.74	0.021
202436_s_at	CYP1B1	⇧	1.75	0.015	233074_at	---	⇩	1.75	1.80E-03	1554089_s_at	SBDS	⇩	1.74	0.021
64371_at	SFRS14	⇧	1.75	0.015	1570054_at	---	⇧	1.75	1.70E-03	236554_x_at	TMC8	⇧	1.74	0.019
239597_at	---	⇧	1.75	0.014	237133_at	---	⇧	1.75	1.60E-03	1560456_at	LSDP5	⇧	1.74	0.018
237618_at	---	⇧	1.75	0.014	216499_at	---	⇧	1.75	1.20E-03	236696_at	SR140	⇧	1.74	0.018
213109_at	TNIK	⇧	1.75	0.013	204238_s_at	C6orf108	⇩	1.75	1.20E-03	229262_at	LRRC68	⇧	1.74	0.017
220823_at	---	⇧	1.75	0.012	215978_x_at	LOC152719	⇧	1.75	1.20E-03	204064_at	THOC1	⇧	1.74	0.016
241786_at	---	⇧	1.75	0.010	209193_at	PIM1	⇧	1.75	1.10E-03	233658_at	---	⇧	1.74	0.015
1561181_at	---	⇧	1.75	0.010	243793_at	AHDC1	⇧	1.75	8.40E-04	233152_x_at	---	⇧	1.74	0.014
233271_at	---	⇧	1.75	0.010	211387_x_at	RNGTT	⇧	1.75	4.80E-04	1557167_at	HCG11	⇧	1.74	0.014
1556658_a_at	---	⇧	1.75	9.30E-03	205193_at	MAFF	⇧	1.75	4.50E-04	205296_at	RBL1	⇧	1.74	0.014

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

1562364_at	GVINP1	⇧	1.74	0.013	221387_at	NPFFR1	⇧	1.74	7.50E-04	223010_s_at	OCIAD1	⇩	1.73	0.015
223462_at	TMEM175	⇧	1.74	0.013	1554697_at	ADAMTS9	⇧	1.74	7.10E-04	225739_at	RAB11FIP4	⇩	1.73	0.014
240128_at	---	⇧	1.74	0.011	210213_s_at	EIF6	⇩	1.74	5.20E-04	217832_at	SYNCRIP	⇩	1.73	0.014
219802_at	PYROXD1	⇧	1.74	0.011	216460_at	FLJ00049	⇧	1.74	5.00E-04	202191_s_at	GAS7	⇧	1.73	0.012
215824_at	NUDT7	⇧	1.74	9.00E-03	215674_at	KIAA1659	⇧	1.74	3.70E-04	203778_at	MANBA	⇩	1.73	0.011
227278_at	TAF13	⇧	1.74	8.30E-03	218634_at	PHLDA3	⇧	1.74	3.70E-04	1558445_at	---	⇧	1.73	0.010
242109_at	SYTL3	⇧	1.74	7.80E-03	233902_at	GUCA1C	⇧	1.74	3.20E-04	228916_at	CWF19L2	⇩	1.73	9.90E-03
1554251_at	HP1BP3	⇧	1.74	7.20E-03	242687_at	FAM160A1	⇧	1.74	2.10E-04	1559420_x_at	CACNB2	⇧	1.73	9.60E-03
234235_at	---	⇧	1.74	7.10E-03	209650_s_at	TBC1D22A	⇧	1.74	1.30E-04	231863_at	ING3	⇧	1.73	9.60E-03
241062_at	---	⇧	1.74	6.30E-03	1566670_at	PDXK	⇧	1.74	7.50E-05	56919_at	WDR48	⇧	1.73	8.60E-03
239060_at	---	⇧	1.74	6.00E-03	223774_at	SNHG12	⇩	1.74	3.50E-05	231242_at	BHLHE41	⇧	1.73	5.70E-03
1558075_at	LOC339047	⇧	1.74	5.40E-03	223463_at	RAB23	⇧	1.73	0.045	218906_x_at	KLC2	⇧	1.73	5.70E-03
1552303_a_at	TMEM106A	⇧	1.74	5.40E-03	217100_s_at	UBXN7	⇧	1.73	0.045	229735_s_at	NIPAL3	⇧	1.73	5.30E-03
244279_at	SOBP	⇧	1.74	5.30E-03	212492_s_at	KDM4B	⇧	1.73	0.043	242912_at	P704P	⇧	1.73	5.30E-03
208624_s_at	EIF4G1	⇧	1.74	5.00E-03	232371_at	MARCH7	⇧	1.73	0.039	1559771_at	---	⇧	1.73	5.00E-03
201011_at	RPN1	⇧	1.74	4.50E-03	209389_x_at	DBI	⇩	1.73	0.038	243103_at	---	⇧	1.73	4.90E-03
233645_s_at	C1RL	⇧	1.74	4.20E-03	1570135_at	ZNF230	⇧	1.73	0.037	237316_at	ANKDD1A	⇧	1.73	4.80E-03
1553365_at	DEPDC4	⇧	1.74	3.90E-03	1561092_at	---	⇧	1.73	0.035	215763_at	---	⇧	1.73	4.60E-03
1555843_at	HNRNPM	⇩	1.74	3.60E-03	240743_at	---	⇧	1.73	0.030	1564204_at	FAM91A2	⇧	1.73	4.50E-03
244872_at	RBBP4	⇧	1.74	3.10E-03	201409_s_at	PPP1CB	⇧	1.73	0.027	212862_at	CDS2	⇧	1.73	4.30E-03
228254_at	STAM2	⇧	1.74	3.00E-03	209691_s_at	DOK4	⇧	1.73	0.024	217679_x_at	---	⇧	1.73	4.20E-03
219470_x_at	CCNJ	⇧	1.74	2.90E-03	1560145_at	MKLN1	⇩	1.73	0.022	200761_s_at	ARL6IP5	⇧	1.73	3.60E-03
1562428_at	LOC654780	⇧	1.74	2.60E-03	228412_at	LOC643072	⇩	1.73	0.021	241993_x_at	---	⇧	1.73	3.50E-03
232107_at	---	⇧	1.74	2.30E-03	227472_at	DDA1	⇧	1.73	0.019	218113_at	TMEM2	⇧	1.73	3.50E-03
208195_at	TTN	⇩	1.74	2.20E-03	227934_at	KPNA5	⇧	1.73	0.019	1568986_x_at	PIGT	⇧	1.73	3.30E-03
1553037_a_at	SYN2	⇧	1.74	2.10E-03	216748_at	PYHIN1	⇧	1.73	0.019	211919_s_at	CXCR4	⇩	1.73	3.10E-03
203816_at	DGUOK	⇩	1.74	2.00E-03	1554565_x_at	UNQ1887	⇧	1.73	0.019	1557224_at	---	⇧	1.73	2.60E-03
241757_x_at	DYNC2LI1	⇧	1.74	2.00E-03	217608_at	SFRS12IP1	⇧	1.73	0.018	37170_at	BMP2K	⇧	1.73	2.60E-03
227507_at	ZNF592	⇧	1.74	1.90E-03	218923_at	CTBS	⇧	1.73	0.017	227860_at	CPXM1	⇧	1.73	2.30E-03
210389_x_at	TUBD1	⇧	1.74	1.70E-03	1564155_x_at	---	⇧	1.73	0.016	214085_x_at	GLIPR1	⇧	1.73	1.80E-03
200908_s_at	RPLP2	⇩	1.74	1.60E-03	237492_at	---	⇧	1.73	0.015	240867_at	---	⇧	1.73	1.70E-03
1555978_s_at	MYL12A	⇧	1.74	1.50E-03	1557736_at	NKTR	⇧	1.73	0.015	1561346_at	---	⇧	1.73	1.50E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student’s t-test p<0.05, FC ≥ ±1.50]

226888_at	CSNK1G1	⇧	1.73	1.20E-03	238041_at	TCF12	⇧	1.72	0.018	206556_at	CLUL1	⇧	1.72	3.60E-04
204175_at	ZNF593	⇩	1.73	1.20E-03	226018_at	C7orf41	⇧	1.72	0.016	1561614_at	SLC8A1	⇧	1.72	3.30E-04
237123_x_at	KLHL9	⇧	1.73	1.00E-03	224400_s_at	CHST9	⇩	1.72	0.016	208598_s_at	HUWE1	⇩	1.72	2.70E-04
1557501_a_at	---	⇧	1.73	9.20E-04	1556416_s_at	---	⇧	1.72	0.015	200881_s_at	DNAJA1	⇩	1.72	2.50E-04
222329_x_at	---	⇩	1.73	9.00E-04	218043_s_at	AZI2	⇧	1.72	0.014	1562669_at	---	⇧	1.72	1.50E-04
235797_x_at	HMCN2	⇩	1.73	7.90E-04	243826_at	---	⇧	1.72	0.013	239980_at	C22orf28	⇧	1.72	1.30E-04
206056_x_at	SPN	⇧	1.73	7.10E-04	216323_x_at	TUBA3D	⇩	1.72	0.013	1556383_at	---	⇩	1.72	1.20E-04
214902_x_at	---	⇧	1.73	5.70E-04	226965_at	FAM116A	⇧	1.72	0.012	242520_s_at	C1orf228	⇩	1.72	5.30E-05
1557068_at	KRT37	⇧	1.73	5.00E-04	208583_x_at	HIST1H2AJ	⇩	1.72	0.011	1562036_at	---	⇧	1.72	6.40E-06
205998_x_at	CYP3A4	⇧	1.73	4.20E-04	212651_at	RHOBTB1	⇩	1.72	0.011	AFFX-BioB-M_at	---	⇩	1.72	2.97E-04
216343_at	PCDHGA3	⇧	1.73	3.20E-04	206293_at	SULT2A1	⇧	1.72	0.011	203828_s_at	IL32	⇩	1.71	0.048
233399_x_at	ZNF252	⇧	1.73	2.70E-04	225980_at	C14orf43	⇩	1.72	7.80E-03	230180_at	DDX17	⇧	1.71	0.047
214294_at	KIAA0485	⇧	1.73	2.60E-04	223309_x_at	PNPLA8	⇧	1.72	7.40E-03	1557300_s_at	---	⇧	1.71	0.044
203171_s_at	RRP8	⇩	1.73	1.60E-04	217052_x_at	---	⇧	1.72	4.90E-03	239175_at	---	⇧	1.71	0.039
1562142_at	SKIV2L2	⇧	1.73	1.20E-04	223012_at	UBXN6	⇧	1.72	4.60E-03	238892_at	---	⇧	1.71	0.039
211881_x_at	IGLJ3	⇩	1.73	8.80E-05	216442_x_at	FN1	⇩	1.72	4.00E-03	202335_s_at	UBE2B	⇧	1.71	0.035
200599_s_at	HSP90B1	⇩	1.72	0.046	1557842_at	---	⇧	1.72	3.00E-03	240314_at	---	⇧	1.71	0.031
207310_s_at	NOS1	⇩	1.72	0.045	212119_at	RHOQ	⇧	1.72	2.60E-03	226587_at	SNRPN	⇧	1.71	0.030
211358_s_at	CIZ1	⇩	1.72	0.043	216310_at	TAOK1	⇧	1.72	2.30E-03	244826_at	---	⇧	1.71	0.024
243552_at	MBTD1	⇧	1.72	0.043	1558560_s_at	BLZF1	⇧	1.72	1.80E-03	241849_at	---	⇧	1.71	0.024
41657_at	STK11	⇧	1.72	0.042	214951_at	SLC26A10	⇧	1.72	1.80E-03	1561829_at	---	⇧	1.71	0.023
1561973_at	SMARCC2	⇧	1.72	0.038	223718_at	ACRBP	⇩	1.72	1.60E-03	233078_at	API5	⇧	1.71	0.023
233114_at	---	⇧	1.72	0.032	240251_at	IFT80	⇧	1.72	1.60E-03	234260_at	---	⇧	1.71	0.021
1565598_at	---	⇧	1.72	0.031	235907_at	TMEM33	⇧	1.72	1.50E-03	225797_at	MRPL54	⇩	1.71	0.019
214544_s_at	SNAP23	⇩	1.72	0.031	214707_x_at	ALMS1	⇧	1.72	1.20E-03	238070_at	CHD1L	⇧	1.71	0.017
215284_at	---	⇧	1.72	0.024	207339_s_at	LTB	⇩	1.72	9.00E-04	218708_at	NXT1	⇩	1.71	0.017
216682_s_at	FAM48A	⇧	1.72	0.023	201871_s_at	UBXN1	⇩	1.72	8.70E-04	206995_x_at	SCARF1	⇧	1.71	0.017
233229_at	SCFD1	⇧	1.72	0.023	210169_at	SEC14L5	⇩	1.72	7.20E-04	235760_at	NSD1	⇧	1.71	0.014
242274_x_at	SLC25A42	⇧	1.72	0.021	236060_at	---	⇧	1.72	5.30E-04	244061_at	---	⇧	1.71	0.013
203252_at	CDK2AP2	⇩	1.72	0.018	1565269_s_at	ATF1	⇩	1.72	4.40E-04	215913_s_at	GULP1	⇧	1.71	0.012
203181_x_at	SRPK2	⇧	1.72	0.018	232703_at	GLUD1P7	⇧	1.72	4.00E-04	212593_s_at	PDCD4	⇧	1.71	0.012

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

227601_at	METTL14	⇧	1.71	0.011
217550_at	ATF6	⇧	1.71	8.40E-03
214295_at	KIAA0485	⇧	1.71	7.80E-03
229128_s_at	ANP32E	⇧	1.71	7.50E-03
216491_x_at	IGHM	⇩	1.71	7.50E-03
207126_x_at	UGT1A1	⇩	1.71	7.40E-03
235601_at	---	⇧	1.71	7.20E-03
203893_at	TAF9	⇩	1.71	6.60E-03
208866_at	CSNK1A1	⇧	1.71	6.50E-03
232350_x_at	GPR161	⇧	1.71	6.20E-03
1554196_at	IZUMO1	⇩	1.71	6.00E-03
222368_at	---	⇧	1.71	5.50E-03
243471_at	---	⇧	1.71	5.50E-03
230966_at	IL4I1	⇩	1.71	5.50E-03
225204_at	PPTC7	⇧	1.71	5.30E-03
240870_at	---	⇧	1.71	5.10E-03
222481_at	FXC1	⇧	1.71	4.90E-03
205219_s_at	GALK2	⇩	1.71	4.90E-03
236130_at	SNORA37	⇧	1.71	3.90E-03
225444_at	UBN2	⇧	1.71	3.80E-03
202736_s_at	LSM4	⇩	1.71	3.60E-03
214669_x_at	IGKC	⇩	1.71	3.30E-03
203100_s_at	CDYL	⇩	1.71	3.10E-03
209055_s_at	CDC5L	⇩	1.71	3.00E-03
1553909_x_at	FAM178A	⇧	1.71	3.00E-03
1562353_x_at	---	⇧	1.71	2.80E-03
232002_at	---	⇧	1.71	2.40E-03
240800_x_at	---	⇧	1.71	2.30E-03
226716_at	PRR12	⇧	1.71	2.30E-03
217625_x_at	LOC100506190	⇧	1.71	2.20E-03
203219_s_at	APRT	⇩	1.71	2.00E-03
234120_at	---	⇧	1.71	9.80E-04
242896_at	C2orf21	⇧	1.71	5.90E-04
216187_x_at	---	⇧	1.71	4.80E-04
242025_at	---	⇧	1.71	2.90E-04
207804_s_at	FCN2	⇩	1.71	2.70E-04
235792_x_at	PIK3C2A	⇧	1.71	2.20E-04
203079_s_at	CUL2	⇧	1.71	1.90E-04
240568_at	---	⇧	1.71	1.40E-04
219965_s_at	MAGIX	⇩	1.71	1.20E-04
229277_at	ADRB1	⇧	1.71	1.10E-04
AFFX-r2-Ec-bioB-5_at	---	⇩	1.71	2.34E-04
241938_at	QKI	⇧	1.70	0.045
232156_at	MUDENG	⇧	1.70	0.044
201164_s_at	PUM1	⇩	1.70	0.041
236974_at	---	⇧	1.70	0.039
202555_s_at	MYLK	⇩	1.70	0.037
224820_at	FAM36A	⇧	1.70	0.036
238446_at	SMA4	⇧	1.70	0.036
232174_at	---	⇧	1.70	0.035
237218_at	---	⇧	1.70	0.034
233359_at	---	⇧	1.70	0.033
241434_at	---	⇧	1.70	0.033
216384_x_at	LOC643287	⇧	1.70	0.032
214042_s_at	RPL22	⇩	1.70	0.030
201281_at	ADRM1	⇩	1.70	0.029
217677_at	PLEKHA2	⇧	1.70	0.028
201921_at	GNG10	⇧	1.70	0.026
206098_at	ZBTB6	⇩	1.70	0.025
208808_s_at	HMGB2	⇧	1.70	0.024
237077_at	---	⇧	1.70	0.023
225160_x_at	MDM2	⇩	1.70	0.023
227847_at	EPM2AIP1	⇧	1.71	1.70E-03
201532_at	PSMA3	⇩	1.70	0.023
240515_at	---	⇧	1.70	0.018
208310_s_at	C7orf28A/B	⇩	1.70	0.018
242760_x_at	PIGB	⇧	1.70	0.018
1570194_x_at	---	⇧	1.70	0.017
239187_at	C4orf30	⇩	1.70	0.017
1555653_at	HNRNPA3	⇧	1.70	0.017
208057_s_at	GLI2	⇩	1.70	0.016
221085_at	TNFSF15	⇧	1.70	0.015
244651_at	---	⇧	1.70	0.013
213462_at	NPAS2	⇩	1.70	0.013
242254_at	---	⇧	1.70	0.012
242797_x_at	---	⇧	1.70	0.012
215579_at	APOBEC3G	⇧	1.70	0.012
1554316_at	PGLS	⇧	1.70	0.012
1557571_at	VPS13D	⇧	1.70	0.012
230795_at	---	⇧	1.70	0.011
203643_at	ERF	⇧	1.70	0.011
239213_at	SERPINB1	⇧	1.70	0.011
244077_at	C10orf113	⇧	1.70	0.010
1565873_at	---	⇧	1.70	8.80E-03
215208_x_at	RPL35A	⇧	1.70	8.80E-03
210829_s_at	SSBP2	⇩	1.70	7.20E-03
234596_at	---	⇧	1.70	6.50E-03
201478_s_at	DKC1	⇩	1.70	6.20E-03
234306_s_at	SLAMF7	⇩	1.70	5.70E-03
211997_x_at	H3F3B	⇩	1.70	5.20E-03
1556951_at	---	⇧	1.70	4.40E-03
219929_s_at	ZFYVE21	⇩	1.70	4.40E-03
227068_at	PGK1	⇧	1.70	3.40E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test $p<0.05$, FC ≥ ±1.50]

241777_x_at	---	⇧	1.70	2.80E-03
241637_at	---	⇧	1.70	2.60E-03
224597_at	LOC647979	⇧	1.70	2.50E-03
1569129_s_at	C3orf38	⇧	1.70	2.30E-03
1560779_a_at	ZNF568	⇧	1.70	1.80E-03
243442_x_at	---	⇧	1.70	1.60E-03
238489_at	PRKAA2	⇧	1.70	1.30E-03
201510_at	ELF3	⇧	1.70	1.20E-03
1564444_at	LOC100130264	⇧	1.70	1.20E-03
244489_at	---	⇧	1.70	1.00E-03
222364_at	SLC44A1	⇧	1.70	9.60E-04
231695_at	---	⇧	1.70	9.50E-04
232215_x_at	PRR11	⇧	1.70	9.50E-04
217348_x_at	ARHGEF15	⇧	1.70	9.20E-04
236880_at	RAD52	⇧	1.70	9.10E-04
238474_at	NUP43	⇧	1.70	8.50E-04
1554039_at	C14orf159	⇧	1.70	7.00E-04
1556072_at	C22orf37	⇧	1.70	6.60E-04
211625_s_at	DRD3	⇧	1.70	3.00E-04
239934_x_at	---	⇧	1.70	2.40E-04
1553282_at	C21orf128	⇩	1.70	2.10E-04
213624_at	SMPDL3A	⇧	1.70	7.50E-05
212051_at	WIPF2	⇩	1.70	7.30E-05
201616_s_at	CALD1	⇧	1.70	6.90E-05
240621_at	---	⇧	1.70	3.10E-05
1561101_at	LOC153469	⇩	1.70	2.60E-05
240155_x_at	ZNF273	⇧	1.69	0.048
243546_at	---	⇧	1.69	0.047
219364_at	DHX58	⇩	1.69	0.045
239432_at	FLJ31306	⇧	1.69	0.045
215992_s_at	RAPGEF2	⇧	1.69	0.043
209917_s_at	TP53TG1	⇩	1.69	0.038
233415_at	---	⇧	1.69	0.035
243282_at	CCDC93	⇧	1.69	0.032
201534_s_at	UBL3	⇧	1.69	0.032
201326_at	CCT6A	⇩	1.69	0.031
226217_at	SLC30A7	⇧	1.69	0.031
236472_at	---	⇧	1.69	0.028
222887_s_at	TMEM127	⇩	1.69	0.028
207460_at	GZMM	⇧	1.69	0.024
1560156_at	---	⇧	1.69	0.020
239549_at	---	⇧	1.69	0.017
220694_at	DDEF1IT1	⇧	1.69	0.015
214153_at	ELOVL5	⇧	1.69	0.015
243985_at	GTF2A2	⇧	1.69	0.015
1568857_a_at	NBR1	⇧	1.69	0.015
205946_at	VIPR2	⇩	1.69	0.015
1557504_at	---	⇧	1.69	0.014
214808_at	---	⇧	1.69	0.013
201846_s_at	RYBP	⇧	1.69	0.013
239212_at	LTV1	⇧	1.69	0.012
206674_at	FLT3	⇩	1.69	0.011
224252_s_at	FXYD5	⇩	1.69	0.011
234884_x_at	IGL	⇩	1.69	0.011
209244_s_at	KIF1C	⇧	1.69	0.011
236470_at	---	⇧	1.69	0.010
218061_at	MEA1	⇩	1.69	0.010
201844_s_at	RYBP	⇧	1.69	0.010
237414_at	F7	⇧	1.69	9.90E-03
1555088_x_at	STAT5B	⇧	1.69	9.20E-03
242554_at	TPCN2	⇧	1.69	8.50E-03
224580_at	SLC38A1	⇧	1.69	7.30E-03
235626_at	CAMK1D	⇧	1.69	6.90E-03
221530_s_at	BHLHE41	⇩	1.69	6.50E-03
216040_x_at	---	⇧	1.69	6.30E-03
1554608_at	TGOLN2	⇧	1.69	6.00E-03
1565162_s_at	MGST1	⇩	1.69	5.40E-03
235058_at	---	⇧	1.69	5.00E-03
229265_at	SKI	⇧	1.69	4.80E-03
232962_x_at	---	⇧	1.69	4.30E-03
1558672_at	---	⇧	1.69	4.30E-03
204181_s_at	ZBTB43	⇧	1.69	3.70E-03
1565752_at	FGD2	⇧	1.69	3.40E-03
1570329_at	---	⇧	1.69	3.30E-03
223043_at	TMEM85	⇩	1.69	3.30E-03
202156_s_at	CUGBP2	⇧	1.69	3.10E-03
230490_x_at	RSU1	⇧	1.69	2.90E-03
1564317_at	---	⇧	1.69	2.80E-03
1569999_at	---	⇧	1.69	2.80E-03
1556336_at	RBMX	⇧	1.69	2.10E-03
204768_s_at	FEN1	⇩	1.69	2.00E-03
1566887_x_at	---	⇧	1.69	1.90E-03
233428_at	---	⇧	1.69	1.50E-03
230784_at	PRAC	⇧	1.69	1.50E-03
232685_at	---	⇧	1.69	1.30E-03
215179_x_at	PGF	⇧	1.69	1.20E-03
231212_x_at	---	⇧	1.69	9.70E-04
216811_at	---	⇧	1.69	8.00E-04
215850_s_at	NDUFA5	⇧	1.69	6.70E-04
236519_at	C9orf135	⇧	1.69	6.60E-04
222015_at	CSNK1E	⇧	1.69	5.50E-04
230125_at	GUSB	⇧	1.69	4.30E-04
243120_at	---	⇧	1.69	2.70E-04
1570229_at	---	⇧	1.69	2.60E-04
203630_s_at	COG5	⇧	1.69	2.50E-04
1561140_at	---	⇧	1.69	2.30E-04

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

240909_at	---	⇧	1.69	1.70E-04
231965_at	FAM113A	⇧	1.69	4.60E-05
209689_at	CCDC93	⇩	1.68	0.046
224412_s_at	TRPM6	⇩	1.68	0.044
232582_at	---	⇧	1.68	0.043
1570038_at	ZNF595	⇩	1.68	0.043
209177_at	NDUFAF3	⇩	1.68	0.040
240829_at	---	⇧	1.68	0.034
217185_s_at	ZNF259	⇩	1.68	0.034
213528_at	C1orf156	⇩	1.68	0.029
202112_at	VWF	⇩	1.68	0.029
223717_s_at	ACRBP	⇩	1.68	0.028
225961_at	KLHDC5	⇧	1.68	0.026
209207_s_at	SEC22B	⇧	1.68	0.025
211992_at	WNK1	⇧	1.68	0.025
224102_at	P2RY12	⇩	1.68	0.023
230958_s_at	---	⇧	1.68	0.022
1570111_at	C14orf48	⇧	1.68	0.022
230689_at	---	⇧	1.68	0.021
232500_at	C20orf74	⇧	1.68	0.021
215109_at	RC3H1	⇧	1.68	0.020
223173_at	SPNS1	⇧	1.68	0.020
206661_at	DBF4B	⇧	1.68	0.019
206416_at	ZNF205	⇧	1.68	0.019
201163_s_at	IGFBP7	⇧	1.68	0.018
212044_s_at	RPL27A	⇧	1.68	0.018
238356_at	DOCK11	⇧	1.68	0.017
212843_at	NCAM1	⇧	1.68	0.016
236557_at	ZBTB38	⇧	1.68	0.016
241697_at	---	⇩	1.68	0.015
212107_s_at	DHX9	⇧	1.68	0.015
221651_x_at	IGK	⇩	1.68	0.015
212667_at	SPARC	⇩	1.68	0.015
1557341_x_at	---	⇧	1.68	0.013
1562300_at	---	⇧	1.68	0.013
239070_at	---	⇧	1.68	0.013
233904_at	---	⇧	1.68	0.013
1555241_at	C8orf59	⇧	1.68	0.013
206398_s_at	CD19	⇩	1.68	0.012
201694_s_at	EGR1	⇩	1.68	0.010
217620_s_at	PIK3CB	⇧	1.68	0.010
1556817_a_at	---	⇩	1.68	7.20E-03
203582_s_at	RAB4A	⇩	1.68	7.00E-03
218618_s_at	FNDC3B	⇩	1.68	6.20E-03
201627_s_at	INSIG1	⇩	1.68	6.10E-03
217480_x_at	---	⇩	1.68	5.70E-03
243379_at	---	⇧	1.68	5.10E-03
1563643_at	---	⇧	1.68	4.10E-03
1562579_at	---	⇧	1.68	4.00E-03
210601_at	CDH6	⇧	1.68	3.50E-03
232498_at	HEATR7A	⇧	1.68	3.00E-03
1566207_at	TCEA1	⇧	1.68	2.60E-03
237561_x_at	---	⇧	1.68	2.30E-03
214395_x_at	EEF1D	⇩	1.68	2.30E-03
227130_s_at	TLE1	⇩	1.68	2.20E-03
224029_x_at	SCN11A	⇧	1.68	2.10E-03
201278_at	DAB2	⇩	1.68	2.00E-03
234565_x_at	---	⇧	1.68	1.80E-03
244822_at	GART	⇧	1.68	1.70E-03
217434_at	MC2R	⇧	1.68	1.70E-03
241695_s_at	---	⇧	1.68	1.50E-03
204403_x_at	FAM115A	⇧	1.68	1.30E-03
1553472_at	FLJ32955	⇩	1.68	1.10E-03
220368_s_at	SMEK1	⇧	1.68	9.40E-04
1563310_a_at	---	⇧	1.68	9.30E-04
1554657_a_at	C20orf26	⇧	1.68	7.20E-04
1568813_at	LOC100506392	⇧	1.68	6.70E-04
244714_at	---	⇧	1.68	5.00E-04
241066_at	ZNF449	⇧	1.68	3.30E-04
244533_at	PTPN14	⇧	1.68	1.90E-04
1560033_at	MCCC2	⇧	1.68	7.30E-05
208115_x_at	C10orf137	⇩	1.68	4.50E-05
241905_at	PIK3C2A	⇧	1.67	0.048
1566166_at	---	⇧	1.67	0.046
227854_at	---	⇧	1.67	0.044
1558586_at	ZNF33B	⇧	1.67	0.044
208782_at	FSTL1	⇩	1.67	0.043
1552318_at	GIMAP1	⇧	1.67	0.042
203168_at	ATF6B	⇧	1.67	0.041
205921_s_at	SLC6A6	⇧	1.67	0.037
204028_s_at	RABGAP1	⇧	1.67	0.035
232705_at	LRRFIP2	⇧	1.67	0.034
233866_at	KLHL5	⇧	1.67	0.033
207794_at	CCR2	⇩	1.67	0.032
231920_s_at	CSNK1G1	⇧	1.67	0.032
220960_x_at	RPL22	⇩	1.67	0.030
230337_at	SOS1	⇧	1.67	0.030
223490_s_at	EXOSC3	⇩	1.67	0.028
1553906_s_at	FGD2	⇧	1.67	0.028
244047_at	---	⇧	1.67	0.026
236505_at	NUP62	⇧	1.67	0.022
232344_at	---	⇧	1.67	0.021
216657_at	ATXN3	⇧	1.67	0.021
210222_s_at	RTN1	⇩	1.67	0.021
239723_at	---	⇧	1.67	0.020
229312_s_at	GKAP1	⇧	1.67	0.018

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

205628_at	PRIM2	⇧	1.67	0.018	243153_at	CDK5RAP2	⇧	1.67	3.70E-03	215650_at	---	⇧	1.66	2.10E-03
209484_s_at	NSL1	⇧	1.67	0.017	240168_at	XPO7	⇧	1.67	3.60E-03	213457_at	MFHAS1	⇧	1.66	0.048
204929_s_at	VAMP5	⇩	1.67	0.017	233128_at	---	⇧	1.67	3.50E-03	228655_at	---	⇧	1.66	0.046
235060_at	LOC100190986	⇧	1.67	0.016	210663_s_at	KYNU	⇩	1.67	3.30E-03	238462_at	UBASH3B	⇩	1.66	0.040
224919_at	MRPS6	⇩	1.67	0.016	206355_at	GNAL	⇧	1.67	3.00E-03	202947_s_at	GYPC	⇧	1.66	0.039
231357_at	CLEC12B	⇧	1.67	0.015	243760_at	LOC650794	⇧	1.67	2.90E-03	1555363_s_at	LOC284440	⇧	1.66	0.039
226122_at	PLEKHG1	⇩	1.67	0.015	206330_s_at	SHC3	⇩	1.67	2.80E-03	241489_at	---	⇧	1.66	0.038
218354_at	TRAPPC2L	⇩	1.67	0.015	228443_s_at	SETD8	⇧	1.67	2.70E-03	203280_at	SAFB2	⇧	1.66	0.038
240302_at	---	⇧	1.67	0.014	242889_x_at	LOC645431	⇧	1.67	2.60E-03	242140_at	ERVK3-1	⇧	1.66	0.036
1564165_at	PRKRIP1	⇧	1.67	0.013	222195_s_at	C9orf156	⇩	1.67	2.40E-03	234764_x_at	IGL	⇩	1.66	0.036
1554539_a_at	RHOF	⇩	1.67	0.013	227398_s_at	MIDN	⇩	1.67	2.40E-03	201416_at	SOX4	⇩	1.66	0.033
213956_at	CEP350	⇧	1.67	0.012	1566278_at	---	⇧	1.67	2.10E-03	242216_at	---	⇧	1.66	0.032
1563471_at	KIAA1632	⇧	1.67	0.012	205971_s_at	CTRB1/B2	⇧	1.67	2.10E-03	57739_at	DND1	⇧	1.66	0.031
1561015_at	---	⇧	1.67	0.011	204232_at	FCER1G	⇩	1.67	1.80E-03	244031_at	---	⇧	1.66	0.029
1555460_a_at	SLC39A6	⇩	1.67	0.011	225940_at	EIF4E3	⇧	1.67	1.70E-03	203401_at	PRPS2	⇧	1.66	0.027
226934_at	CPSF6	⇧	1.67	0.010	208548_at	IFNA6	⇧	1.67	1.70E-03	230292_at	---	⇧	1.66	0.026
212188_at	KCTD12	⇧	1.67	9.80E-03	215968_at	---	⇧	1.67	1.60E-03	201211_s_at	DDX3X	⇩	1.66	0.025
210553_x_at	PCSK6	⇧	1.67	9.60E-03	210618_at	RAP1GAP	⇧	1.67	1.30E-03	234789_at	---	⇧	1.66	0.022
212880_at	WDR7	⇩	1.67	9.60E-03	224321_at	TMEFF2	⇩	1.67	1.30E-03	239780_at	---	⇧	1.66	0.022
214633_at	SOX3	⇧	1.67	9.10E-03	242949_x_at	CCDC157	⇧	1.67	1.10E-03	201353_s_at	BAZ2A	⇧	1.66	0.022
237999_at	---	⇧	1.67	8.60E-03	215063_x_at	LRRC40	⇧	1.67	8.30E-04	225526_at	MKLN1	⇩	1.66	0.021
215162_at	GARNL1	⇧	1.67	7.80E-03	238690_at	---	⇩	1.67	7.20E-04	202753_at	PSMD6	⇩	1.66	0.021
202050_s_at	ZMYM4	⇩	1.67	7.60E-03	224137_at	CACNG7	⇧	1.67	6.80E-04	221671_x_at	IGK	⇩	1.66	0.018
224582_s_at	NUCKS1	⇧	1.67	7.40E-03	219206_x_at	TMBIM4	⇧	1.67	6.00E-04	201986_at	MED13	⇧	1.66	0.018
244154_at	DDHD1	⇧	1.67	6.90E-03	207419_s_at	RAC2	⇩	1.67	5.40E-04	1557759_at	ATP5SL	⇧	1.66	0.017
1563263_at	PLCG2	⇧	1.67	6.20E-03	231162_at	CLDND2	⇧	1.67	3.40E-04	213897_s_at	MRPL23	⇩	1.66	0.017
1555439_at	GTF3C3	⇧	1.67	5.80E-03	1569409_x_at	---	⇧	1.67	2.50E-04	224760_at	SP1	⇧	1.66	0.017
216751_at	---	⇧	1.67	5.00E-03	233515_at	---	⇧	1.67	2.40E-04	1554670_at	GGA1	⇧	1.66	0.014
228225_at	PXMP3	⇧	1.67	4.60E-03	230216_at	C12orf51	⇧	1.67	5.00E-05	227025_at	PPHLN1	⇧	1.66	0.013
204817_at	ESPL1	⇧	1.67	4.30E-03	231349_at	GPR150	⇧	1.66	0.011	204240_s_at	SMC2	⇩	1.66	0.013
1570032_at	AP3B2	⇧	1.67	4.00E-03	203380_x_at	SFRS5	⇧	1.66	5.51E-04	221166_at	FGF23	⇩	1.66	0.012
233775_x_at	LOC100289333	⇧	1.67	4.00E-03	210120_s_at	RANBP3	⇧	1.66	0.012	232112_at	RALGPS2	⇩	1.66	0.012

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

212762_s_at	TCF7L2	⇧	1.66	0.012
208899_x_at	ATP6V1D	⇩	1.66	0.011
205322_s_at	MTF1	⇧	1.66	0.011
240347_at	---	⇧	1.66	0.010
1557621_at	KCP	⇧	1.66	9.70E-03
221553_at	MAGT1	⇧	1.66	9.70E-03
240875_at	C17orf68	⇧	1.66	9.60E-03
1560199_x_at	LOC728153	⇧	1.66	9.60E-03
1557905_s_at	CD44	⇩	1.66	8.30E-03
209329_x_at	HIGD2A	⇩	1.66	7.80E-03
1555994_at	DIAPH3-AS1	⇧	1.66	7.60E-03
225331_at	CCDC50	⇩	1.66	7.10E-03
220905_at	---	⇧	1.66	6.70E-03
227921_at	---	⇩	1.66	6.60E-03
206429_at	F2RL1	⇩	1.66	6.30E-03
1566646_at	LOC149086	⇧	1.66	6.20E-03
202105_at	IGBP1	⇩	1.66	5.90E-03
1564424_at	---	⇧	1.66	5.80E-03
208278_s_at	---	⇧	1.66	5.60E-03
218336_at	PFDN2	⇩	1.66	4.80E-03
213794_s_at	NGDN	⇩	1.66	4.70E-03
209645_s_at	ALDH1B1	⇩	1.66	4.50E-03
231884_at	CNTROB	⇧	1.66	4.50E-03
224606_at	KLF6	⇧	1.66	4.00E-03
208793_x_at	SMARCA4	⇩	1.66	4.00E-03
201688_s_at	TPD52	⇩	1.66	3.70E-03
211962_s_at	ZFP36L1	⇧	1.66	3.70E-03
211318_s_at	RAE1	⇩	1.66	3.60E-03
214535_s_at	ADAMTS2	⇧	1.66	3.50E-03
238884_at	---	⇧	1.66	3.30E-03
216509_x_at	MLLT10	⇧	1.66	3.10E-03
1554583_a_at	C12orf72	⇧	1.66	2.80E-03
219341_at	CLN8	⇧	1.66	2.80E-03
215609_at	---	⇧	1.66	2.60E-03
216463_at	---	⇧	1.66	2.60E-03
234283_at	C22orf28	⇧	1.66	2.30E-03
233182_x_at	ATXN3	⇧	1.66	1.90E-03
231992_x_at	LOC493754	⇧	1.66	1.70E-03
206048_at	OVOL2	⇧	1.66	1.50E-03
214605_x_at	GPR1	⇧	1.66	1.30E-03
232942_at	PYROXD2	⇧	1.66	1.30E-03
208246_x_at	---	⇧	1.66	1.20E-03
240548_at	---	⇧	1.66	1.10E-03
232420_x_at	LOC286260	⇧	1.66	1.00E-03
204590_x_at	VPS33A	⇧	1.66	9.10E-04
1552432_at	MFSD6L	⇧	1.66	8.50E-04
1564635_a_at	FHAD1	⇩	1.66	8.10E-04
1559807_at	---	⇧	1.66	7.80E-04
232921_at	KIAA1549	⇧	1.66	6.30E-04
220838_at	EXD3	⇧	1.66	6.00E-04
215404_x_at	FGFR1	⇧	1.66	4.50E-04
206334_at	LIPF	⇧	1.66	4.40E-04
217120_s_at	MED14	⇧	1.66	4.10E-04
220955_x_at	RAB23	⇧	1.66	3.20E-04
1555717_at	---	⇧	1.66	2.50E-04
233013_x_at	LOC220906	⇧	1.66	2.50E-04
221250_s_at	MXD3	⇧	1.66	1.50E-04
232083_at	KIF16B	⇧	1.66	1.40E-04
236410_x_at	---	⇧	1.66	1.30E-04
1569983_at	---	⇧	1.66	1.10E-04
204977_at	DDX10	⇩	1.66	1.10E-04
215072_x_at	C10orf137	⇩	1.66	5.70E-05
223189_x_at	MLL5	⇧	1.65	0.048
234649_at	---	⇧	1.65	0.046
208962_s_at	FADS1	⇩	1.65	0.045
208949_s_at	LGALS3	⇧	1.65	0.043
242521_at	LOC100505812	⇧	1.65	0.042
225644_at	CCDC117	⇧	1.65	0.041
218402_s_at	HPS4	⇩	1.65	0.034
224332_s_at	MRPL43	⇩	1.65	0.034
1558105_a_at	SLC9A7	⇩	1.65	0.033
242080_at	---	⇧	1.65	0.032
209006_s_at	C1orf63	⇧	1.65	0.032
210527_x_at	TUBA3C	⇩	1.65	0.032
239804_at	---	⇧	1.65	0.031
243431_at	---	⇧	1.65	0.031
1560303_at	FKBP4	⇩	1.65	0.030
235093_at	PEX13	⇧	1.65	0.030
208074_s_at	AP2S1	⇩	1.65	0.029
201444_s_at	ATP6AP2	⇩	1.65	0.027
215013_s_at	USP34	⇧	1.65	0.027
1557339_at	---	⇧	1.65	0.022
223466_x_at	COL4A3BP	⇧	1.65	0.021
244144_at	SYNE1	⇧	1.65	0.021
216614_at	---	⇧	1.65	0.020
238700_at	PIAS2	⇧	1.65	0.020
203760_s_at	SLA	⇧	1.65	0.020
203745_at	HCCS	⇧	1.65	0.019
1553123_at	WDR62	⇧	1.65	0.019
234723_x_at	---	⇧	1.65	0.018
236367_at	SMG7	⇧	1.65	0.017
1560334_at	MEGF11	⇧	1.65	0.016
216278_at	---	⇧	1.65	0.015
205690_s_at	BUD31	⇩	1.65	0.015
227678_at	XRCC6BP1	⇩	1.65	0.015
206976_s_at	HSPH1	⇩	1.65	0.012

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208698_s_at	NONO	⇧	1.65	0.012	227651_at	NACC1	⇧	1.65	1.00E-03	224707_at	C5orf32	⇧	1.64	0.029
236703_at	NT5C2	⇧	1.65	0.012	208082_x_at	MKRN1	⇧	1.65	9.00E-04	243918_at	---	⇩	1.64	0.028
49306_at	RASSF4	⇧	1.65	0.012	229988_at	---	⇧	1.65	8.70E-04	216890_at	---	⇩	1.64	0.026
218833_at	ZAK	⇧	1.65	0.011	1570632_at	---	⇧	1.65	8.00E-04	200757_s_at	CALU	⇧	1.64	0.025
236732_at	---	⇧	1.65	9.20E-03	208476_s_at	FRMD4A	⇧	1.65	7.90E-04	1556553_at	---	⇧	1.64	0.024
202334_s_at	UBE2B	⇧	1.65	8.80E-03	216875_x_at	HAB1	⇧	1.65	6.00E-04	205789_at	CD1D	⇩	1.64	0.023
1557505_a_at	---	⇧	1.65	8.30E-03	243474_at	---	⇧	1.65	5.90E-04	208909_at	UQCRFS1	⇩	1.64	0.022
1552607_at	CXorf52	⇧	1.65	6.30E-03	207822_at	FGFR1	⇧	1.65	5.50E-04	239151_at	---	⇧	1.64	0.021
223439_at	NKAP	⇩	1.65	5.90E-03	211703_s_at	TM2D1	⇩	1.65	5.50E-04	223739_at	PADI1	⇩	1.64	0.021
244611_at	MED13	⇧	1.65	4.80E-03	236850_at	CAPRIN1	⇧	1.65	3.70E-04	232284_at	PSMD6	⇧	1.64	0.020
235317_at	LOC284454	⇧	1.65	4.40E-03	215048_at	ZNF280B	⇩	1.65	3.70E-04	224365_s_at	TIGD7	⇩	1.64	0.020
1552400_a_at	C15orf27	⇩	1.65	4.30E-03	236772_s_at	---	⇧	1.65	3.50E-04	1569500_at	---	⇧	1.64	0.019
244197_x_at	---	⇧	1.65	4.20E-03	1566882_at	---	⇧	1.65	2.30E-04	204050_s_at	CLTA	⇩	1.64	0.019
216110_x_at	---	⇧	1.65	4.10E-03	227095_at	LEPROT	⇧	1.65	2.30E-04	227992_s_at	NCRNA00085	⇧	1.64	0.019
210156_s_at	PCMT1	⇩	1.65	3.80E-03	209927_s_at	C1orf77	⇩	1.65	2.20E-04	223743_s_at	MRPL4	⇩	1.64	0.017
232877_at	---	⇧	1.65	3.50E-03	1553887_at	FLJ40235	⇧	1.65	2.00E-04	223638_at	NBPF3	⇩	1.64	0.015
204221_x_at	GLIPR1	⇧	1.65	3.10E-03	211600_at	PTPRO	⇧	1.65	1.50E-04	209328_x_at	HIGD2A	⇩	1.64	0.014
233868_x_at	ADAM33	⇧	1.65	3.00E-03	212106_at	FAF2	⇧	1.65	1.10E-04	232150_at	---	⇧	1.64	0.013
226520_at	LCOR	⇧	1.65	3.00E-03	210667_s_at	C21orf33	⇩	1.65	1.80E-05	242490_at	LOC100653004	⇧	1.64	0.013
210830_s_at	PON2	⇩	1.65	3.00E-03	216814_at	---	⇩	1.65	8.80E-06	200750_s_at	RAN	⇩	1.64	0.013
233721_x_at	---	⇧	1.65	2.80E-03	AFFX-r2-Ec-bioC-3_at	---	⇩	1.64	1.59E-04	1564729_at	---	⇧	1.64	0.012
210920_x_at	---	⇧	1.65	2.40E-03	213154_s_at	BICD2	⇩	1.64	0.048	238130_at	NFATC2IP	⇧	1.64	0.011
216733_s_at	GATM	⇩	1.65	2.40E-03	240939_x_at	---	⇧	1.64	0.045	243909_x_at	GUSBL2	⇩	1.64	0.010
1560499_at	C14orf64	⇧	1.65	2.30E-03	244443_at	CHD2	⇧	1.64	0.042	234140_s_at	STIM2	⇩	1.64	0.010
215038_s_at	SETD2	⇩	1.65	2.20E-03	223705_s_at	GPBP1	⇩	1.64	0.039	204203_at	CEBPG	⇩	1.64	9.90E-03
212266_s_at	SFRS5	⇧	1.65	1.90E-03	236908_at	---	⇧	1.64	0.035	215529_x_at	DIP2A	⇧	1.64	9.60E-03
215067_x_at	PRDX2	⇧	1.65	1.70E-03	239035_at	MTHFR	⇧	1.64	0.035	224495_at	TMEM107	⇧	1.64	7.20E-03
1563565_at	INPP5B	⇧	1.65	1.60E-03	227208_at	CCDC84	⇧	1.64	0.033	238943_at	FIBCD1	⇧	1.64	7.00E-03
206967_at	CCNT1	⇧	1.65	1.50E-03	201055_s_at	HNRNPA0	⇧	1.64	0.033	221547_at	PRPF18	⇩	1.64	6.90E-03
233087_at	FBXL17	⇧	1.65	1.10E-03	223565_at	MGC29506	⇩	1.64	0.032	243170_at	---	⇧	1.64	6.30E-03
233296_x_at	---	⇧	1.65	1.00E-03	230395_at	---	⇧	1.64	0.031	233487_s_at	LRRC8A	⇧	1.64	6.10E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

221434_s_at	C14orf156	⇩	1.64	6.00E-03	205832_at	CPA4	⇧	1.64	5.40E-05	218081_at	C20orf27	⇧	1.63	0.018
212533_at	WEE1	⇧	1.64	6.00E-03	1565558_at	---	⇧	1.64	4.80E-05	242369_x_at	---	⇧	1.63	0.017
206500_s_at	C14orf106	⇧	1.64	5.90E-03	1554960_at	C1orf110	⇧	1.64	2.30E-05	1562497_at	---	⇧	1.63	0.017
234938_at	BACH1	⇧	1.64	5.30E-03	1566606_a_at	TEX9	⇧	1.64	2.10E-05	231727_s_at	MIF4GD	⇩	1.63	0.017
209105_at	NCOA1	⇩	1.64	4.70E-03	212141_at	MCM4	⇩	1.64	1.80E-05	237264_at	---	⇧	1.63	0.016
1554441_a_at	WAPAL	⇩	1.64	4.40E-03	224297_s_at	SPTBN4	⇧	1.64	4.40E-07	1569540_at	---	⇧	1.63	0.014
244837_at	---	⇧	1.64	4.20E-03	203594_at	RTCD1	⇩	1.63	0.046	1553843_at	C10orf67	⇧	1.63	0.014
234408_at	IL17F	⇩	1.64	4.00E-03	241755_at	UQCRC2	⇧	1.63	0.046	214965_at	SPATA2L	⇧	1.63	0.014
1555157_at	---	⇧	1.64	3.30E-03	222326_at	---	⇧	1.63	0.044	212302_at	RTF1	⇧	1.63	0.013
205829_at	HSD17B1	⇧	1.64	3.30E-03	1566342_at	SOD2	⇩	1.63	0.043	223461_at	TBC1D7	⇩	1.63	0.013
224494_x_at	HSD17B14	⇧	1.64	3.30E-03	242202_at	---	⇧	1.63	0.041	1570192_at	---	⇧	1.63	0.012
210253_at	HTATIP2	⇧	1.64	2.60E-03	1556035_s_at	ZNF207	⇧	1.63	0.041	1563513_at	SYTL4	⇧	1.63	0.012
202417_at	KEAP1	⇧	1.64	2.40E-03	1556338_at	---	⇧	1.63	0.040	244835_at	C16orf52	⇧	1.63	0.010
231945_at	FILIP1	⇧	1.64	2.30E-03	216557_x_at	IGH	⇩	1.63	0.039	240363_at	ANK1	⇧	1.63	9.90E-03
241301_at	---	⇧	1.64	1.80E-03	230751_at	WNT4	⇩	1.63	0.037	209153_s_at	TCF3	⇧	1.63	9.30E-03
236707_at	DAPP1	⇧	1.64	1.80E-03	200638_s_at	YWHAZ	⇧	1.63	0.037	206181_at	SLAMF1	⇩	1.63	8.60E-03
1569668_at	---	⇧	1.64	1.70E-03	219474_at	C3orf52	⇧	1.63	0.035	200862_at	DHCR24	⇩	1.63	8.40E-03
202613_at	CTPS	⇩	1.64	1.40E-03	220529_at	FLJ11710	⇧	1.63	0.033	232754_at	---	⇧	1.63	7.20E-03
233958_at	---	⇧	1.64	1.30E-03	232963_at	---	⇧	1.63	0.032	242355_at	CRAMP1L	⇧	1.63	6.90E-03
243180_at	---	⇧	1.64	1.20E-03	1557910_at	HSP90AB1	⇩	1.63	0.032	244814_at	UGGT1	⇩	1.63	6.80E-03
224177_s_at	CXorf26	⇩	1.64	1.10E-03	208887_at	EIF3G	⇩	1.63	0.031	201728_s_at	KIAA0100	⇩	1.63	5.40E-03
243525_at	---	⇧	1.64	9.40E-04	229119_s_at	ZSWIM7	⇩	1.63	0.031	242377_x_at	THUMPD3	⇧	1.63	4.90E-03
243801_x_at	MRPL30	⇧	1.64	7.00E-04	244599_at	---	⇧	1.63	0.030	1566480_x_at	FLJ35848	⇧	1.63	4.00E-03
217713_x_at	---	⇧	1.64	6.90E-04	208670_s_at	EID1	⇧	1.63	0.030	238502_at	---	⇧	1.63	3.90E-03
242311_x_at	---	⇧	1.64	6.70E-04	223737_x_at	CHST9	⇩	1.63	0.027	241851_x_at	LOC100130429	⇧	1.63	3.80E-03
1569921_at	---	⇧	1.64	5.20E-04	216068_at	---	⇧	1.63	0.025	239815_at	---	⇧	1.63	3.70E-03
209639_s_at	RGS12	⇧	1.64	4.20E-04	1554816_at	ASTN2	⇧	1.63	0.025	244722_at	---	⇧	1.63	3.70E-03
241302_at	---	⇩	1.64	3.50E-04	239876_at	---	⇧	1.63	0.023	212863_x_at	CTBP1	⇧	1.63	3.70E-03
1556345_s_at	---	⇧	1.64	3.20E-04	223175_s_at	FEM1A	⇧	1.63	0.022	216768_x_at	TTC38	⇧	1.63	3.30E-03
1562415_a_at	SPOCD1	⇧	1.64	3.20E-04	225177_at	RAB11FIP1	⇩	1.63	0.021	243147_x_at	---	⇧	1.63	3.10E-03
228541_x_at	---	⇧	1.64	1.90E-04	231017_at	STK11	⇧	1.63	0.020	216883_x_at	PDE6D	⇩	1.63	2.90E-03
1564391_at	---	⇩	1.64	6.80E-05	1557486_at	---	⇧	1.63	0.018	214816_x_at	C19orf40	⇧	1.63	2.70E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

237960_at	---	⇩	1.63	2.50E-03	222113_s_at	EPS15L1	⇧	1.62	0.041	210565_at	GCGR	⇩	1.62	9.00E-03
226027_at	C9orf119	⇩	1.63	2.30E-03	219049_at	CSGALNACT1	⇩	1.62	0.040	216527_at	---	⇧	1.62	8.90E-03
217957_at	C16orf80	⇩	1.63	1.90E-03	218566_s_at	CHORDC1	⇧	1.62	0.037	217179_x_at	---	⇩	1.62	8.60E-03
223104_at	JAGN1	⇩	1.63	1.60E-03	222061_at	CD58	⇩	1.62	0.035	244326_at	---	⇩	1.62	8.10E-03
1553755_at	NXNL1	⇧	1.63	1.60E-03	236301_at	IKZF3	⇩	1.62	0.035	205272_s_at	PRH1/2	⇧	1.62	7.40E-03
1563120_at	LOC100129029	⇧	1.63	1.50E-03	238888_at	---	⇧	1.62	0.030	1561966_at	---	⇧	1.62	7.00E-03
213329_at	SRGAP2	⇩	1.63	1.50E-03	211086_x_at	NEK1	⇧	1.62	0.030	1557553_at	PPP1R12B	⇧	1.62	6.70E-03
228551_at	DENND5B	⇩	1.63	1.40E-03	203844_at	VHL	⇧	1.62	0.030	234886_at	TRBV24-1	⇩	1.62	6.40E-03
211776_s_at	EPB41L3	⇩	1.63	1.00E-03	204097_s_at	RBMX2	⇧	1.62	0.029	230528_s_at	MGC2752	⇧	1.62	6.10E-03
242398_x_at	---	⇧	1.63	9.90E-04	203403_s_at	RNF6	⇩	1.62	0.029	224467_s_at	PDCD2L	⇩	1.62	6.00E-03
241137_at	DPCR1	⇧	1.63	8.70E-04	236921_at	---	⇧	1.62	0.028	209182_s_at	C10orf10	⇧	1.62	5.50E-03
207953_at	RP5-886K2.1	⇧	1.63	8.10E-04	219236_at	PAQR6	⇧	1.62	0.028	228055_at	NAPSB	⇩	1.62	5.30E-03
226823_at	PHACTR4	⇩	1.63	5.20E-04	201810_s_at	SH3BP5	⇧	1.62	0.028	1559780_at	---	⇧	1.62	4.00E-03
201564_s_at	FSCN1	⇧	1.63	4.50E-04	1560426_at	C12orf55	⇧	1.62	0.025	1561653_at	---	⇧	1.62	3.60E-03
244626_at	---	⇧	1.63	3.30E-04	1570339_x_at	---	⇧	1.62	0.022	237475_x_at	CCDC152	⇧	1.62	3.50E-03
215383_x_at	SPG21	⇧	1.63	3.30E-04	242876_at	AKT3	⇧	1.62	0.021	214200_s_at	COL6A1	⇧	1.62	3.50E-03
220411_x_at	PODNL1	⇧	1.63	2.70E-04	213920_at	CUX2	⇩	1.62	0.021	233004_x_at	---	⇧	1.62	3.30E-03
228375_at	IGSF11	⇩	1.63	1.80E-04	1560358_at	PHKA2	⇧	1.62	0.021	1553551_s_at	ND2	⇧	1.62	3.00E-03
233148_at	PODN	⇩	1.63	1.40E-04	200749_at	RAN	⇧	1.62	0.021	229680_at	CCDC44	⇧	1.62	2.80E-03
220089_at	L2HGDH	⇧	1.63	1.20E-04	205427_at	ZNF354A	⇩	1.62	0.020	242229_at	NAPEPLD	⇧	1.62	2.70E-03
242730_at	MYRIP	⇧	1.63	1.20E-04	203747_at	AQP3	⇩	1.62	0.018	220539_at	C10orf92	⇩	1.62	2.60E-03
205010_at	GNL3L	⇧	1.63	9.10E-05	220925_at	MAK10	⇧	1.62	0.016	231770_x_at	C2orf86	⇧	1.62	2.60E-03
222087_at	PVT1	⇧	1.63	7.50E-05	221212_x_at	PBRM1	⇧	1.62	0.016	213899_at	METAP2	⇧	1.62	2.60E-03
212711_at	CAMSAP1	⇩	1.63	1.30E-05	222816_s_at	ZCCHC2	⇧	1.62	0.016	215861_at	---	⇧	1.62	2.30E-03
217210_at	---	⇩	1.63	6.90E-06	227154_at	IGSF21	⇩	1.62	0.015	232665_x_at	---	⇧	1.62	2.30E-03
222934_s_at	CLEC4E	⇩	1.62	0.049	1558527_at	---	⇧	1.62	0.014	220797_at	METT10D	⇩	1.62	2.30E-03
200067_x_at	SNX3	⇧	1.62	0.049	207914_x_at	EVX1	⇧	1.62	0.014	1553927_at	C7orf33	⇩	1.62	2.20E-03
202760_s_at	---	⇧	1.62	0.048	1569857_s_at	TPP2	⇧	1.62	0.013	215864_at	---	⇧	1.62	2.10E-03
231735_s_at	MALAT1	⇧	1.62	0.048	1566897_at	---	⇧	1.62	0.012	1562947_x_at	---	⇧	1.62	2.10E-03
202941_at	NDUFV2	⇩	1.62	0.046	231111_at	---	⇧	1.62	0.012	216136_at	---	⇧	1.62	2.10E-03
237875_at	---	⇧	1.62	0.043	200087_s_at	TMED2	⇧	1.62	0.011	201551_s_at	LAMP1	⇩	1.62	1.90E-03
221498_at	SNX27	⇩	1.62	0.043	237582_at	---	⇩	1.62	9.40E-03	233702_x_at	---	⇧	1.62	1.70E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

1555199_at	GOSR1	⇧	1.62	1.70E-03
228576_s_at	MXRA8	⇧	1.62	1.60E-03
219105_x_at	ORC6L	⇧	1.62	1.60E-03
1557342_a_at	LOC400931	⇧	1.62	1.40E-03
1568847_at	---	⇧	1.62	1.10E-03
1555811_at	ARHGDIB	⇩	1.62	1.10E-03
211277_x_at	APP	⇧	1.62	1.00E-03
201119_s_at	COX8A	⇩	1.62	8.80E-04
201199_s_at	PSMD1	⇩	1.62	7.50E-04
1564970_at	SETDB2	⇧	1.62	7.10E-04
206466_at	ACSBG1	⇧	1.62	6.30E-04
222012_at	C19orf72	⇩	1.62	6.00E-04
203091_at	FUBP1	⇧	1.62	5.60E-04
226053_at	MAP2K7	⇧	1.62	1.90E-04
215455_at	TIMELESS	⇧	1.62	1.70E-04
212924_s_at	LSM4	⇧	1.62	1.50E-04
234050_at	TAGAP	⇧	1.62	8.40E-05
233226_at	PTPN9	⇧	1.62	3.60E-05
AFFX-r2-Ec-bioB-M_at	---	⇩	1.61	7.88E-04
243054_at	---	⇧	1.61	0.048
213688_at	CALM1	⇧	1.61	0.047
208979_at	NCOA6	⇩	1.61	0.047
205560_at	PCSK5	⇩	1.61	0.047
209959_at	NR4A3	⇧	1.61	0.046
214794_at	PA2G4	⇩	1.61	0.043
239695_at	JAK1	⇧	1.61	0.041
233284_at	---	⇧	1.61	0.036
204490_s_at	CD44	⇩	1.61	0.036
243249_at	---	⇧	1.61	0.035
212582_at	OSBPL8	⇧	1.61	0.035
1553185_at	RASEF	⇧	1.61	0.035
228818_at	---	⇧	1.61	0.032
1562511_at	LYST	⇧	1.61	0.031
1553768_a_at	DCBLD1	⇧	1.61	0.029
225579_at	PQLC3	⇩	1.61	0.029
211637_x_at	IGH	⇩	1.61	0.028
210958_s_at	MAST4	⇩	1.61	0.028
218526_s_at	RANGRF	⇩	1.61	0.027
222790_s_at	RSBN1	⇧	1.61	0.027
214806_at	BICD1	⇧	1.61	0.025
202487_s_at	H2AFV	⇩	1.61	0.025
1564897_at	TNR	⇧	1.61	0.025
239577_at	---	⇧	1.61	0.024
221071_at	---	⇧	1.61	0.024
228993_s_at	NCRNA00081	⇧	1.61	0.023
232180_at	UGP2	⇧	1.61	0.023
219062_s_at	ZCCHC2	⇩	1.61	0.023
216096_s_at	NRXN1	⇧	1.61	0.022
201108_s_at	THBS1	⇩	1.61	0.022
234627_at	FLJ21408	⇩	1.61	0.020
201748_s_at	SAFB	⇧	1.61	0.020
244834_at	C1orf134	⇧	1.61	0.019
201252_at	PSMC4	⇩	1.61	0.019
205835_s_at	YTHDC2	⇩	1.61	0.019
213813_x_at	---	⇩	1.61	0.018
234442_at	---	⇩	1.61	0.017
239991_at	---	⇧	1.61	0.016
207820_at	ADH1A	⇩	1.61	0.016
212786_at	CLEC16A	⇩	1.61	0.016
208281_x_at	DAZ1-4	⇧	1.61	0.016
242829_x_at	FBXL3	⇧	1.61	0.016
221692_s_at	MRPL34	⇩	1.61	0.015
235152_at	---	⇧	1.61	0.014
217655_at	---	⇧	1.61	0.014
1561086_at	---	⇩	1.61	0.013
237502_at	CRLS1	⇧	1.61	0.013
220575_at	FAM106A	⇧	1.61	0.012
243677_at	GORASP1	⇩	1.61	0.012
220140_s_at	SNX11	⇩	1.61	0.012
212312_at	BCL2L1	⇧	1.61	0.011
235623_at	ELP2	⇧	1.61	0.011
214836_x_at	IGKC	⇩	1.61	0.011
239640_at	LOC401320	⇧	1.61	0.011
232097_at	TOX4	⇧	1.61	0.011
207134_x_at	TPSB2	⇧	1.61	0.011
234849_at	TRA	⇩	1.61	0.011
230599_at	---	⇧	1.61	0.010
233615_at	CGA	⇧	1.61	0.010
217868_s_at	METTL9	⇧	1.61	0.010
211367_s_at	CASP1	⇩	1.61	9.00E-03
1552291_at	PIGX	⇧	1.61	8.50E-03
217586_x_at	---	⇧	1.61	7.60E-03
238826_x_at	---	⇧	1.61	7.50E-03
208404_x_at	KCNJ5	⇧	1.61	6.70E-03
236248_x_at	TADA2B	⇧	1.61	6.30E-03
234765_at	---	⇧	1.61	5.90E-03
216101_at	---	⇧	1.61	4.90E-03
208576_s_at	HIST1H3B	⇩	1.61	4.30E-03
215810_x_at	DST	⇧	1.61	4.20E-03
206551_x_at	KLHL24	⇧	1.61	3.90E-03
237246_at	---	⇧	1.61	3.60E-03
209226_s_at	TNPO1	⇧	1.61	3.60E-03
234089_at	---	⇧	1.61	3.30E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

1554950_at	ACAN	⇧	1.61	3.30E-03	231116_at	---	⇧	1.60	0.033	226293_at	MED19	⇧	1.60	6.40E-03
207365_x_at	USP34	⇧	1.61	3.20E-03	236895_at	---	⇧	1.60	0.033	241947_at	LOC100233209	⇧	1.60	6.10E-03
237865_x_at	---	⇧	1.61	3.10E-03	209524_at	HDGFRP3	⇧	1.60	0.033	211495_x_at	TNFSF13	⇩	1.60	6.10E-03
217579_x_at	---	⇧	1.61	2.90E-03	234377_at	TRBV7-8	⇩	1.60	0.031	215191_at	---	⇧	1.60	4.90E-03
215200_x_at	---	⇧	1.61	2.80E-03	1569345_at	---	⇧	1.60	0.029	227087_at	INPP4A	⇧	1.60	4.20E-03
208066_s_at	GTF2B	⇩	1.61	2.80E-03	200723_s_at	CAPRIN1	⇩	1.60	0.029	201545_s_at	PABPN1	⇧	1.60	3.90E-03
223281_s_at	COX15	⇧	1.61	2.50E-03	222734_at	WARS2	⇩	1.60	0.029	232065_x_at	CENPL	⇧	1.60	3.80E-03
1552782_at	SLC44A5	⇧	1.61	2.40E-03	237800_at	---	⇧	1.60	0.021	210495_x_at	FN1	⇩	1.60	3.80E-03
234613_at	---	⇧	1.61	1.80E-03	1554388_at	VPS29	⇧	1.60	0.021	216064_s_at	AGA	⇩	1.60	3.70E-03
205820_s_at	APOC3	⇧	1.61	1.70E-03	215882_at	CEP152	⇩	1.60	0.018	209136_s_at	USP10	⇧	1.60	3.70E-03
234773_x_at	---	⇩	1.61	1.50E-03	209883_at	GLT25D2	⇧	1.60	0.017	223871_x_at	ING5	⇧	1.60	3.30E-03
207965_at	NEUROG3	⇩	1.61	1.50E-03	200734_s_at	ARF3	⇧	1.60	0.015	229038_at	CWF19L1	⇩	1.60	3.00E-03
1566096_x_at	---	⇧	1.61	1.30E-03	238809_at	C5orf51	⇩	1.60	0.015	202738_s_at	PHKB	⇩	1.60	3.00E-03
211672_s_at	ARPC4	⇩	1.61	8.10E-04	203076_s_at	SMAD2	⇩	1.60	0.015	215373_x_at	---	⇧	1.60	2.90E-03
229701_at	DNAJC9	⇧	1.61	7.90E-04	239341_at	---	⇩	1.60	0.014	234788_x_at	---	⇧	1.60	2.80E-03
214399_s_at	KRT4	⇧	1.61	7.90E-04	241790_at	---	⇧	1.60	0.014	216786_at	LOC159110	⇧	1.60	2.50E-03
243069_at	---	⇧	1.61	7.50E-04	208529_at	BTF3L1	⇩	1.60	0.014	1570210_x_at	SAPS2	⇧	1.60	2.50E-03
241857_at	---	⇧	1.61	7.50E-04	216705_s_at	ADA	⇩	1.60	0.013	237959_at	---	⇧	1.60	2.40E-03
220593_s_at	CCDC40	⇧	1.61	5.60E-04	224447_s_at	C17orf37	⇩	1.60	0.013	222824_at	NUDT5	⇧	1.60	2.40E-03
221678_at	ABHD6	⇩	1.61	3.20E-04	228625_at	CITED4	⇩	1.60	0.013	217810_x_at	LARS	⇧	1.60	2.30E-03
215403_at	---	⇧	1.61	1.90E-04	212647_at	RRAS	⇩	1.60	0.012	223912_s_at	CLN8	⇧	1.60	1.80E-03
1561512_at	---	⇧	1.61	6.80E-05	207917_at	---	⇧	1.60	0.011	221470_s_at	IL1F7	⇩	1.60	1.80E-03
1552311_a_at	RAX2	⇧	1.61	1.50E-05	203720_s_at	ERCC1	⇩	1.60	0.011	229650_s_at	C19orf42	⇩	1.60	1.70E-03
201546_at	TRIP12	⇩	1.60	0.048	214995_s_at	APOBEC3F/G	⇩	1.60	0.010	244541_x_at	---	⇧	1.60	1.60E-03
202308_at	SREBF1	⇩	1.60	0.047	243662_at	---	⇧	1.60	8.60E-03	208453_s_at	XPNPEP1	⇩	1.60	1.50E-03
1560013_at	PDXDC1	⇧	1.60	0.044	232163_at	WDR19	⇧	1.60	8.50E-03	1561905_at	---	⇩	1.60	1.40E-03
202929_s_at	DDT	⇩	1.60	0.043	1560104_at	---	⇧	1.60	8.40E-03	236903_at	---	⇩	1.60	1.30E-03
227606_s_at	STAMBPL1	⇩	1.60	0.043	232323_s_at	TTC17	⇧	1.60	8.20E-03	211827_s_at	KCND3	⇧	1.60	1.30E-03
1555659_a_at	TREML1	⇩	1.60	0.043	238738_at	PSMD7	⇧	1.60	8.00E-03	231625_at	SLC22A9	⇧	1.60	6.70E-04
209921_at	SLC7A11	⇩	1.60	0.042	219180_s_at	PEX26	⇧	1.60	7.30E-03	228038_at	SOX2	⇩	1.60	6.00E-04
218912_at	GCC1	⇩	1.60	0.040	225634_at	ZC3HAV1	⇩	1.60	6.70E-03	206420_at	IGSF6	⇧	1.60	5.50E-04
208854_s_at	STK24	⇩	1.60	0.035	225666_at	TMTC4	⇩	1.60	6.50E-03	235327_x_at	UBXN2A	⇧	1.60	5.50E-04

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

234201_x_at	---	⇧	1.60	4.90E-04
219393_s_at	AKT3	⇧	1.60	4.30E-04
241064_at	hCG_1776047	⇧	1.60	4.20E-04
231659_at	ST3GAL3	⇩	1.60	3.40E-04
238017_at	SDR16C5	⇩	1.60	3.20E-04
207515_s_at	POLR1C	⇩	1.60	1.70E-04
1558832_at	FLJ32224	⇧	1.60	1.50E-04
1555278_a_at	CKAP5	⇩	1.60	4.30E-05
AFFX-BioC-5_at	---	⇩	1.59	5.46E-05
1568815_a_at	DDX50	⇧	1.59	0.050
206237_s_at	NRG1	⇧	1.59	0.046
201896_s_at	PSRC1	⇩	1.59	0.045
202483_s_at	RANBP1	⇩	1.59	0.045
242433_at	ZBTB11	⇧	1.59	0.045
242836_at	---	⇧	1.59	0.042
224790_at	ASAP1	⇩	1.59	0.042
218439_s_at	COMMD10	⇩	1.59	0.042
216427_at	---	⇧	1.59	0.036
243256_at	MKNK1	⇧	1.59	0.035
212587_s_at	PTPRC	⇧	1.59	0.035
1560116_a_at	NEDD1	⇧	1.59	0.034
234131_at	---	⇧	1.59	0.031
238591_at	HEXDC	⇧	1.59	0.030
212770_at	TLE3	⇧	1.59	0.030
242512_at	MYO9A	⇧	1.59	0.027
208680_at	PRDX1	⇩	1.59	0.027
1557520_a_at	---	⇧	1.59	0.026
49878_at	PEX16	⇧	1.59	0.025
231255_at	MPRIP	⇧	1.59	0.023
210876_at	ANXA2P1	⇩	1.59	0.022
229065_at	SLC35F3	⇩	1.59	0.021
209461_x_at	WDR18	⇩	1.59	0.021
218011_at	UBL5	⇧	1.59	0.020
241351_at	---	⇧	1.59	0.019
219366_at	AVEN	⇩	1.59	0.019
239851_at	---	⇧	1.59	0.016
225269_s_at	RBMS1	⇧	1.59	0.016
1555883_s_at	SPIN3	⇧	1.59	0.016
232731_x_at	LOC100190938	⇧	1.59	0.015
227574_at	OBSL1	⇩	1.59	0.015
234731_at	---	⇧	1.59	0.014
200074_s_at	RPL14	⇩	1.59	0.014
218851_s_at	WDR33	⇩	1.59	0.014
201307_at	SEPT11	⇩	1.59	0.013
1560491_at	---	⇧	1.59	0.012
227435_at	KIAA2018	⇧	1.59	0.011
206238_s_at	YAF2	⇩	1.59	0.011
223137_at	ZDHHC4	⇧	1.59	0.010
210988_s_at	PRUNE	⇩	1.59	9.50E-03
204387_x_at	MRP63	⇧	1.59	9.20E-03
200848_at	AHCYL1	⇧	1.59	8.60E-03
233290_at	---	⇧	1.59	8.30E-03
240529_at	---	⇧	1.59	8.10E-03
202059_s_at	KPNA1	⇧	1.59	7.70E-03
221596_s_at	C7orf64	⇧	1.59	7.20E-03
1556346_at	COTL1	⇧	1.59	6.90E-03
1569940_at	SLC6A16	⇩	1.59	6.90E-03
203694_s_at	DHX16	⇩	1.59	6.60E-03
219959_at	MOCOS	⇩	1.59	6.50E-03
244780_at	SGPP2	⇧	1.59	6.50E-03
223060_at	C14orf119	⇩	1.59	6.10E-03
233553_at	---	⇧	1.59	6.00E-03
1560457_x_at	LSDP5	⇧	1.59	6.00E-03
225083_at	GTF3C6	⇧	1.59	5.80E-03
234266_at	---	⇧	1.59	5.70E-03
219512_at	DSN1	⇩	1.59	5.30E-03
207476_at	LOC100507630	⇧	1.59	5.30E-03
1553224_at	LUZP1	⇧	1.59	5.20E-03
231736_x_at	MGST1	⇩	1.59	5.20E-03
1556327_a_at	---	⇧	1.59	5.10E-03
204380_s_at	FGFR3	⇧	1.59	5.00E-03
206529_x_at	SLC26A4	⇧	1.59	4.50E-03
1554798_at	SNED1	⇩	1.59	4.50E-03
1558561_at	HM13	⇧	1.59	4.10E-03
1564679_at	ASB15	⇧	1.59	4.00E-03
217394_at	---	⇩	1.59	3.70E-03
233024_at	---	⇧	1.59	3.70E-03
225756_at	CSNK1E	⇧	1.59	3.50E-03
211008_s_at	UBE2I	⇧	1.59	3.50E-03
243545_at	---	⇧	1.59	3.40E-03
214074_s_at	CTTN	⇩	1.59	3.30E-03
207263_x_at	VEZT	⇧	1.59	3.20E-03
222252_x_at	UBQLN4	⇧	1.59	3.10E-03
229542_at	C20orf85	⇩	1.59	2.90E-03
242675_x_at	---	⇧	1.59	2.80E-03
1557403_s_at	---	⇧	1.59	2.60E-03
213767_at	KSR1	⇩	1.59	2.60E-03
202288_at	FRAP1	⇩	1.59	2.30E-03
231459_at	---	⇧	1.59	2.20E-03
229442_at	C18orf54	⇧	1.59	2.20E-03
236109_at	RPUSD4	⇧	1.59	2.00E-03
224620_at	MAPK1	⇧	1.59	1.60E-03
234762_x_at	NLN	⇧	1.59	1.10E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student’s t-test p<0.05, FC ≥ ±1.50]

201716_at	SNX1	⇩	1.59	1.10E-03
207743_at	---	⇧	1.59	1.00E-03
213238_at	ATP10D	⇩	1.59	1.00E-03
240049_at	---	⇧	1.59	8.20E-04
219392_x_at	PRR11	⇧	1.59	8.00E-04
208157_at	SIM2	⇧	1.59	7.80E-04
222907_x_at	TMEM50B	⇧	1.59	7.50E-04
211127_x_at	EDA	⇧	1.59	6.20E-04
214189_s_at	GGA2	⇧	1.59	6.10E-04
216778_s_at	CYLC1	⇩	1.59	6.00E-04
218112_at	MRPS34	⇩	1.59	5.20E-04
206978_at	CCR2	⇩	1.59	4.20E-04
1562764_at	LOC100507351	⇩	1.59	4.10E-04
220311_at	N6AMT1	⇧	1.59	1.40E-04
1563043_at	LOC285375	⇧	1.59	9.90E-05
231328_s_at	RASGRP4	⇩	1.59	9.60E-05
1554466_a_at	C16orf13	⇩	1.59	3.50E-05
1563075_s_at	---	⇧	1.58	0.049
239931_at	---	⇩	1.58	0.048
210350_x_at	ING1	⇩	1.58	0.047
1554492_at	THADA	⇧	1.58	0.047
224963_at	SLC26A2	⇧	1.58	0.045
209164_s_at	CYB561	⇧	1.58	0.043
1555334_s_at	SLC30A5	⇩	1.58	0.043
238875_at	---	⇧	1.58	0.042
218029_at	FAM65A	⇩	1.58	0.040
235381_at	RSF1	⇧	1.58	0.039
223273_at	C14orf142	⇩	1.58	0.038
211047_x_at	AP2S1	⇩	1.58	0.033
58994_at	CC2D1A	⇧	1.58	0.033
227809_at	ZC3H6	⇧	1.58	0.033
232021_at	GLT8D3	⇧	1.58	0.032
1552662_a_at	PCDHGB7	⇩	1.58	0.032
234072_at	SEMA4A	⇧	1.58	0.030
208816_x_at	ANXA2P2	⇩	1.58	0.029
240024_at	SEC14L2	⇩	1.58	0.028
206386_at	SERPINA7	⇧	1.58	0.027
1565886_at	---	⇧	1.58	0.026
224151_s_at	AK3	⇧	1.58	0.026
205504_at	BTK	⇩	1.58	0.026
239768_x_at	GPATCH2	⇧	1.58	0.026
238899_at	---	⇩	1.58	0.025
200956_s_at	SSRP1	⇩	1.58	0.025
211948_x_at	BAT2D1	⇩	1.58	0.024
211752_s_at	NDUFS7	⇩	1.58	0.024
1562161_at	---	⇧	1.58	0.022
1563076_x_at	---	⇧	1.58	0.022
223318_s_at	ALKBH7	⇩	1.58	0.022
230296_at	C16orf52	⇧	1.58	0.022
238353_at	RASL11A	⇧	1.58	0.022
240527_at	---	⇧	1.58	0.021
232409_x_at	FBXL16	⇩	1.58	0.019
1558557_at	C16orf62	⇧	1.58	0.018
223059_s_at	FAM107B	⇧	1.58	0.018
204621_s_at	NR4A2	⇧	1.58	0.018
215387_x_at	---	⇧	1.58	0.017
204868_at	ICT1	⇩	1.58	0.016
212616_at	CHD9	⇧	1.58	0.014
213492_at	COL2A1	⇧	1.58	0.013
200043_at	ERH	⇧	1.58	0.013
215749_s_at	GORASP1	⇩	1.58	0.013
225452_at	MED1	⇧	1.58	0.013
202616_s_at	MECP2	⇧	1.58	0.012
1562321_at	PDK4	⇧	1.58	0.012
243295_at	RBM27	⇧	1.58	0.012
1569503_at	HEATR5B	⇧	1.58	0.011
209080_x_at	GLRX3	⇩	1.58	0.010
201031_s_at	HNRNPH1	⇧	1.58	0.010
213199_at	C2CD3	⇩	1.58	9.90E-03
222373_at	---	⇧	1.58	9.80E-03
223287_s_at	FOXP1	⇧	1.58	9.60E-03
1566178_x_at	---	⇧	1.58	9.50E-03
225772_s_at	C12orf62	⇩	1.58	9.40E-03
235984_at	---	⇧	1.58	9.30E-03
217672_x_at	EIF1	⇧	1.58	8.70E-03
236737_at	C17orf56	⇧	1.58	8.60E-03
221315_s_at	FGF22	⇧	1.58	8.30E-03
219163_at	ZNF562	⇧	1.58	8.10E-03
1569091_at	---	⇧	1.58	7.90E-03
1553567_s_at	---	⇧	1.58	7.00E-03
210355_at	PTHLH	⇧	1.58	7.00E-03
233509_at	HERC4	⇧	1.58	6.80E-03
1554329_x_at	STXBP4	⇧	1.58	6.60E-03
211647_x_at	IGHA1	⇩	1.58	6.30E-03
219397_at	COQ10B	⇧	1.58	4.70E-03
207972_at	GLRA1	⇧	1.58	4.00E-03
215615_x_at	---	⇧	1.58	3.30E-03
1564552_at	---	⇧	1.58	2.70E-03
236169_at	---	⇧	1.58	2.40E-03
230619_at	ARNT	⇧	1.58	2.40E-03
1556651_at	---	⇧	1.58	1.90E-03
239025_at	---	⇧	1.58	1.60E-03
243673_at	---	⇧	1.58	1.50E-03
206718_at	LMO1	⇧	1.58	1.40E-03
1556484_at	LRRC52	⇧	1.58	1.40E-03
237972_at	---	⇩	1.58	1.10E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

217136_at	PPIAL4A	⇩	1.58	9.90E-04	217356_s_at	PGK1	⇩	1.57	0.035	229436_x_at	BRCC3	⇧	1.57	0.011
207613_s_at	CAMK2A	⇧	1.58	9.30E-04	202316_x_at	UBE4B	⇩	1.57	0.034	212181_s_at	NUDT4	⇧	1.57	0.011
242309_at	---	⇧	1.58	9.00E-04	226562_at	ZSCAN29	⇧	1.57	0.033	214813_at	ZNF75D	⇩	1.57	0.010
216966_at	ITGA2B	⇧	1.58	8.90E-04	225016_at	APCDD1	⇩	1.57	0.032	1554480_a_at	ARMC10	⇧	1.57	9.90E-03
214667_s_at	TP53I11	⇧	1.58	7.70E-04	223525_at	DLL4	⇩	1.57	0.032	230147_at	F2RL2	⇧	1.57	9.80E-03
233221_at	DEFB118	⇧	1.58	6.80E-04	235520_at	ZNF280C	⇧	1.57	0.032	1560176_s_at	PPP4R1L	⇩	1.57	9.20E-03
1560017_at	TMTC3	⇧	1.58	5.50E-04	1561139_at	---	⇧	1.57	0.029	219226_at	CRKRS	⇧	1.57	9.10E-03
1560181_at	LOC100288122	⇧	1.58	4.70E-04	225878_at	KIF1B	⇧	1.57	0.029	1569277_at	ZNF91	⇧	1.57	8.10E-03
221354_s_at	MCHR1	⇩	1.58	4.10E-04	241425_at	NUPL1	⇧	1.57	0.029	1559936_at	---	⇧	1.57	7.80E-03
1556929_at	PAPOLG	⇧	1.58	3.90E-04	225095_at	SPTLC2	⇩	1.57	0.029	221368_at	NEU2	⇧	1.57	7.70E-03
230054_at	LOC100130536	⇧	1.58	2.50E-04	206555_s_at	THUMPD1	⇧	1.57	0.028	235759_at	---	⇧	1.57	7.60E-03
235952_at	---	⇧	1.58	2.30E-04	225737_s_at	FBXO22	⇩	1.57	0.027	1563208_s_at	C3orf65	⇧	1.57	7.60E-03
241749_at	MURC	⇧	1.58	2.20E-04	205867_at	PTPN11	⇧	1.57	0.027	229961_x_at	YJEFN3	⇧	1.57	6.70E-03
243065_at	---	⇧	1.58	2.00E-04	204675_at	SRD5A1	⇧	1.57	0.027	230862_at	---	⇧	1.57	6.10E-03
208846_s_at	VDAC3	⇩	1.58	1.60E-04	226318_at	TBRG1	⇧	1.57	0.027	201104_x_at	NBPF10	⇩	1.57	6.00E-03
211130_x_at	EDA	⇧	1.58	1.10E-04	234041_at	---	⇧	1.57	0.026	222713_s_at	FANCF	⇩	1.57	5.80E-03
1561612_at	---	⇧	1.58	8.00E-05	212269_s_at	MCM3AP	⇩	1.57	0.025	227090_at	PHF21A	⇧	1.57	5.40E-03
207488_at	---	⇧	1.58	4.70E-05	202396_at	TCERG1	⇧	1.57	0.022	220253_s_at	LRP12	⇧	1.57	5.30E-03
217458_at	---	⇧	1.58	6.70E-06	207958_at	UGT2A1/2	⇩	1.57	0.020	214031_s_at	KRT7	⇧	1.57	4.90E-03
AFFX-BioB-5_at	---	⇩	1.58	6.65E-04	219081_at	ANKHD1	⇩	1.57	0.019	234133_s_at	LOC728543	⇧	1.57	4.70E-03
214188_at	---	⇧	1.57	0.048	212983_at	HRAS	⇩	1.57	0.018	1565888_at	---	⇧	1.57	4.20E-03
212073_at	CSNK2A1	⇧	1.57	0.048	239585_at	KAT2B	⇧	1.57	0.018	223619_x_at	PECR	⇧	1.57	4.10E-03
1568713_a_at	TBC1D1	⇩	1.57	0.047	243745_at	---	⇧	1.57	0.016	234013_at	TRD	⇩	1.57	4.10E-03
215212_at	---	⇧	1.57	0.046	222111_at	FAM63B	⇧	1.57	0.016	233769_at	---	⇧	1.57	4.00E-03
233931_at	---	⇧	1.57	0.045	45749_at	FAM65A	⇩	1.57	0.016	243531_at	ORAOV1	⇩	1.57	4.00E-03
1560609_at	CRYZL1	⇧	1.57	0.045	223538_at	SERF1A	⇧	1.57	0.016	213219_at	ADCY2	⇧	1.57	3.80E-03
215669_at	HLA-DRB4	⇧	1.57	0.041	207490_at	TUBA4B	⇩	1.57	0.014	1566098_at	---	⇧	1.57	3.70E-03
205133_s_at	HSPE1	⇩	1.57	0.041	1563303_at	---	⇧	1.57	0.012	33778_at	TBC1D22A	⇧	1.57	3.40E-03
232262_at	PIGL	⇧	1.57	0.041	220690_s_at	DHRS7B	⇩	1.57	0.012	204209_at	PCYT1A	⇩	1.57	2.90E-03
231718_at	SLU7	⇧	1.57	0.040	241923_x_at	NANS	⇧	1.57	0.012	223647_x_at	HSCB	⇧	1.57	2.80E-03
213048_s_at	---	⇧	1.57	0.037	228628_at	SRGAP2P1	⇧	1.57	0.012	233374_at	---	⇧	1.57	2.70E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student’s t-test p<0.05, FC ≥ ±1.50]

1570411_at	---	⇧	1.57	2.70E-03	244168_s_at	ULK4	⇧	1.56	0.045	1558076_at	ANKRD32	⇧	1.56	0.015
207645_s_at	CHD1L	⇧	1.57	2.40E-03	238822_at	---	⇩	1.56	0.044	1562650_at	FRYL	⇧	1.56	0.015
232768_at	CCNB2	⇧	1.57	2.20E-03	1555243_x_at	C8orf59	⇧	1.56	0.043	213197_at	ASTN1	⇧	1.56	0.014
231557_at	---	⇩	1.57	2.00E-03	218930_s_at	TMEM106B	⇧	1.56	0.043	218443_s_at	DAZAP1	⇧	1.56	0.014
1563315_s_at	ERICH1	⇩	1.57	2.00E-03	242051_at	---	⇧	1.56	0.040	226320_at	THOC4	⇧	1.56	0.014
201216_at	ERP29	⇩	1.57	2.00E-03	207223_s_at	ROD1	⇩	1.56	0.040	233270_x_at	---	⇧	1.56	0.013
233041_x_at	---	⇧	1.57	1.90E-03	200832_s_at	SCD	⇩	1.56	0.038	212243_at	GCOM1	⇧	1.56	0.013
241724_x_at	---	⇧	1.57	1.80E-03	201922_at	TINP1	⇩	1.56	0.038	205498_at	GHR	⇩	1.56	0.013
221552_at	ABHD6	⇩	1.57	1.80E-03	208891_at	DUSP6	⇩	1.56	0.037	216755_at	OSBPL10	⇧	1.56	0.013
1555944_at	FAM120A	⇧	1.57	1.70E-03	235440_at	SPTY2D1	⇧	1.56	0.037	1562295_at	LOC730057	⇧	1.56	0.012
1553243_at	ITIH5	⇧	1.57	1.70E-03	202155_s_at	NUP214	⇩	1.56	0.034	226816_s_at	KIAA1143	⇧	1.56	0.011
234382_x_at	---	⇧	1.57	1.50E-03	217235_x_at	IGL	⇩	1.56	0.031	222169_x_at	SH2D3A	⇧	1.56	0.011
241596_at	NUDT10	⇧	1.57	1.30E-03	236375_at	---	⇧	1.56	0.030	215193_x_at	HLA-DRB1/3/4	⇩	1.56	0.010
1564658_at	C7orf52	⇧	1.57	1.00E-03	212798_s_at	ANKMY2	⇩	1.56	0.027	231601_at	LOC100507224	⇧	1.56	0.010
232190_x_at	LOC115110	⇧	1.57	1.00E-03	202093_s_at	PAF1	⇩	1.56	0.027	206340_at	NR1H4	⇩	1.56	0.010
213604_at	TCEB3	⇩	1.57	1.00E-03	1558742_at	---	⇧	1.56	0.026	200053_at	SPAG7	⇩	1.56	0.010
216184_s_at	RIMS1	⇧	1.57	9.00E-04	201506_at	TGFBI	⇩	1.56	0.026	216057_at	RAB3GAP2	⇧	1.56	8.40E-03
224712_x_at	C19orf42	⇧	1.57	8.60E-04	230998_at	---	⇧	1.56	0.025	203829_at	ELP4	⇩	1.56	8.30E-03
222187_x_at	G3BP1	⇧	1.57	7.80E-04	1566991_at	ARID1B	⇩	1.56	0.023	222339_x_at	---	⇧	1.56	8.10E-03
233456_at	---	⇩	1.57	6.90E-04	242293_at	ING3	⇧	1.56	0.023	205547_s_at	TAGLN	⇧	1.56	7.80E-03
1563841_at	---	⇧	1.57	5.90E-04	240733_at	---	⇧	1.56	0.020	202706_s_at	UMPS	⇩	1.56	7.20E-03
207986_x_at	CYB561	⇧	1.57	2.60E-04	221290_s_at	MUM1	⇧	1.56	0.020	204573_at	CROT	⇧	1.56	7.10E-03
231413_at	---	⇧	1.57	2.40E-04	202205_at	VASP	⇧	1.56	0.019	1555575_a_at	KDELR1	⇧	1.56	6.80E-03
237813_at	PCBP2	⇧	1.57	1.90E-04	213889_at	PIGL	⇩	1.56	0.018	1560424_at	---	⇧	1.56	6.40E-03
1567286_at	OR5L2	⇩	1.57	9.20E-05	232140_at	---	⇩	1.56	0.017	210878_s_at	KDM3B	⇧	1.56	6.00E-03
1554396_at	UEVLD	⇩	1.57	3.60E-05	225941_at	EIF4E3	⇧	1.56	0.017	214801_at	TOR1AIP2	⇧	1.56	6.00E-03
214233_at	GGA2	⇩	1.57	3.40E-05	239062_at	LOC100131096	⇩	1.56	0.017	240777_at	SYNE2	⇧	1.56	5.00E-03
215626_at	---	⇧	1.56	0.049	234166_at	UBE3A	⇩	1.56	0.017	217005_at	LDLR	⇧	1.56	4.90E-03
230213_at	C19orf43	⇧	1.56	0.048	240154_at	---	⇧	1.56	0.016	225152_at	ZNF622	⇩	1.56	4.80E-03
238431_at	---	⇧	1.56	0.047	211779_x_at	AP2A2	⇩	1.56	0.016	1569916_at	---	⇧	1.56	4.70E-03
210685_s_at	UBE4B	⇩	1.56	0.047	238804_at	LOC100131701	⇧	1.56	0.016	223697_x_at	C9orf64	⇧	1.56	4.70E-03
224635_s_at	BIRC6	⇧	1.56	0.045	1563975_at	RNF130	⇧	1.56	0.016	1554564_a_at	UNQ1887	⇧	1.56	4.70E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

234897_s_at	LY6G6F	⇩	1.56	4.60E-03
1562063_x_at	NBPF1	⇧	1.56	4.60E-03
1564049_at	LOC339593	⇧	1.56	4.50E-03
212247_at	NUP205	⇩	1.56	4.00E-03
1558714_at	---	⇧	1.56	3.70E-03
217374_x_at	TARP	⇩	1.56	3.40E-03
1555078_at	ZNF843	⇧	1.56	3.30E-03
1561205_at	---	⇧	1.56	3.10E-03
215533_s_at	UBE4B	⇩	1.56	3.00E-03
212920_at	REST	⇧	1.56	2.70E-03
207598_x_at	XRCC2	⇧	1.56	2.70E-03
230641_at	LOC100505938	⇩	1.56	2.60E-03
222913_at	KLF3	⇧	1.56	2.50E-03
1563472_at	---	⇧	1.56	2.30E-03
208252_s_at	CHST3	⇩	1.56	2.30E-03
1561300_at	---	⇧	1.56	2.20E-03
217042_at	RDH11	⇧	1.56	2.00E-03
209449_at	LSM2	⇩	1.56	1.80E-03
1553761_at	C22orf30	⇧	1.56	1.60E-03
216204_at	COMT	⇧	1.56	1.60E-03
229839_at	SCARA5	⇩	1.56	1.50E-03
207300_s_at	F7	⇧	1.56	1.30E-03
234293_x_at	---	⇧	1.56	1.20E-03
243712_at	XIST	⇩	1.56	1.10E-03
214516_at	HIST1H4B	⇧	1.56	1.00E-03
239748_x_at	OCIAD1	⇧	1.56	9.70E-04
214943_s_at	RBM34	⇩	1.56	8.80E-04
216123_x_at	---	⇧	1.56	7.00E-04
1563571_at	LOC285463	⇧	1.56	6.90E-04
225616_at	SPRYD4	⇩	1.56	6.90E-04
215595_x_at	---	⇧	1.56	6.20E-04
216072_at	---	⇧	1.56	4.90E-04
221681_s_at	DSPP	⇧	1.56	4.80E-04
1552609_s_at	IL28A/B	⇧	1.56	3.30E-04
233016_at	---	⇧	1.56	2.70E-04
237606_at	CD53	⇩	1.56	2.60E-04
217919_s_at	MRPL42	⇩	1.56	2.40E-04
215553_x_at	---	⇧	1.56	2.30E-04
1564446_at	LOC284930	⇧	1.56	2.30E-04
208871_at	ATN1	⇧	1.56	2.10E-04
230456_at	---	⇧	1.56	1.80E-04
226519_s_at	AGXT2L2	⇧	1.56	1.50E-04
1554985_at	ZNF396	⇧	1.56	9.60E-05
238517_at	KLF7	⇧	1.56	3.40E-05
202115_s_at	NOC2L	⇧	1.55	1.31E-03
201756_at	RPA2	⇩	1.55	0.024
227292_at	C11orf84	⇧	1.55	0.035
202783_at	NNT	⇩	1.55	0.016
212069_s_at	BAT2L	⇩	1.55	0.042
223200_s_at	LSG1	⇧	1.55	0.012
238036_at	SHE	⇧	1.55	4.57E-03
209939_x_at	CFLAR	⇧	1.55	0.042
1563241_at	---	⇧	1.55	4.51E-03
232612_s_at	ATG16L1	⇧	1.55	2.58E-03
216745_x_at	---	⇧	1.55	3.21E-03
228087_at	CCDC126	⇧	1.55	0.024
218021_at	DHRS4	⇩	1.55	1.03E-03
61297_at	CASKIN2	⇩	1.55	2.51E-03
224073_at	FLJ20464	⇩	1.55	9.85E-03
207520_at	TROVE2	⇧	1.55	0.039
243216_x_at	---	⇧	1.55	8.38E-03
1561578_s_at	MCART6	⇧	1.55	0.041
211609_x_at	PSMD4	⇩	1.55	1.18E-03
219051_x_at	METRN	⇩	1.55	4.54E-03
236259_at	STK4	⇧	1.55	0.012
1558120_at	DDX3X	⇧	1.55	0.012
212204_at	TMEM87A	⇩	1.55	0.032
239377_at	EIF1AD	⇧	1.55	0.010
1560340_s_at	RP9P	⇧	1.55	0.013
1564227_at	---	⇧	1.55	0.011
1558784_at	---	⇧	1.55	0.013
205917_at	ZNF264	⇧	1.55	5.23E-03
205895_s_at	NOLC1	⇩	1.55	9.13E-04
1569078_at	RNF213	⇧	1.55	0.024
230579_at	LOC728705	⇧	1.55	0.010
214606_at	TSPAN2	⇧	1.55	0.024
210838_s_at	ACVRL1	⇩	1.55	3.31E-03
210251_s_at	RUFY3	⇧	1.55	0.042
243643_x_at	SLC30A6	⇧	1.55	0.022
241686_x_at	---	⇧	1.55	7.84E-04
229060_at	YPEL2	⇧	1.55	2.46E-03
203729_at	EMP3	⇩	1.55	0.048
240047_at	---	⇧	1.55	0.016
203142_s_at	AP3B1	⇩	1.55	1.04E-03
230018_at	DPP9	⇧	1.55	0.011
1570366_x_at	ZNF709	⇧	1.55	1.55E-04
202569_s_at	MARK3	⇧	1.55	8.77E-04
1569527_at	---	⇧	1.55	0.020
236594_at	LLGL1	⇧	1.55	0.010
242968_at	---	⇧	1.55	0.027
204698_at	ISG20	⇩	1.55	0.022
1559987_at	---	⇧	1.55	0.010
234628_at	---	⇧	1.55	9.90E-03
221625_at	---	⇧	1.55	2.50E-03
231801_at	NFATC2	⇧	1.55	1.60E-04
242778_at	LPXN	⇧	1.55	1.30E-03

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219717_at	C4orf30	⇧	1.55	0.015	243792_x_at	PTPN13	⇧	1.55	4.94E-03	211166_at	FAM153A	⇧	1.54	4.73E-04
1569202_x_at	---	⇧	1.55	0.033	218242_s_at	SUV420H1	⇧	1.55	0.029	224639_at	UNQ1887	⇧	1.54	8.65E-03
242131_at	LOC440552	⇧	1.55	0.038	201167_x_at	ARHGDIA	⇩	1.55	3.92E-03	221620_s_at	APOO	⇩	1.54	0.044
236494_x_at	---	⇧	1.55	0.011	212544_at	ZNHIT3	⇩	1.55	0.018	1561073_at	---	⇧	1.54	5.81E-04
213394_at	MAPKBP1	⇧	1.55	0.011	214322_at	CAMK2G	⇩	1.55	0.027	222914_s_at	TMEM121	⇩	1.54	2.12E-03
242456_at	MRE11A	⇧	1.55	0.034	1565823_at	---	⇧	1.55	6.67E-03	232376_at	PCCA	⇧	1.54	0.044
243971_x_at	LOC731789	⇧	1.55	2.57E-03	210161_at	---	⇧	1.55	3.57E-04	214531_s_at	SNX1	⇩	1.54	3.06E-03
236599_at	---	⇧	1.55	6.51E-03	222272_x_at	SCIN	⇧	1.55	0.016	236971_at	---	⇧	1.54	9.27E-03
220636_at	DNAI2	⇧	1.55	5.39E-03	226598_s_at	GTPBP5	⇧	1.55	0.048	211639_x_at	IGHA1-2	⇩	1.54	0.047
1568821_at	TTC23	⇧	1.55	1.58E-05	227658_s_at	PLEKHA3	⇧	1.55	0.048	227513_s_at	LRRFIP1	⇧	1.54	4.65E-03
222547_at	MAP4K4	⇩	1.55	3.27E-03	1564121_at	---	⇧	1.55	7.18E-03	225674_at	BCAP29	⇧	1.54	0.019
1557025_a_at	---	⇧	1.55	0.039	208739_x_at	SUMO2	⇩	1.55	6.15E-03	216161_at	SBNO1	⇧	1.54	6.00E-03
202296_s_at	RER1	⇩	1.55	0.034	1554576_a_at	ETV4	⇧	1.55	6.85E-04	231567_s_at	CCDC62	⇧	1.54	1.90E-03
244454_at	---	⇧	1.55	0.045	1555595_at	SCRN3	⇧	1.55	3.82E-04	238840_at	LRRFIP1	⇧	1.54	0.036
219924_s_at	ZMYM6	⇩	1.55	4.36E-04	218156_s_at	TSR1	⇩	1.54	3.18E-03	1562468_at	---	⇧	1.54	0.040
219275_at	PDCD5	⇩	1.55	0.024	228515_at	LOC90784	⇩	1.54	0.022	228544_s_at	CSRP2BP	⇩	1.54	0.027
91826_at	EPS8L1	⇩	1.55	1.12E-03	209620_s_at	ABCB7	⇩	1.54	5.76E-03	1553386_at	MFSD2	⇧	1.54	0.017
227825_at	NAIF1	⇩	1.55	8.45E-03	243242_at	---	⇧	1.54	0.024	234096_at	---	⇧	1.54	6.21E-03
204558_at	RAD54L	⇧	1.55	3.28E-04	1566798_at	SLC35E1	⇧	1.54	1.90E-03	1569573_at	---	⇧	1.54	3.01E-03
232569_at	---	⇧	1.55	0.014	1558385_at	---	⇧	1.54	0.013	227120_at	FOXP4	⇧	1.54	4.34E-03
229434_at	---	⇧	1.55	0.028	1553036_at	GPR111	⇧	1.54	8.35E-03	244048_x_at	---	⇧	1.54	5.50E-03
244464_at	---	⇧	1.55	4.48E-03	223218_s_at	NFKBIZ	⇧	1.54	0.023	215636_at	UBR4	⇧	1.54	8.37E-03
219013_at	GALNT11	⇧	1.55	0.031	1555259_at	ZAK	⇧	1.54	8.00E-04	220071_x_at	HAUS2	⇧	1.54	4.56E-03
237410_x_at	---	⇧	1.55	0.014	206262_at	ADH1C	⇩	1.54	1.39E-03	1566673_at	---	⇧	1.54	0.012
242875_at	---	⇧	1.55	0.014	233900_at	---	⇧	1.54	2.92E-05	40016_g_at	MAST4	⇩	1.54	0.015
228151_at	---	⇧	1.55	7.41E-03	1560137_at	---	⇧	1.54	4.41E-03	216524_x_at	---	⇧	1.54	1.58E-03
209625_at	PIGH	⇩	1.55	0.048	208907_s_at	MRPS18B	⇩	1.54	3.27E-03	1559668_s_at	---	⇧	1.54	5.58E-03
208728_s_at	CDC42	⇧	1.55	0.013	212559_at	PRKAR1B	⇩	1.54	0.011	1562970_at	---	⇧	1.54	1.36E-03
214957_at	ACTL8	⇧	1.55	4.80E-03	202120_x_at	AP2S1	⇩	1.54	0.032	226926_at	DMKN	⇧	1.54	9.53E-04
214773_x_at	TIPRL	⇧	1.55	0.036	1565874_at	---	⇧	1.54	1.51E-04	1559490_at	LRCH3	⇧	1.54	1.90E-03
200909_s_at	RPLP2	⇩	1.55	0.045	1565692_at	---	⇧	1.54	3.83E-03	203199_s_at	MTRR	⇩	1.54	0.011
1553217_s_at	ZNF41	⇩	1.55	5.83E-03	203033_x_at	FH	⇩	1.54	5.52E-03	209004_s_at	FBXL5	⇧	1.54	0.011

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

239981_x_at	LOC728902	⇧	1.54	1.87E-03	233642_s_at	HEATR5B	⇩	1.54	0.032	231715_s_at	PYCR2	⇩	1.54	4.16E-03
243943_x_at	C6orf52	⇧	1.54	0.027	219846_at	GON4L	⇧	1.54	7.18E-03	200772_x_at	PTMA	⇧	1.53	0.034
205770_at	GSR	⇩	1.54	0.012	210149_s_at	ATP5H	⇩	1.54	0.027	244813_at	---	⇧	1.53	0.023
224918_x_at	MGST1	⇩	1.54	0.017	226023_at	MAP2K7	⇧	1.54	5.84E-03	241376_at	LOC100130097	⇧	1.53	4.04E-03
241770_x_at	---	⇧	1.54	7.65E-03	230628_at	EP400	⇧	1.54	1.04E-03	200665_s_at	SPARC	⇩	1.53	0.043
215494_at	---	⇩	1.54	0.027	233163_at	LOC731157	⇩	1.54	8.84E-03	216771_at	---	⇧	1.53	0.016
1555718_x_at	---	⇧	1.54	1.28E-04	222763_s_at	WDR33	⇩	1.54	2.38E-03	222098_s_at	---	⇩	1.53	5.56E-03
AFFX-BioC-3_at	---	⇩	1.54	2.97E-04	201417_at	SOX4	⇩	1.54	8.97E-03	235021_at	KIAA2026	⇧	1.53	0.022
237560_at	MRPS5	⇧	1.54	0.041	214617_at	PRF1	⇧	1.54	0.049	210577_at	CASR	⇩	1.53	4.41E-03
243641_at	---	⇧	1.54	0.020	242474_s_at	VMA21	⇧	1.54	3.16E-03	216045_at	CCDC144A	⇧	1.53	0.029
231972_at	---	⇩	1.54	0.033	226758_at	LUC7L2	⇩	1.54	0.017	222299_x_at	---	⇧	1.53	3.16E-04
1563529_at	HYDIN2	⇧	1.54	0.016	1560762_at	LOC285972	⇩	1.54	0.031	1570022_at	---	⇧	1.53	0.029
230309_at	---	⇩	1.54	4.12E-03	217376_at	---	⇧	1.54	5.17E-03	225623_at	KIAA1737	⇩	1.53	0.041
244787_at	---	⇧	1.54	0.030	203945_at	ARG2	⇩	1.54	0.035	222593_s_at	SPATS2	⇧	1.53	0.033
237225_at	---	⇧	1.54	0.033	223369_at	METTL11A	⇩	1.54	5.73E-04	242711_x_at	FANCM	⇧	1.53	0.034
1556682_s_at	---	⇧	1.54	0.024	228277_at	FBXL19	⇧	1.54	2.80E-03	217188_s_at	C14orf1	⇩	1.53	2.30E-03
218323_at	RHOT1	⇧	1.54	0.022	222280_at	---	⇧	1.54	6.35E-03	227687_at	HYLS1	⇩	1.53	0.012
213175_s_at	SNRPB	⇧	1.54	0.041	AFFX-BioDn-5_at	---	⇩	1.54	7.42E-03	1570272_at	---	⇧	1.53	1.50E-04
243414_at	PPIL2	⇧	1.54	0.034	206680_at	CD5L	⇩	1.54	2.17E-03	1563679_at	LOC150577	⇧	1.53	5.91E-03
207925_at	CST5	⇩	1.54	0.017	221040_at	CAPN10	⇩	1.54	5.98E-03	224904_at	PDPR	⇩	1.53	0.026
213121_at	SNRNP70	⇧	1.54	1.21E-05	205981_s_at	ING2	⇩	1.54	0.014	209518_at	SMARCD1	⇧	1.53	7.99E-04
227670_at	ZNF75A	⇩	1.54	0.045	1556543_at	---	⇧	1.54	0.034	229420_at	---	⇩	1.53	4.76E-03
217894_at	KCTD3	⇩	1.54	0.048	232168_x_at	MACF1	⇧	1.54	7.82E-03	209638_x_at	RGS12	⇧	1.53	5.46E-04
222843_at	FIGNL1	⇩	1.54	0.041	218459_at	TOR3A	⇩	1.54	0.033	213684_s_at	PDLIM5	⇧	1.53	0.035
215597_x_at	---	⇧	1.54	0.015	226368_at	CHST11	⇧	1.54	0.025	241018_at	TMEM59	⇧	1.53	0.045
221997_s_at	MRPL52	⇧	1.54	6.76E-04	232804_at	---	⇧	1.54	0.015	205496_at	KIAA0408	⇧	1.53	1.36E-04
1561305_at	---	⇧	1.54	0.011	219670_at	BEND5	⇩	1.54	0.030	224316_at	LOC100131728	⇧	1.53	0.016
218942_at	PIP4K2C	⇧	1.54	2.76E-03	238149_at	ZNF818P	⇩	1.54	7.37E-03	206127_at	ELK3	⇧	1.53	9.18E-04
201576_s_at	GLB1	⇩	1.54	2.51E-03	217281_x_at	IGHA1-2	⇩	1.54	4.50E-03	216957_at	USP22	⇧	1.53	0.013
230401_at	---	⇧	1.54	2.10E-03	233485_at	---	⇩	1.54	5.51E-03	231496_at	FCAMR	⇩	1.53	0.046

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

233427_x_at	---	⇧	1.53	3.43E-03	234981_x_at	CMBL	⇧	1.53	3.71E-04	237759_at	CD48	⇧	1.53	0.016
230316_at	SEC14L2	⇩	1.53	0.040	217548_at	LOC100129502	⇧	1.53	2.97E-03	1569353_at	CP110	⇧	1.53	0.012
212159_x_at	AP2A2	⇩	1.53	0.015	226713_at	CCDC50	⇩	1.53	4.46E-03	201583_s_at	SEC23B	⇩	1.53	6.29E-03
234294_x_at	GATAD2A	⇧	1.53	3.16E-03	1569772_x_at	---	⇩	1.53	0.030	208322_s_at	ST3GAL1	⇩	1.53	0.021
233457_at	---	⇧	1.53	2.63E-03	223064_at	RNF181	⇩	1.53	0.015	243378_at	---	⇧	1.53	0.022
203258_at	DRAP1	⇩	1.53	0.019	217772_s_at	MTCH2	⇩	1.53	3.32E-03	217165_x_at	MT1F	⇩	1.53	0.015
1557172_x_at	NEK8	⇧	1.53	7.80E-03	1554171_at	ZMYM3	⇧	1.53	0.041	205451_at	FOXO4	⇧	1.53	0.014
244452_at	C2orf30	⇧	1.53	4.89E-03	208238_x_at	---	⇧	1.53	5.22E-03	238382_x_at	---	⇧	1.53	0.038
243594_x_at	SPIRE2	⇧	1.53	1.85E-03	228568_at	GCOM1	⇩	1.53	0.036	242995_at	---	⇧	1.53	5.92E-03
204526_s_at	TBC1D8	⇩	1.53	9.76E-04	215840_at	DNAH2	⇧	1.53	0.047	212109_at	HN1L	⇧	1.53	6.28E-03
1553227_s_at	BRWD1	⇩	1.53	0.026	215852_x_at	C20orf117	⇧	1.53	7.20E-04	209271_at	BPTF	⇩	1.53	9.35E-03
238778_at	MPP7	⇧	1.53	0.046	209233_at	EMG1	⇩	1.53	0.032	1562010_x_at	---	⇧	1.53	1.88E-03
218700_s_at	RAB7L1	⇧	1.53	0.021	1570414_x_at	FLJ13197	⇧	1.53	3.08E-03	227186_s_at	MRPL41	⇩	1.53	8.85E-03
1566535_at	---	⇧	1.53	0.014	206877_at	MXD1	⇩	1.53	0.031	200841_s_at	EPRS	⇧	1.53	0.029
211354_s_at	LEPR	⇩	1.53	3.80E-03	201386_s_at	DHX15	⇩	1.53	0.043	200853_at	H2AFZ	⇩	1.53	0.014
224002_s_at	FKBP7	⇧	1.53	8.24E-04	241329_s_at	---	⇧	1.53	2.21E-03	1555467_a_at	CUGBP1	⇩	1.53	0.042
242036_x_at	ATP2B3	⇧	1.53	2.27E-03	218835_at	SFTPA2/B	⇩	1.53	0.017	214403_x_at	SPDEF	⇧	1.53	9.76E-04
213040_s_at	NPTXR	⇧	1.53	0.034	225317_at	ACBD6	⇩	1.53	1.95E-03	213768_s_at	ASCL1	⇧	1.53	2.44E-04
233976_at	---	⇧	1.53	0.035	214538_x_at	RGS6	⇩	1.53	0.021	221578_at	RASSF4	⇩	1.53	1.23E-03
216853_x_at	IGLV3-19	⇩	1.53	1.03E-03	207499_x_at	UNC45A	⇧	1.53	4.76E-03	1554627_a_at	ASCC1	⇩	1.53	2.02E-04
221861_at	---	⇩	1.53	5.00E-03	207343_at	LYZL6	⇩	1.53	5.06E-03	228420_at	PDCD2	⇧	1.53	0.011
214385_s_at	MUC5AC	⇧	1.53	7.59E-04	242936_at	---	⇧	1.53	0.012	239536_at	---	⇧	1.53	0.014
1556672_a_at	RBM6	⇧	1.53	0.029	242235_x_at	---	⇧	1.53	4.24E-03	230212_at	LOC729345	⇩	1.53	7.46E-03
236387_at	LOC100129961	⇧	1.53	1.70E-03	1554867_a_at	PRR16	⇩	1.53	0.011	1556742_at	LOC728411	⇧	1.53	5.93E-04
234531_at	---	⇧	1.53	7.62E-04	230790_x_at	---	⇧	1.53	8.89E-03	244093_at	---	⇧	1.52	3.64E-03
204683_at	ICAM2	⇩	1.53	0.033	240123_at	---	⇧	1.53	0.012	229609_at	LOC728190	⇩	1.52	0.010
1554339_a_at	COG3	⇧	1.53	0.031	207740_s_at	NUP62	⇩	1.53	6.51E-03	235248_at	BTBD9	⇧	1.52	1.67E-03
236702_at	C20orf43	⇩	1.53	0.036	233330_s_at	---	⇩	1.53	5.93E-03	241531_at	---	⇧	1.52	2.07E-03
204638_at	ACP5	⇧	1.53	0.037	208572_at	HIST3H3	⇧	1.53	2.79E-03	208096_s_at	COL21A1	⇩	1.52	1.00E-04
210032_s_at	SPAG6	⇩	1.53	2.43E-04	239807_at	LOC728842	⇧	1.53	7.25E-03	228623_at	---	⇧	1.52	0.026
241286_at	---	⇩	1.53	0.037	224121_x_at	PLEKHB2	⇧	1.53	7.02E-03	240232_at	---	⇧	1.52	0.039
215006_at	---	⇧	1.53	0.039	244788_at	---	⇧	1.53	0.016	215600_x_at	FBXW12	⇧	1.52	5.75E-03

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student’s t-test p<0.05, FC ≥ ±1.50]

225849_s_at	SFT2D1	⇧	1.52	5.20E-03	236072_at	---	⇧	1.52	0.013	224370_s_at	CAPS2	⇧	1.52	0.017
210801_at	DIMT1L	⇧	1.52	3.53E-03	236571_at	---	⇧	1.52	3.20E-03	229165_at	MRPL12	⇩	1.52	0.047
225783_at	UBE2F	⇧	1.52	0.019	221503_s_at	KPNA3	⇧	1.52	4.86E-03	202246_s_at	CDK4	⇩	1.52	5.66E-03
218678_at	NES	⇩	1.52	0.011	1561919_at	---	⇧	1.52	2.07E-05	230742_at	RBM6	⇧	1.52	0.043
215246_at	LARP7	⇧	1.52	2.72E-03	1557203_at	PABPC1L2B	⇩	1.52	0.021	235958_at	PLA2G4F	⇧	1.52	5.65E-03
1566787_at	---	⇧	1.52	5.00E-03	227384_s_at	LOC727820	⇧	1.52	0.047	238486_at	FRS2	⇧	1.52	5.38E-05
214651_s_at	HOXA9	⇩	1.52	0.019	238119_at	---	⇧	1.52	0.022	1553901_x_at	ZNF486	⇧	1.52	5.69E-04
244875_at	NCRNA00105	⇩	1.52	7.61E-03	201734_at	CLCN3	⇩	1.52	0.035	1568619_s_at	ITPRIPL2	⇧	1.52	4.79E-03
1562981_at	HBB	⇧	1.52	5.91E-04	1554494_at	MTHFSD	⇩	1.52	0.040	223513_at	CENPJ	⇩	1.52	0.017
211960_s_at	RAB7A	⇧	1.52	3.69E-03	235810_at	ZNF182	⇧	1.52	0.032	31861_at	IGHMBP2	⇩	1.52	7.76E-04
1559434_at	---	⇧	1.52	8.11E-04	229078_s_at	KIAA1704	⇧	1.52	0.028	234330_at	---	⇧	1.52	7.79E-03
1554154_at	GDAP2	⇧	1.52	0.024	236961_at	---	⇧	1.52	5.45E-03	1561019_at	---	⇧	1.52	2.46E-05
207194_s_at	ICAM4	⇧	1.52	0.038	206316_s_at	KNTC1	⇩	1.52	0.012	220753_s_at	CRYL1	⇩	1.52	0.027
215507_x_at	---	⇧	1.52	2.95E-03	221781_s_at	DNAJC10	⇩	1.52	0.010	214962_s_at	NUP160	⇩	1.52	2.29E-03
212471_at	AVL9	⇩	1.52	0.031	236797_at	---	⇧	1.52	3.88E-06	231129_at	LOC728012	⇩	1.52	1.07E-03
228108_at	---	⇩	1.52	0.029	224413_s_at	TM2D2	⇩	1.52	1.85E-03	215052_at	FRMPD4	⇧	1.52	7.37E-04
1562281_at	---	⇧	1.52	6.66E-04	1554668_a_at	FAM151A	⇩	1.52	3.62E-04	237112_at	---	⇧	1.52	0.049
242371_x_at	---	⇧	1.52	9.94E-03	209358_at	TAF11	⇧	1.52	0.044	1566208_at	TCEA1	⇩	1.52	0.010
216206_x_at	MAP2K7	⇧	1.52	0.021	208644_at	PARP1	⇩	1.52	7.97E-03	242194_at	CUL4A	⇧	1.52	0.010
201643_x_at	KDM3B	⇧	1.52	6.12E-03	224533_s_at	C6orf142	⇩	1.52	3.01E-03	240350_at	---	⇧	1.52	7.69E-04
1561389_at	---	⇩	1.52	0.032	216231_s_at	B2M	⇩	1.52	0.019	231009_at	PLA2G12B	⇩	1.52	0.029
240606_at	---	⇧	1.52	1.75E-03	242472_x_at	FNBP4	⇧	1.52	0.020	222070_at	DND1	⇧	1.52	0.034
216115_at	NF1	⇧	1.52	2.31E-03	231734_at	RBP2	⇩	1.52	0.018	1558124_at	NUDCD2	⇧	1.52	0.024
221192_x_at	MFSD11	⇧	1.52	4.33E-03	209174_s_at	QRICH1	⇧	1.52	0.022	223057_s_at	XPO5	⇩	1.52	2.93E-04
203883_s_at	RAB11FIP2	⇧	1.52	0.032	232716_at	---	⇧	1.52	0.016	213747_at	LOC100134128	⇧	1.52	0.018
243125_x_at	---	⇧	1.52	5.13E-03	1563026_at	---	⇧	1.52	0.018	201774_s_at	NCAPD2	⇩	1.52	0.016
206106_at	MAPK12	⇩	1.52	4.19E-04	202486_at	AFG3L2	⇩	1.52	5.70E-03	226109_at	C21orf91	⇧	1.52	0.032
216709_at	---	⇧	1.52	0.016	219290_x_at	DAPP1	⇧	1.52	3.55E-03	221903_s_at	CYLD	⇩	1.52	7.58E-03
210934_at	BLK	⇧	1.52	3.30E-03	1563426_a_at	LOC644613	⇧	1.52	4.60E-03	203789_s_at	SEMA3C	⇩	1.52	0.050
1556595_at	---	⇧	1.52	0.034	1565602_at	---	⇧	1.52	0.015	232615_at	---	⇧	1.52	0.039
230559_x_at	FGD4	⇧	1.52	0.047	211371_at	MAP2K5	⇩	1.52	4.88E-04	239076_at	SEPT13	⇧	1.52	9.74E-03
211267_at	HESX1	⇧	1.52	0.016	210717_at	---	⇧	1.52	0.032	1570473_at	LOC338579	⇧	1.52	8.50E-03

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210134_x_at	SHOX2	⇩	1.52	9.50E-03	228377_at	KLHL14	⇩	1.51	0.035	212815_at	ASCC3	⇩	1.51	0.014
229700_at	ZNF738	⇧	1.52	0.020	226986_at	WIPI2	⇧	1.51	0.018	216503_s_at	MLLT10	⇩	1.51	0.028
201589_at	SMC1A	⇩	1.52	0.017	205692_s_at	CD38	⇩	1.51	1.88E-03	217750_s_at	UBE2Z	⇧	1.51	7.57E-04
1557588_at	LOC100128946	⇧	1.52	2.76E-03	210933_s_at	FSCN1	⇧	1.51	0.034	203304_at	BAMBI	⇩	1.51	5.63E-03
218695_at	EXOSC4	⇩	1.52	2.14E-03	1562608_at	---	⇧	1.51	8.06E-03	1562946_at	---	⇧	1.51	0.011
1569905_at	HSD11B1L	⇧	1.52	5.91E-04	1564067_x_at	TMEM151B	⇧	1.51	0.039	204804_at	TRIM21	⇩	1.51	0.023
228902_at	NUP214	⇩	1.52	8.65E-04	221385_s_at	FFAR3	⇩	1.51	8.09E-04	220367_s_at	SAP130	⇩	1.51	2.32E-04
244522_at	SYVN1	⇧	1.51	0.011	202928_s_at	PHF1	⇩	1.51	0.013	238158_at	MEIG1	⇧	1.51	0.021
226914_at	ARPC5L	⇧	1.51	0.048	1562273_at	CNGA4	⇧	1.51	1.37E-03	1553099_at	TIGD1	⇩	1.51	6.65E-03
225367_at	PGM2	⇧	1.51	0.020	231961_at	RBPMS	⇧	1.51	0.037	242641_at	---	⇧	1.51	9.19E-03
236291_at	RDH5	⇧	1.51	6.49E-03	1562270_at	ARHGEF7	⇧	1.51	0.021	207819_s_at	ABCB4	⇩	1.51	0.028
1553218_a_at	ZNF512	⇩	1.51	3.38E-03	1553349_at	ARID2	⇧	1.51	0.046	229881_at	KLF12	⇧	1.51	0.028
227939_s_at	TRA2A	⇧	1.51	0.019	214542_x_at	HIST1H2AI	⇩	1.51	0.023	1561419_at	---	⇧	1.51	5.98E-03
223294_at	CXorf26	⇩	1.51	0.021	215607_x_at	---	⇧	1.51	0.031	214719_at	SLC46A3	⇧	1.51	0.038
239885_at	---	⇧	1.51	1.54E-03	207190_at	ZZEF1	⇩	1.51	0.011	1565829_at	KIAA1731	⇧	1.51	1.20E-04
220152_at	C10orf95	⇧	1.51	0.040	237236_x_at	LOC731789	⇧	1.51	1.84E-04	238058_at	LOC150381	⇧	1.51	0.041
231809_x_at	PDCD7	⇧	1.51	0.040	59999_at	HIF1AN	⇧	1.51	9.40E-04	232250_at	KIAA1257	⇧	1.51	0.010
202053_s_at	ALDH3A2	⇩	1.51	8.95E-03	207232_s_at	DZIP3	⇩	1.51	4.67E-05	207433_at	IL10	⇧	1.51	1.18E-03
211713_x_at	KIAA0101	⇧	1.51	9.13E-03	229370_at	---	⇩	1.51	5.10E-03	231552_at	---	⇧	1.51	0.034
238684_at	---	⇧	1.51	0.011	1554020_at	BICD1	⇩	1.51	0.016	1570393_at	EML5	⇧	1.51	4.70E-03
212655_at	ZCCHC14	⇩	1.51	0.023	228457_at	---	⇩	1.51	2.12E-03	218583_s_at	DCUN1D1	⇧	1.51	0.047
230203_at	FLJ46875	⇧	1.51	2.81E-03	209902_at	ATR	⇩	1.51	0.036	211649_x_at	IGHA1-2	⇩	1.51	4.60E-03
239252_at	---	⇧	1.51	5.98E-03	241195_at	---	⇧	1.51	5.33E-04	216924_s_at	DRD2	⇧	1.51	2.00E-04
228009_x_at	ZNRD1	⇩	1.51	0.044	236935_at	---	⇧	1.51	0.022	216002_at	---	⇧	1.51	0.043
218264_at	BCCIP	⇩	1.51	0.015	1562034_at	NCRNA00163	⇩	1.51	8.39E-03	206770_s_at	SLC35A3	⇧	1.51	0.048
240887_at	---	⇧	1.51	9.77E-03	227046_at	SLC39A11	⇩	1.51	1.15E-03	223674_s_at	CDC42SE1	⇩	1.51	0.010
216640_s_at	PDIA6	⇩	1.51	0.011	47083_at	C7orf26	⇩	1.51	0.040	210460_s_at	PSMD4	⇩	1.51	6.45E-03
1554176_a_at	C3orf33	⇧	1.51	0.020	1569577_x_at	---	⇧	1.51	0.041	1561942_x_at	---	⇧	1.51	0.034
219575_s_at	COG8	⇩	1.51	7.61E-03	242342_at	---	⇩	1.51	1.23E-03	1565861_at	---	⇧	1.51	1.05E-03
206528_at	TRPC6	⇧	1.51	1.69E-04	240240_at	---	⇧	1.51	0.048	239959_x_at	---	⇩	1.51	2.98E-03
213124_at	ZNF473	⇩	1.51	0.011	225149_at	PCID2	⇩	1.51	7.64E-03	1560745_at	---	⇩	1.51	4.24E-03
235433_at	APOOL	⇧	1.51	3.51E-03	229656_s_at	EML6	⇩	1.51	0.014	244423_at	---	⇧	1.50	0.031

Table A2: RR Ambion® GLOBINClear™ Gene List (n=4,520) [GeneSpring unpaired student's t-test p<0.05, FC ≥ ±1.50]

201969_at	NASP	⇩	1.50	2.35E-03	238257_at	MLLT10	⇧	1.50	0.033	210433_at	POFUT1	⇧	1.50	0.023
211190_x_at	CD84	⇩	1.50	9.25E-03	219038_at	MORC4	⇩	1.50	0.049	203426_s_at	IGFBP5	⇩	1.50	0.032
239324_at	---	⇩	1.50	0.037	228662_at	SOCS7	⇧	1.50	0.034	1552927_at	MAP3K7IP3	⇧	1.50	0.041
1555189_a_at	TAT	⇧	1.50	3.33E-03	212079_s_at	MLL	⇧	1.50	0.035	228536_at	LOC90826	⇩	1.50	0.012
227177_at	CORO2A	⇩	1.50	7.54E-03	242555_at	C16orf87	⇧	1.50	0.028	203447_at	PSMD5	⇧	1.50	0.014
1566716_at	---	⇧	1.50	0.019	243675_at	---	⇧	1.50	0.032	224667_x_at	C10orf104	⇧	1.50	3.64E-03
223781_x_at	ADH4	⇧	1.50	8.92E-03	207966_s_at	GLG1	⇧	1.50	0.048	223643_at	CRYGS	⇧	1.50	0.011
1565628_at	---	⇩	1.50	0.014	226993_at	---	⇧	1.50	0.034	201299_s_at	MOBKL1B	⇧	1.50	0.016
210185_at	CACNB1	⇧	1.50	4.90E-03	209448_at	HTATIP2	⇧	1.50	0.027	220242_x_at	ZNF701	⇧	1.50	3.63E-03
234135_x_at	---	⇧	1.50	7.60E-04	217703_x_at	---	⇧	1.50	1.27E-03	200878_at	EPAS1	⇩	1.50	0.029
209646_x_at	ALDH1B1	⇩	1.50	0.017	230090_at	GDNF	⇩	1.50	1.98E-03	208346_at	PPBPL2	⇧	1.50	0.024
1564972_x_at	SETDB2	⇧	1.50	1.58E-03	233873_x_at	MTPAP	⇧	1.50	2.52E-03	212192_at	KCTD12	⇧	1.50	0.026
204214_s_at	RAB32	⇩	1.50	0.015	239992_at	---	⇧	1.50	0.028	219217_at	NARS2	⇩	1.50	4.25E-03
228652_at	ZNF776	⇧	1.50	0.018	1558444_at	---	⇩	1.50	0.013	217492_s_at	PTEN	⇩	1.50	0.047
208216_at	DLX4	⇧	1.50	6.36E-03	210521_s_at	FETUB	⇧	1.50	0.048	224989_at	---	⇧	1.50	0.031
220778_x_at	SEMA6B	⇧	1.50	0.013	210193_at	MOBP	⇩	1.50	2.68E-04	204413_at	TRAF2	⇩	1.50	6.21E-03
234562_x_at	LOC728678	⇧	1.50	0.021	233930_at	DMRT3	⇩	1.50	0.022	1564773_x_at	---	⇧	1.50	0.024
227175_at	LOC100131311	⇩	1.50	0.043	216170_at	---	⇧	1.50	0.038	244011_at	PPM1K	⇧	1.50	0.021
241085_at	---	⇩	1.50	0.018	224795_x_at	IGKC	⇩	1.50	0.035	243746_at	IGHMBP2	⇩	1.50	0.037
209123_at	QDPR	⇩	1.50	8.95E-03	214637_at	OSM	⇧	1.50	3.05E-03	234088_at	---	⇧	1.50	0.046

APPENDIX B: ECACC LCL STUDY

List of Figures

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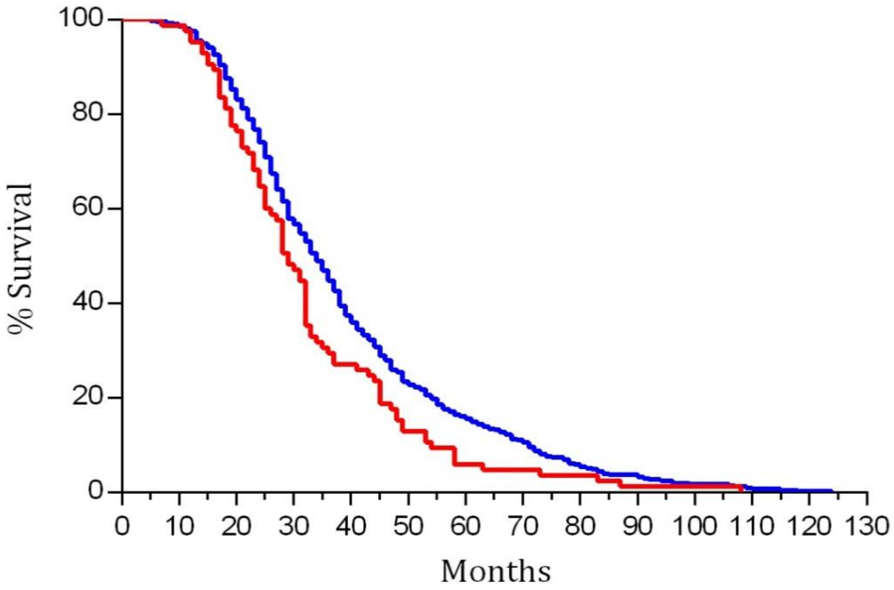
Figure B1: Kaplan-Meier Survival Curve for LCL's in the ECACC Discovery and Replication Cohort



Key 🟥 *C9ORF72+* 🟦 non*C9ORF72*-related_SALS

Abbreviations: ALS - Amyotrophic Lateral Sclerosis, *C9ORF72* - chromosome 9 open reading frame 72, ECACC - European Collection of Cell Cultures, LCL - lymphoblastoid cell line and S - sporadic.

Table B1: Clinical Information Relating to Control LCL's in the ECACC Discovery Cohort

ID	ECACC	Sex	Age	ID	ECACC	Sex	Age	ID	ECACC	Sex	Age	ID	ECACC	Sex	Age	ID	ECACC	Sex	Age
C001	SMa0033	M	65	C021	LCa0076	M	69	C041	BC6397	M	52	C061	SC3150	M	36	C081	SC3738	M	49
C002	BLi0245	M	61	C022	SPr0086	F	69	C042	SC3247	F	56	C062	LC0101	M	75	C082	BC6477	F	52
C003	BC6548	M	69	C023	SC3672	M	71	C043	BC6231	M	62	C063	SC3293	F	76	C083	BLi0269	M	65
C004	SNc0091	M	43	C024	SNt0035	M	51	C044	SNc0041	F	67	C064	SC3692	M	78	C084	LC0669	F	66
C005	LPo0033	M	50	C025	SNc0218	M	61	C045	SC3406	M	47	C065	BLi0123	M	57	C085	SNc0035	M	68
C006	LC0455	F	52	C026	BC6295	F	65	C046	LSh0023	M	70	C066	LC0262	M	48	C086	BLi0217	F	69
C007	SNc0038	M	72	C027	LC0216	M	64	C047	SNc0149	M	73	C067	SC3504	F	48	C087	BC6166	M	39
C008	SPr0050	M	75	C028	SC3452	F	39	C048	SNt0005	F	74	C068	LRo0007	M	67	C088	BC6323	M	61
C009	SNc0103	F	79	C029	SNc0023	M	59	C049	SC3052	M	64	C069	BC6253	F	68	C089	SC3594	M	72
C010	SPr0014	M	58	C030	LC0675	M	77	C050	LC0194	M	33	C070	SC3312	M	69	C090	BOx0073	F	57
C011	SNc0045	F	63	C031	SC3709	F	84	C051	BC6300	M	57	C071	LC0583	M	72	C091	SC3741	M	57
C012	LSh0025	M	55	C032	LC0573	M	46	C052	SNt0073	F	59	C072	SPr0048	M	52	C092	SC3690	M	75
C013	SDu0012	F	66	C033	SMa0183	F	53	C053	LPo0062	M	69	C073	BC6091	F	63	C093	BLi0196	F	77
C014	LC0433	M	70	C034	SC3151	M	66	C054	LNh0075	F	70	C074	SPr0068	M	64	C094	SC3699	M	78
C015	LSh0032	M	63	C035	SC3021	F	67	C055	LC0367	M	72	C075	LC0311	M	71	C095	BLi0029	M	70
C016	SC3489	F	69	C036	SMa0156	M	56	C056	LC0249	M	60	C076	SNc0106	F	71	C096	LC0692	M	71
C017	LPo0027	M	71	C037	BC6448	F	59	C057	BC6335	F	65	C077	SMa0047	M	60	C097	BLi0083	F	72
C018	SNc0096	F	73	C038	LSh0022	M	70	C058	SC3278	F	41	C078	BC6374	M	63	C098	BC6234	M	54
C019	LCa0022	F	58	C039	BLi0169	M	73	C059	SC3246	M	78	C079	SC3279	F	56	C099	SC3282	F	63
C020	BBe0006	F	36	C040	LRf0014	F	74	C060	BC6507	M	67	C080	BC6317	F	66	C100	BC6376	M	63

Table B2: Clinical Information Relating to Familial LCL's in the ECACC Discovery Cohort

ID	ECACC	Sex	Age	EEC	Diagnosis	Genotype	Survival	Presentation	ALSFRS-R	Riluzole	Meds Other	Supplements	Smoking
F001	LP0137	M	61	Definite	ALS	Unknown	32	Limb	34	Y	None	None	?
F002	LNh0101	M	67	Probable	ALS	*C9ORF72*	16	Bulbar	19	Y	None	None	?
F003	LP0048	M	27	Definite	ALS	*FUS*	13	Mixed	0	Y	None	None	?
F004	LP0614	M	38	Probable	ALS	Unknown	20	Mixed	42	N	None	None	?
F005	LP0225	F	40	Probable	ALS	Unknown	19	Limb	46	N	None	Vitamin E	?
F006	BP6206	M	45	Probable	ALS	Unknown	10	Bulbar	15	Y	None	None	?
F007	LP0388	F	48	Definite	ALS	Unknown	17	Bulbar	45	N	None	None	?
F008	BP6074	M	46	Definite	ALS	Unknown	33	Bulbar	31	Y	None	None	?
F009	BP6061	F	50	Probable	ALS	Unknown	38	Unknown	34	Unknown	None	None	?
F010	SPr0085	M	70	Probable	ALS	Unknown	Unknown	Mixed	24	Y	None	None	?
F011	LP0637	F	68	Probable	ALS	*C9ORF72*	63	Limb	41	Y	None	None	?
F012	SP3474	F	74	Probable	ALS	Unknown	Unknown	Limb	40	Y	None	None	N
F013	BP6494	M	58	Probable	ALS	*C9ORF72*	Alive	Limb	33	N	None	None	?
F014	LCa0111	F	63	Definite	ALS	Unknown	35	Bulbar	0	Y	None	None	?
F015	LP0460	M	46	Definite	ALS	*TARDBP*	Alive	Unknown	33	Unknown	None	None	?
F016	LP0328	M	53	Definite	ALS	Unknown	20	Bulbar	45	Y	None	None	?
F017	BP6072	F	56	Probable	ALS	*C9ORF72*	33	Bulbar	30	Y	None	None	?
F018	LP0631	M	63	Probable	ALS	Unknown	30	Limb	40	Y	None	None	?
F019	BP6391	M	60	Probable	ALS	*C9ORF72*	28	Limb	41	Y	None	None	?
F020	BLi0236	F	71	Probable	ALS	*C9ORF72*	33	Mixed	35	N	None	None	?
F021	LP0125	M	57	Probable	ALS	*C9ORF72*	25	Limb	0	Y	None	None	?
F022	LP0294	M	56	Probable	ALS	Unknown	75	Limb	47	Y	None	None	?
F023	BP6054	F	61	Definite	ALS	Unknown	35	Limb	31	Y	None	None	?
F024	SP3148	F	28	Definite	ALS+EL	*C9ORF72*	14	Bulbar	18	Y	None	Vitamin C/E	N
F025	SPr0059	F	69	Probable	ALS	*C9ORF72*	18	Bulbar	24	Y	None	None	?
F026	LP0657	M	70	Definite	ALS	*C9ORF72*	18	Mixed	45	N	None	None	?
F027	SNc0204	F	48	Definite	ALS	*C9ORF72*	41	Unknown	40	Unknown	None	None	?
F028	SMa0020	M	49	Definite	ALS	Unknown	29	Mixed	39	Y	None	None	?
F029	LPy0018	F	52	PBP	PBP	*C9ORF72*	58	Bulbar	45	Y	None	None	?
F030	LP0475	M	59	Probable	ALS	*C9ORF72*	30	Limb	42	Y	None	None	?
F031	SP3526	M	60	Definite	ALS+EL	*SOD1*	24	Respiratory	36	N	None	None	N
F032	BP6550	F	61	Definite	ALS	Unknown	39	Bulbar	29	Y	None	None	?

Table B2: Clinical Information Relating to Familial LCL's in the ECACC Discovery Cohort

F033	SP3006	M	62	Definite	ALS	*C9ORF72*	32	Limb	32	Y	None	Vitamin C/E	N
F034	BP6508	F	64	Probable	ALS	Unknown	49	Limb	40	Y	None	Vitamin C	?
F035	SP3590	M	63	Definite	ALS	Unknown	39	Limb	37	Y	None	None	?
F036	LP0193	F	31	Probable	ALS	*FUS*	Unknown	Limb	43	Unknown	None	None	?
F037	LP0529	M	33	Definite	ALS	Unknown	22	Limb	45	Y	None	Vitamin C/E	?
F038	BLi0249	M	40	Definite	ALS	Unknown	10	Mixed	40	Y	None	None	?
F039	BP6447	M	56	Probable	ALS	Unknown	26	Bulbar	41	Y	None	Multivitamin	?
F040	SP3068	M	57	Probable	ALS	*TARDBP*	Unknown	Bulbar	46	Y	None	None	N
F041	LP0440	F	58	PBP	PBP	*C9ORF72*	22	Bulbar	38	Unknown	None	None	?
F042	SP3303	F	78	Definite	ALS	Unknown	11	Bulbar	36	Y	None	None	N
F043	LNh0046	M	43	Definite	ALS	Unknown	32	Respiratory	29	Y	None	None	?
F044	LP0456	F	45	Definite	ALS	Unknown	18	Bulbar	27	Y	None	None	?
F045	BLi0254	M	49	Definite	ALS	*C9ORF72*	Unknown	Limb	41	Y	None	None	?
F046	LP0008	M	69	Definite	ALS	*C9ORF72*	19	Limb	29	Y	None	None	?
F047	BP6502	M	53	Probable	ALS	*C9ORF72*	Alive	Limb	44	Y	None	Multivitamin	?
F048	BBr0015	F	71	Definite	ALS	*C9ORF72*	19	Mixed	Unknown	N	None	None	?
F049	LP0497	M	53	Probable	ALS	*C9ORF72*	13	Bulbar	43	Y	None	None	?
F050	BP6308	F	55	Definite	ALS	*C9ORF72*	47	Limb	29	Y	None	None	?
F051	LP0305	M	57	Probable	ALS	*C9ORF72*	21	Limb	27	Y	None	None	?
F052	LCa0026	F	65	PBP	PBP	*C9ORF72*	Unknown	Bulbar	35	N	None	None	?
F053	SP3610	M	59	Probable	ALS	*SOD1*	24	Limb	26	Y	Lithium	None	?
F054	SP3048	M	47	Definite	ALS	Unknown	Alive	Mixed	48	Y	None	None	N
F055	LP0682	M	49	Probable	ALS	Unknown	Unknown	Bulbar	41	Y	None	None	?
F056	SP3462	F	50	Probable	ALS	*C9ORF72-OPTN*	28	Bulbar	31	Y	None	None	N
F057	LP0717	M	71	Definite	ALS	*C9ORF72*	32	Limb	36	N	None	None	?
F058	LPo0036	M	62	PBP	PBP	*C9ORF72*	27	Bulbar	38	Y	None	None	?
F059	BP6124	F	32	Definite	ALS	Unknown	Unknown	Limb	29	Y	None	None	?
F060	SP3528	M	33	Probable	ALS	Unknown	16	Limb	35	Y	None	None	N
F061	LP0296	M	57	Probable	ALS	Unknown	33	Limb	36	Y	None	None	?
F062	LP0148	M	67	Definite	ALS	Unknown	17	Bulbar	0	N	None	None	?
F063	LP0405	F	72	Probable	ALS	Unknown	21	Mixed	34	Y	None	None	?
F064	SNc0063	M	56	Definite	ALS	Unknown	69	Mixed	24	Y	None	Vitamin C/E	?
F065	LP0033	F	61	Probable	ALS	Unknown	14	Limb	14	Y	None	None	?

Table B2: Clinical Information Relating to Familial LCL's in the ECACC Discovery Cohort

F066	SP3659	M	39	Definite	ALS	Unknown	44	Limb	44	Y	None	None	?
F067	SP3086	F	40	Definite	ALS	*TARDBP*	224	Limb	15	N	None	None	Y
F068	LP0075	M	44	Definite	ALS	*SOD1*	33	Mixed	0	Y	None	None	?
F069	LP0157	F	44	Probable	ALS	Unknown	78	Unknown	43	Unknown	None	None	?
F070	BP6531	F	78	Probable	ALS	Unknown	33	Limb	28	Y	None	None	?
F071	SNc0031	M	63	Definite	ALS	Unknown	67	Limb	39	Y	None	Vitamin C/E	?
F072	BLi0251	F	70	Definite	ALS	*C9ORF72*	23	Bulbar	20	Y	None	None	?
F073	BP6165	F	35	Definite	ALS	*C9ORF72*	53	Limb	31	Y	Minocycline	Vitamin E	?
F074	BLi0272	M	36	Definite	ALS	Unknown	Unknown	Limb	46	Y	None	None	?
F075	BP6551	M	41	Probable	ALS	Unknown	Unknown	Limb	45	Y	None	Vitamin C/E	?
F076	SP3670	F	82	Probable	ALS	Unknown	35	Limb	38	Y	None	None	?
F077	LP0437	M	54	Definite	ALS	*C9ORF72*	6	Bulbar	26	Y	None	None	?
F078	BOx0029	F	57	Probable	ALS	*C9ORF72*	20	Mixed	29	N	None	None	?
F079	LNh0050	M	43	Probable	ALS	Unknown	19	Limb	42	Y	None	None	?
F080	SP3508	F	47	Probable	ALS	Unknown	40	Limb	40	Y	None	None	N
F081	SMa0006	M	62	Probable	ALS	*C9ORF72*	107	Limb	45	Y	None	None	?
F082	LP0584	F	70	Definite	ALS	Unknown	Unknown	Bulbar	28	Y	None	None	?
F083	LP0665	F	69	Definite	ALS	*C9ORF72*	28	Mixed	34	N	None	None	?
F084	BP6063	M	71	Definite	ALS	*C9ORF72*	23	Bulbar	0	Y	None	None	?
F085	LP0013	M	48	Definite	ALS	Unknown	35	Limb	41	Y	None	None	?
F086	LP0051	M	49	Probable	ALS	*FUS*	79	Limb	48	Y	None	None	?
F087	SP3216	F	50	PLS	PLS+EL	Unknown	48	Limb	0	N	None	None	N
F088	LP0091	M	62	Definite	ALS	*C9ORF72*	25	Bulbar	21	N	None	None	?
F089	SP3331	F	61	Definite	ALS	*C9ORF72*	24	Bulbar	14	Y	None	Vitamin C/E	N
F090	SP3063	M	61	Probable	ALS	Unknown	6	Limb	0	Y	None	Vitamin C/E	N
F091	SP3534	F	63	Probable	ALS	*C9ORF72*	83	Limb	35	Y	BDNF-trial	None	N
F092	SP3154	M	57	Probable	ALS	*TARDBP*	36	Limb	40	Y	None	Vitamin C/E	Ex-smoker
F093	SP3033	M	59	Definite	ALS	Unknown	23	Bulbar	34	Y	None	None	?
F094	BLi0246	F	60	Probable	ALS	*C9ORF72*	Unknown	Limb	28	Y	None	None	?
F095	SMa0008	M	62	Probable	ALS	Unknown	78	Mixed	10	Y	None	None	?
F096	LP0480	M	59	Probable	ALS	*C9ORF72*	16	Unknown	46	Unknown	None	None	?
F097	SP3277	M	43	Probable	ALS	Unknown	21	Limb	23	Y	None	None	Y
F098	SP3127	F	45	Probable	ALS	*C9ORF72*	35	Bulbar	22	Y	None	None	N

Table B2: Clinical Information Relating to Familial LCL's in the ECACC Discovery Cohort

F099	LP0073	F	61	Definite	ALS	*C9ORF72*	45	Mixed	35	Y	None	None	?
F100	SP3070	M	63	PBP	PBP	*C9ORF72*	19	Bulbar	36	N	None	None	Y
F101	SPr0026	F	64	Definite	ALS	*C9ORF72*	32	Bulbar	12	Y	None	None	?
F102	LSh0038	M	65	Probable	ALS	*C9ORF72*	87	Limb	38	Y	None	None	?
F103	BLi0265	M	23	Definite	ALS	*SOD1*	Unknown	Limb	46	Y	None	None	?
F104	BP6535	M	37	Probable	ALS	Unknown	Unknown	Limb	47	Y	None	None	?
F105	BP6504	F	39	Definite	ALS	Unknown	35	Limb	39	Y	None	Vitamin C	?
F106	BP6029	F	55	Definite	ALS	*C9ORF72*	53	Limb	42	Y	None	None	?
F107	BP6334	M	56	Probable	ALS	*C9ORF72*	31	Limb	36	Y	None	Vitamin C/E	?
F108	SMa0078	M	59	Definite	ALS	Unknown	22	Limb	36	Y	None	None	?
F109	SNc0202	M	71	Definite	ALS	Unknown	Unknown	Unknown	40	Unknown	None	None	?
F110	LP0088	M	55	Probable	ALS	Unknown	58	Limb	45	Y	None	None	?
F111	LP0582	F	73	Definite	ALS	Unknown	Unknown	Bulbar	20	Y	None	None	?
F112	LP0198	M	67	Probable	ALS	Unknown	9	Bulbar	0	N	None	None	?
F113	LP0393	F	69	Definite	ALS	Unknown	32	Bulbar	38	Y	None	None	?
F114	SP3560	M	47	Probable	ALS+PD	*C9ORF72*	17	Limb	0	Y	None	None	N
F115	SP3118	F	50	Definite	ALS+FTD	*C9ORF72*	16	Bulbar	28	Y	None	None	N
F116	BP6077	M	51	Probable	ALS	Unknown	Unknown	Limb	44	N	None	None	?
F117	SMa0166	M	60	Definite	ALS	*C9ORF72*	31	Mixed	24	Y	None	Multivitamin	?
F118	SNc0189	M	59	PBP	PBP	*C9ORF72*	33	Bulbar	12	Unknown	None	None	?
F119	SP3089	F	60	Definite	ALS	Unknown	Alive	Bulbar	43	Y	None	Vitamin C/E	N
F120	SP3218	M	49	Probable	ALS	*SOD1*	21	Limb	44	Y	None	Vitamin C/E	N

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ID	ECACC	Sex	Age	EEC	Diagnosis	Genotype	Survival	Presentation	ALSFRS-R	Riluzole	Meds Other	Supplements	Smoking
S001	LP0061	F	22	Probable	ALS	Unknown	35	Limb	34	Y	None	Vitamin E	?
S002	SP3003	F	82	Definite	ALS	Unknown	16	Mixed	22	Y	None	None	?
S003	LP0021	F	64	Probable	ALS	Unknown	33	Bulbar	43	Y	None	Multivitamin	?
S004	SP3486	M	62	Probable	ALS	Unknown	35	Limb	30	Y	None	Vitamin C/E	N
S005	BBe0007	M	30	Probable	ALS	Unknown	46	Limb	Unknown	Y	None	Vitamin E	?
S006	SP3062	F	38	Definite	ALS+EL	Unknown	58	Bulbar	42	Y	None	None	Y
S007	SP3185	M	44	Probable	ALS	Unknown	11	Mixed	41	Y	None	Vitamin C/E	N
S008	SP3111	F	50	Definite	ALS	Unknown	27	Limb	26	Y	None	None	N
S009	BBe0018	M	47	Probable	ALS	Unknown	18	Limb	Unknown	Y	None	None	?
S010	SP3275	M	48	Probable	ALS	Unknown	21	Limb	25	Y	None	None	N
S011	BP6059	M	50	Probable	ALS	*C9ORF72*	36	Limb	Unknown	Y	None	None	?
S012	SNc0022	F	54	Definite	ALS	Unknown	27	Mixed	14	Y	None	Vitamin C/E	?
S013	LP0129	F	53	Probable	ALS	Unknown	21	Bulbar	40	Y	None	None	?
S014	SP3064	M	53	Probable	ALS	Unknown	49	Limb	33	Y	None	None	N
S015	SP3299	M	54	Probable	ALS-FA	Unknown	70	Limb	32	Y	None	None	Ex-Smoker
S016	SP3162	M	71	Probable	ALS	Unknown	19	Limb	34	Y	None	Vitamin E	N
S017	LP0201	M	72	Probable	ALS	Unknown	71	Limb	43	Y	None	None	?
S018	SP3197	F	75	Probable	ALS	Unknown	25	Limb	0	Y	None	Vitamin C/E	N
S019	SP3172	M	72	Definite	ALS+EL	Unknown	24	Respiratory	33	Y	None	Vitamin C/E	N
S020	SP3059	M	76	Definite	ALS	Unknown	10	Limb	19	Y	None	None	?
S021	SP3249	F	76	Probable	ALS	Unknown	13	Bulbar	27	Y	None	None	N
S022	BP6013	M	83	Probable	ALS	Unknown	17	Limb	Unknown	Y	None	None	?
S023	SP3057	M	59	Definite	ALS	*C9ORF72*	17	Bulbar	0	Y	None	None	?
S024	LP0080	M	61	Probable	ALS	Unknown	30	Limb	43	Y	None	None	?
S025	BP6066	F	63	Probable	ALS	Unknown	51	Limb	Unknown	N	None	None	?
S026	SP3022	F	65	Definite	ALS	Unknown	13	Limb	0	Y	None	None	?
S027	LP0172	M	54	Definite	ALS	Unknown	19	Mixed	45	N	None	None	?
S028	SP3036	M	54	Definite	ALS	Unknown	21	Limb	20	Y	None	None	?
S029	BP6037	F	57	Probable	ALS	Unknown	26	Limb	Unknown	Y	None	None	?
S030	SP3050	F	59	Probable	ALS	Unknown	34	Limb	34	Y	None	Vitamin C/E	?
S031	SP3106	M	66	Probable	ALS	Unknown	29	Bulbar	28	Y	None	None	?
S032	SP3397	M	64	Definite	ALS	Unknown	25	Bulbar	26	Y	None	Vitamin E	Y

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S033	SP3045	F	70	Probable	ALS	Unknown	25	Limb	39	Y	None	None	N
S034	SP3378	F	70	Definite	ALS	Unknown	42	Limb	29	N	None	None	N
S035	LPo0010	M	62	Probable	ALS	Unknown	26	Limb	29	Y	None	None	?
S036	SNt0031	M	61	Definite	ALS	Unknown	13	Limb	39	Y	None	None	?
S037	BP6012	M	61	Definite	ALS	Unknown	24	Limb	Unknown	Y	None	None	?
S038	BP6044	F	66	Probable	ALS	Unknown	48	Bulbar	Unknown	Y	None	None	?
S039	SP3001	F	68	Definite	ALS	Unknown	37	Bulbar	26	Y	None	Vitamin C/E	N
S040	SP3271	M	70	PBP	PBP	Unknown	26	Bulbar	43	Y	None	Vitamin C/E	N
S041	LP0094	M	67	Definite	ALS	Unknown	44	Bulbar	23	Y	None	None	?
S042	SP3122	M	68	Probable	ALS-FA	*C9ORF72*	16	Limb	38	Y	None	None	N
S043	SP3181	F	71	Probable	ALS	Unknown	19	Limb	25	Y	None	None	N
S044	SP3329	F	73	PBP	PBP+EL	Unknown	16	Bulbar	31	Y	None	None	N
S045	SP3289	M	56	PBP	PBP	Unknown	35	Bulbar	39	Y	None	Vitamin C/E	N
S046	SNc0001	M	57	Definite	ALS	Unknown	22	Limb	37	Y	None	Vitamin C/E	?
S047	SP3269	F	61	Probable	ALS+EL	Unknown	44	Bulbar	38	Y	None	None	N
S048	SP3066	F	62	Definite	ALS	Unknown	44	Limb	35	N	None	Vitamin C	?
S049	LP0163	M	38	Definite	ALS	Unknown	50	Limb	27	Y	None	None	?
S050	SP3023	M	45	Probable	ALS	Unknown	39	Limb	35	N	Minocycline	Vitamin C/E	?
S051	SP3437	M	65	Probable	ALS	Unknown	35	Limb	42	Y	None	Vitamin E	N
S052	BBe0016	M	65	Probable	ALS	Unknown	92	Limb	Unknown	Y	None	None	?
S053	SP3371	M	66	Probable	ALS	Unknown	28	Limb	28	Y	None	Vitamin C/E	N
S054	SP3179	F	67	Probable	ALS	Unknown	29	Limb	42	Y	None	Vitamin C/E	N
S055	SP3300	F	68	Probable	ALS	Unknown	47	Bulbar	32	Y	None	None	N
S056	LP0085	F	70	Probable	ALS	Unknown	23	Mixed	40	Y	None	None	?
S057	SP3361	M	70	Probable	ALS	Unknown	27	Bulbar	34	Y	None	None	Ex-Smoker
S058	BBe0001	M	71	Probable	ALS	Unknown	42	Limb	Unknown	N	None	None	?
S059	SP3041	F	71	Definite	ALS	*C9ORF72*	57	Limb	32	Y	None	Vitamin C/E	N
S060	SP3338	M	71	Probable	ALS-FA	Unknown	53	Limb	40	Y	None	Vitamin C/E	N
S061	LP0052	M	50	Probable	ALS	Unknown	27	Limb	36	Y	None	None	?
S062	SP3301	M	49	Probable	ALS	*ANG*	4	Limb	36	Y	None	Vitamin C/E	N
S063	LP0161	F	53	Probable	ALS	Unknown	35	Limb	42	N	None	None	?
S064	LP0317	M	51	Probable	ALS	Unknown	15	Bulbar	12	Y	None	None	?
S065	SP3400	M	57	Definite	ALS+EL	Unknown	21	Bulbar	21	Y	None	None	N

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S066	LP0234	M	59	Definite	ALS	Unknown	41	Limb	41	Y	None	Multivitamin	?
S067	SNt0038	F	63	Probable	ALS	Unknown	27	Limb	40	Y	None	None	?
S068	SP3032	M	60	Definite	ALS	Unknown	38	Limb	34	Y	None	None	?
S069	SP3230	M	60	PMA	PMA	Unknown	53	Limb	41	Y	None	Vitamin C/E	Ex-Smoker
S070	SP3239	F	62	Probable	ALS	Unknown	28	Limb	39	Y	None	None	N
S071	LP0039	F	65	Definite	ALS	Unknown	35	Bulbar	46	Y	None	None	?
S072	BP6058	M	32	Definite	ALS	Unknown	72	Limb	Unknown	Y	None	Vitamin E	?
S073	BP6051	F	35	Definite	ALS	Unknown	23	Limb	Unknown	Y	None	Vitamin C	?
S074	BLi0048	M	35	Probable	ALS	Unknown	82	Limb	Unknown	Unknown	None	None	?
S075	SNt0034	F	42	Probable	ALS	Unknown	42	Limb	45	Y	None	None	?
S076	SP3396	M	55	Definite	ALS+EL	Unknown	38	Bulbar	25	Y	None	None	Ex-Smoker
S077	SNc0042	M	57	Definite	ALS	Unknown	36	Mixed	40	Y	None	Vitamin C/E	?
S078	SP3140	F	59	Probable	ALS+EL	Unknown	18	Limb	28	Y	None	Vitamin C/E	N
S079	LP0155	F	62	Definite	ALS	Unknown	8	Bulbar	36	N	None	None	?
S080	SP3292	M	75	Probable	ALS	Unknown	55	Limb	30	N	None	None	N
S081	SP3355	F	77	Definite	ALS+EL	Unknown	25	Bulbar	11	Y	None	Vitamin C/E	N
S082	SP3346	F	84	Definite	ALS+EL	Unknown	36	Bulbar	31	N	None	None	N
S083	SP3357	M	85	Definite	ALS	Unknown	15	Bulbar	28	Y	None	Vitamin C/E	N
S084	SP3469	M	43	Probable	ALS	*C9ORF72*	52	Limb	42	Y	None	Vitamin C/E	N
S085	BP6032	M	44	Probable	ALS	Unknown	25	Limb	Unknown	Y	None	None	?
S086	BP6017	F	51	Definite	ALS	Unknown	32	Limb	Unknown	Y	None	None	?
S087	BBe0009	M	60	Definite	ALS	Unknown	41	Mixed	Unknown	discontd	None	None	?
S088	SNc0086	M	61	Definite	ALS	*C9ORF72*	29	Limb	40	Y	None	Vitamin C/E	?
S089	SNc0053	M	62	Definite	ALS	Unknown	39	Respiratory	21	Y	None	Vitamin C/E	?
S090	SP3304	F	65	Probable	ALS	Unknown	23	Limb	31	Y	None	None	N
S091	SP3143	F	67	Probable	ALS+EL	Unknown	23	Bulbar	31	Y	None	Vitamin C/E	N
S092	SP3310	M	52	Probable	ALS	Unknown	63	Limb	37	Y	None	None	N
S093	SP3049	M	53	Definite	ALS+FTD	Unknown	37	Bulbar	31	Y	None	None	N
S094	BP6038	F	55	Definite	ALS	Unknown	17	Bulbar	Unknown	Y	None	None	?
S095	SP3095	M	55	Definite	ALS	Unknown	26	Limb	27	Y	None	Vitamin C/E	?
S096	SNt0001	F	58	Definite	ALS	Unknown	72	Limb	45	Y	None	None	?
S097	SP3306	M	67	Probable	ALS	Unknown	21	Limb	39	Y	None	Vitamin C/E	N
S098	BLi0037	F	71	Probable	ALS	Unknown	66	Bulbar	Unknown	Y	None	None	?

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S099	BP6034	M	71	Definite	ALS	Unknown	29	Limb	Unknown	Y	None	Vitamin C/E	?
S100	LP0097	F	71	Definite	ALS	Unknown	49	Mixed	20	Y	None	None	?
S101	SP3046	M	50	Definite	ALS	Unknown	32	Limb	13	Y	None	None	?
S102	SP3266	M	52	Definite	ALS+EL	Unknown	37	Limb	44	Y	None	Vitamin C/E	N
S103	SP3156	F	57	Probable	ALS	Unknown	38	Limb	39	Y	None	Vitamin C/E	Ex-Smoker
S104	SP3101	F	57	Probable	ALS	Unknown	34	Bulbar	30	Y	None	Vitamin E	N
S105	SNc0018	M	59	PBP	PBP	Unknown	42	Bulbar	40	Y	None	Vitamin C/E	?
S106	SNc0077	M	59	PBP	PBP	Unknown	24	Bulbar	46	Y	None	Vitamin C/E	?
S107	SP3341	F	63	Probable	ALS+EL	*C9ORF72*	28	Bulbar	37	Y	None	None	N
S108	SP3384	M	46	Definite	ALS	Unknown	22	Mixed	40	Y	None	Vitamin E	N
S109	SP3414	M	48	Probable	ALS	Unknown	39	Limb	39	Y	None	Vitamin C/E	N
S110	SP3298	F	52	Definite	ALS	*C9ORF72*	24	Limb	33	Y	None	None	N
S111	BP6001	F	52	Definite	ALS	Unknown	40	Limb	Unknown	Y	None	None	?
S112	SP3363	M	70	Definite	ALS	Unknown	13	Respiratory	25	Y	None	Vitamin C/E	Ex-Smoker
S113	SP3347	F	71	Probable	ALS+D	Unknown	49	Limb	42	Y	None	Vitamin C	N
S114	SP3356	M	72	Definite	ALS	Unknown	31	Limb	37	Y	None	Vitamin C/E	Ex-Smoker
S115	SNt0004	M	73	Probable	ALS	Unknown	32	Limb	37	Y	None	None	?
S116	SP3351	M	59	Definite	ALS+D	Unknown	19	Bulbar	33	Y	None	Vitamin C/E	N
S117	SP3087	M	60	Probable	ALS	*C9ORF72*	31	Limb	45	Y	None	Vitamin C/E	N
S118	SP3030	M	62	Probable	ALS	Unknown	64	Limb	38	Y	ONO-trial	Vitamin C/E	N
S119	SP3073	M	63	Definite	ALS+EL	Unknown	29	Limb	43	Y	None	Vitamin C/E	N
S120	SP3409	F	66	Probable	ALS	Unknown	32	Limb	39	Y	None	Vitamin C/E	N
S121	SP3420	F	66	Definite	ALS+EL	*C9ORF72*	32	Bulbar	39	Y	Minocycline	None	Ex-Smoker
S122	BBe0014	M	36	Probable	ALS	Unknown	32	Bulbar	Unknown	Y	None	None	?
S123	BP6021	F	36	Definite	ALS	*C9ORF72*	23	Limb	Unknown	Y	None	Vitamin C/E	?
S124	LP0030	M	53	Definite	ALS	Unknown	24	Limb	45	Y	None	Vitamin C/E	?
S125	SP3335	M	53	Probable	ALS	Unknown	52	Limb	34	Y	None	Vitamin C/E	N
S126	SP3079	M	54	Probable	ALS	Unknown	27	Limb	31	Y	None	Vitamin C/E	Y
S127	LP0215	F	61	Definite	ALS	Unknown	23	Bulbar	25	Y	None	None	?
S128	LP0222	F	58	Probable	ALS	Unknown	37	Bulbar	45	Y	None	None	?
S129	SNt0024	M	68	PBP	PBP	Unknown	38	Bulbar	43	Y	None	Vitamin C/E	?
S130	SNc0010	M	69	Definite	ALS	Unknown	36	Limb	33	Y	None	Vitamin C/E	?
S131	LP0271	F	71	Probable	ALS	Unknown	14	Mixed	34	N	None	None	?

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S132	SP3413	M	56	Definite	ALS	*C9ORF72*	24	Limb	32	Y	ONO-trial	Vitamin C/E	Ex-Smoker
S133	SP3465	M	58	Definite	ALS	Unknown	24	Limb	46	Y	None	Vitamin C/E	N
S134	LP0316	F	62	Definite	ALS	Unknown	44	Bulbar	23	Y	None	None	?
S135	SP3219	F	63	Probable	ALS	Unknown	19	Limb	0	N	None	None	N
S136	SP3417	M	39	Probable	ALS	Unknown	23	Limb	46	Y	None	None	Y
S137	LP0223	M	44	Definite	ALS	Unknown	25	Limb	30	Y	None	None	?
S138a	SNc0016	F	45	Definite	ALS	Unknown	41	Limb	36	N	None	None	?
S138b	SNt0017	M	74	Probable	ALS	Unknown	27	Bulbar	36	Y	None	None	?
S139	SP3098	F	74	Probable	ALS	Unknown	28	Limb	33	Y	None	Vitamin C/E	N
S140	SNt0020	F	75	Definite	ALS	Unknown	18	Limb	45	Y	None	None	?
S141	SNc0071	F	77	Definite	ALS	Unknown	29	Limb	22	Y	None	Vitamin C/E	?
S142	SP3016	M	79	Probable	ALS	Unknown	15	Limb	37	Y	None	None	?
S143	LP0265	M	83	Probable	ALS	Unknown	34	Limb	25	N	None	None	?
S144	LP0286	F	83	Definite	ALS	Unknown	25	Bulbar	41	Y	None	None	?
S145	SP3065	M	65	Probable	ALS	Unknown	13	Limb	40	N	None	None	?
S146	SP3132	M	66	Probable	ALS	Unknown	10	Limb	36	Y	None	None	N
S147	SP3447	M	65	Probable	ALS	Unknown	43	Bulbar	37	Y	None	Vitamin E	N
S148	SP3368	F	67	Probable	ALS	Unknown	36	Limb	39	Y	None	Vitamin C/E	N
S149	SP3391	F	69	Definite	ALS	Unknown	29	Limb	36	Y	ONO-trial	None	N
S150	SP3237	M	24	Definite	ALS	Unknown	45	Limb	18	Y	None	None	N
S151	SP3475	M	38	Definite	ALS	Unknown	32	Mixed	31	Y	None	None	N
S152	SNc0090	F	39	Definite	ALS	Unknown	25	Limb	40	Y	None	Vitamin C/E	?
S153	SP3423	F	75	Probable	ALS+EL	Unknown	20	Bulbar	46	Y	None	None	Ex-Smoker
S154	SP3370	F	81	Probable	ALS	Unknown	25	Bulbar	44	Y	None	None	N
S155	SNc0055	M	82	Definite	ALS	Unknown	80	Limb	36	N	None	Vitamin C	?
S156	SNc0029	M	75	Definite	ALS	Unknown	44	Limb	28	N	None	None	?
S157	LP0015	M	53	Definite	ALS	Unknown	26	Limb	18	Y	Minocycline	None	?
S158	SNt0006	M	52	Definite	ALS	Unknown	47	Bulbar	42	Y	None	None	?
S159	BP6042	M	54	Definite	ALS	Unknown	20	Bulbar	Unknown	Y	None	None	?
S160	BP6039	M	55	Probable	ALS	Unknown	26	Limb	Unknown	Y	None	None	?
S161	SP3174	F	57	Probable	ALS	Unknown	36	Limb	44	Y	None	None	Ex-Smoker
S162	SP3326	M	40	Probable	ALS	Unknown	51	Limb	45	Y	None	None	N
S163	SP3183	M	45	Probable	ALS	*C9ORF72*	14	Limb	36	Y	None	Vitamin C/E	N

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S164	LP0053	M	47	Definite	ALS	Unknown	20	Mixed	41	Y	Minocycline	None	?
S165	SP3222	F	48	PBP	PBP	*C9ORF72*	45	Bulbar	0	Y	None	None	N
S166	SP3082	M	64	Probable	ALS	Unknown	26	Limb	27	Y	None	Vitamin E	N
S167	SP3327	F	64	Probable	ALS	Unknown	31	Limb	40	N	None	Vitamin C/E	N
S168	LP0001	M	66	Probable	ALS	Unknown	37	Limb	30	Y	ONO-trial	Vitamin E	?
S169	BP6006	F	66	Definite	ALS	Unknown	12	Limb	Unknown	Y	None	Vitamin C	?
S170	SP3039	F	71	Definite	ALS	Unknown	26	Bulbar	27	Y	None	Vitamin C/E	N
S171	SP3058	M	71	Definite	ALS	*C9ORF72*	12	Limb	0	Y	None	Vitamin C/E	?
S172	SP3067	M	72	Definite	ALS	Unknown	57	Bulbar	44	Y	None	None	N
S173	SP3103	F	75	Definite	ALS	Unknown	10	Limb	14	Y	None	None	N
S174	LP0005	M	49	Probable	ALS	Unknown	8	Limb	0	N	None	None	?
S175	SP3309	M	49	Probable	ALS	Unknown	68	Limb	43	Y	None	Vitamin C/E	N
S176	SP3385	F	52	Definite	ALS	Unknown	23	Limb	22	Y	Copaxone	Vitamin C/E	N
S177	BP6045	F	54	Definite	ALS	Unknown	23	Bulbar	Unknown	Y	None	Vitamin C/E	?
S178	SP3145	M	62	Definite	ALS+FTD	Unknown	16	Bulbar	36	Y	None	Vitamin C/E	Ex-Smoker
S179	SP3376	M	62	Probable	ALS	Unknown	43	Limb	21	Y	None	None	Y
S180	BP6025	F	64	PBP	PBP	Unknown	39	Bulbar	Unknown	Y	None	None	?
S181	BLi0039	M	67	Definite	ALS	Unknown	61	Mixed	Unknown	Y	None	None	?
S182	SNc0008	M	66	Definite	ALS	Unknown	19	Mixed	38	N	None	None	?
S183	LP0069	F	67	Definite	ALS	Unknown	37	Respiratory	39	Y	None	None	?
S184	LP0307	F	67	Probable	ALS	Unknown	49	Mixed	31	N	None	None	?
S185	SP3383	F	69	Definite	ALS+EL	Unknown	17	Mixed	34	Y	None	Vitamin C/E	N
S186	SP3431	F	57	Definite	ALS+EL	*C9ORF72*	20	Mixed	32	Y	None	Vitamin C/E	N
S187	LP0104	M	55	Probable	ALS	Unknown	55	Limb	41	Y	None	None	?
S188	LP0055	M	56	Definite	ALS	Unknown	49	Mixed	31	Y	None	None	?
S189	SP3090	M	60	Probable	ALS	*C9ORF72*	27	Bulbar	39	Y	None	None	N
S190	SP3232	F	59	Probable	ALS	Unknown	47	Limb	37	Y	None	Vitamin C/E	Ex-Smoker
S191	SP3042	M	59	Probable	ALS+FTD	*C9ORF72*	49	Limb	37	Y	None	Vitamin C/E	N
S192	SP3478	M	59	Probable	ALS	Unknown	14	Limb	19	Y	None	None	N
S193	SNc0024	F	62	Definite	ALS	Unknown	29	Mixed	22	Y	None	Vitamin C/E	?
S194	SP3281	M	61	Probable	ALS	Unknown	35	Limb	43	N	None	None	N
S195	LP0396	F	63	Probable	ALS	Unknown	16	Bulbar	41	N	None	None	?
S196	BBe0013	F	68	Probable	ALS	Unknown	74	Limb	Unknown	Y	None	None	?

Table B3: Clinical Information Relating to Sporadic LCL’s in the ECACC Discovery Cohort

S197	LP0232	M	69	Probable	ALS	Unknown	23	Limb	45	Y	None	Vitamin E	?
S198	SNt0016	M	72	PBP	PBP	Unknown	82	Bulbar	40	Y	None	None	?
S199	LP0176	M	79	Probable	ALS	Unknown	39	Bulbar	32	Y	None	None	?
S200	LP0300	M	40	Probable	ALS	Unknown	37	Limb	30	Y	None	None	?
S201	SP3453	M	44	Probable	ALS	Unknown	32	Limb	38	Y	None	None	N
S202	LP0064	M	46	Definite	ALS	*C9ORF72*	21	Limb	34	Y	None	None	?
S203	SNc0059	F	47	Definite	ALS	*C9ORF72*	73	Limb	30	Y	ONO-trial	Vitamin C/E	?
S204	LP0037	M	62	Definite	ALS	Unknown	23	Limb	42	Y	None	None	?
S205	SP3433	M	63	Definite	ALS+EL	*C9ORF72*	11	Limb	29	Y	None	None	N
S206	SP3471	M	64	Probable	ALS	*C9ORF72*	27	Mixed	41	Y	None	None	Ex-Smoker
S207	SP3018	F	65	Probable	ALS	Unknown	33	Bulbar	44	Y	None	Vitamin C/E	N
S208	SP3078	F	66	Probable	ALS	Unknown	37	Limb	41	N	None	None	Ex-Smoker
S209	SNc0012	M	65	Definite	ALS	Unknown	37	Limb	33	Y	None	Vitamin C/E	?
S210	BP6041	M	66	Definite	ALS	Unknown	32	Bulbar	Unknown	discontd	None	None	?
S211	BP6056	F	69	Probable	ALS	Unknown	18	Bulbar	Unknown	Y	None	None	?
S212	SNc0002	M	27	Definite	ALS	Unknown	43	Mixed	23	Y	Minocycline	Vitamin C/E	?
S213	LP0207	F	37	Probable	ALS	*C9ORF72*	49	Bulbar	45	N	None	None	?
S214	SP3037	M	37	Definite	ALS	Unknown	36	Bulbar	31	Y	None	Vitamin C/E	?
S215	SP3187	M	56	Probable	ALS	Unknown	63	Limb	38	Y	None	Vitamin C/E	Ex-Smoker
S216	SP3288	M	57	Probable	ALS	*C9ORF72*	32	Bulbar	35	Y	None	Vitamin C/E	N
S217	BP6027	M	59	Definite	ALS	Unknown	25	Limb	Unknown	Y	None	None	?
S218	SP3379	F	62	Probable	ALS	Unknown	80	Limb	39	Y	None	None	N
S219	SNt0036	M	71	Probable	ALS	Unknown	85	Limb	38	Y	None	None	?
S220	SP3105	F	70	Probable	ALS+EL	Unknown	48	Limb	34	Y	None	None	N
S221	BP6047	F	71	Definite	ALS	Unknown	32	Bulbar	Unknown	Y	None	Vitamin C/E	?
S222	SP3464	M	72	Probable	ALS	Unknown	37	Mixed	40	Y	None	None	N
S223	SNc0095	M	73	Probable	ALS-FA	Unknown	54	Limb	40	Y	None	Vitamin C/E	?
S224	BP6010	F	74	Definite	ALS	Unknown	22	Bulbar	Unknown	Y	None	None	?
S225	SNc0092	F	53	PBP	PBP	Unknown	21	Bulbar	24	discontd	None	None	?
S226	LP0127	M	54	Probable	ALS	Unknown	43	Limb	45	Y	None	None	?
S227	SP3043	M	54	Definite	ALS	Unknown	21	Bulbar	41	N	None	Vitamin C/E	N
S228	BP6030	M	57	Definite	ALS	Unknown	29	Limb	Unknown	Y	None	None	?
S229	SP3296	F	56	Probable	ALS	Unknown	24	Limb	40	Y	None	Vitamin C/E	N

Table B3: Clinical Information Relating to Sporadic LCL's in the ECACC Discovery Cohort

S230	SP3159	F	75	PBP	PBP+EL	Unknown	27	Bulbar	44	Y	None	Vitamin C/E	N
S231	LP0397	M	81	Probable	ALS	Unknown	19	Bulbar	39	N	None	None	?
S232	SNc0051	F	81	PBP	PBP	Unknown	47	Bulbar	19	N	None	None	?
S233	LP0139	M	86	Definite	ALS	Unknown	12	Limb	0	N	None	None	?
S234	SP3060	M	70	Definite	ALS	Unknown	15	Limb	19	Y	None	Vitamin E	N
S235	SP3243	M	69	Probable	ALS	Unknown	18	Respiratory	31	Y	None	None	Ex-Smoker
S236	SP3286	F	70	Definite	ALS+EL	Unknown	35	Limb	36	Y	None	Vitamin C/E	N
S237	BP6008	M	47	Definite	ALS	Unknown	31	Bulbar	Unknown	Y	ONO-trial	Vitamin E	?
S238	LP0238	M	49	Probable	ALS	Unknown	30	Bulbar	41	Y	None	None	?
S239	BP6049	F	54	Probable	ALS	Unknown	38	Mixed	Unknown	Y	None	Multivitamin	?
S240	SNt0030	M	52	Probable	ALS	Unknown	55	Limb	38	discontd	None	None	?
S241	BP6015	M	59	Definite	ALS	Unknown	27	Limb	Unknown	Y	None	None	?
S242	SP3428	M	61	Definite	ALS	Unknown	27	Bulbar	30	Y	None	Vitamin C/E	N
S243	SP3010	F	61	Definite	ALS	*C9ORF72*	43	Bulbar	8	Y	None	None	?
S244	BP6052	F	63	Probable	ALS	Unknown	25	Bulbar	Unknown	Y	None	None	?
S245	LP0116	F	67	Probable	ALS	Unknown	13	Limb	35	Y	None	None	?
S246	SP3393	M	65	Probable	ALS	Unknown	18	Limb	41	Y	None	None	N
S247	SP3353	F	58	Probable	ALS	Unknown	47	Limb	33	Y	None	Vitamin C/E	Y
S248	BBe0003	F	60	Definite	ALS	Unknown	47	Bulbar	Unknown	Y	None	None	?
S249	SP3056	M	72	Probable	ALS	Unknown	15	Bulbar	33	Y	None	None	N

Table B4: Review of ALS Phase II/III Clinical Drug Trials (ClinicalTrials.gov) (U.S. National Library of Medicine, Bethesda)

Drug Compound	Study Design	Study Period	Patient Criteria for Inclusion	Dosage	Primary Measure	Secondary Measures	Drug Safety & Efficacy	Mechanism(s) of Action	Phase of Trial (ref)
Ozanezumab Novartis Pharmaceutical Ltd. NCT01753076	Multicentre, double-blinded, placebo controlled, randomised parallel-group study	DEC 2012 - ? (n=294) 37 centres in 11 countries	- ALS familial/sporadic - onset ≤30mnths - stable dose Riluzole - SVC ≥65% - 18-80yrs	Subcutaneous injection 15mg/kg every 2wks for a period of 48wks	Time to death and ALSFRS-R	Muscle strength, respiratory function, safety, PK and quality of life	Trial ongoing expected to be completed MAY 2015	Monoclonal Ab against neurite outgrowth inhibitor Nogo-A	Phase II (McCray & Ide 2000)
LiCALS UK-MND Study Group	Multicentre, double-blinded, placebo controlled, randomised parallel-group study	MAY-NOV 2009-2011 (n=214) 10 centres across the UK	- ALS definite/probable or possible - onset ≤36mnths - stable dose Riluzole - >18yrs	Administered orally 295mg three times daily for a period of 18mnths	Time to death	ALSFRS-R, mental health state and quality of life	Safe and well tolerated but no significant improvement in survival or ALSFRS-R	Neuroprotective properties	Phase III (Morrison et al 2013)
ONO-2506 Pharmaceutical Co. Ltd. NCT00403104	Multicentre, double-blinded, placebo controlled, randomised parallel-group study	NOV-DEC 2006-2008 (n=420) 26 centres in 8 countries	- ALS definite/probable or possible - onset ≤14mnths - stable dose Riluzole - 18-74yrs	Administered orally 1,200mg daily for a period of 18mnths	Rate of decline SVC	Time to death, ALS FRS-R, muscle strength and quality of life	DATA NOT PUBLISHED	Modulatory compound of astrocytic function	Phase II (McCray & Ide 2000)
Copaxone® TEVA Pharmaceutical Industries Ltd. NCT0326625	Multicentre, double-blinded, placebo controlled, randomised parallel-	JUL-DEC 2006 (n=366) 13 centres in 6 countries	- ALS definite/probable - onset <3yrs - stable dose Riluzole - SVC ≥70% - 18-70yrs - ALSFRS-R of 10 points or	Subcutaneous injection 40mg daily for a period of 52wks	ALSFRS-R	Time to death or permanent assisted ventilation	Safe and well tolerated but no significant improvement in survival or ALSFRS-R	Neuroprotective and immune-modulatory compound used to treat relapsing and remitting MS	Phase II (Meininger et al 2009)

Table B4: Review of ALS Phase II/III Clinical Drug Trials (ClinicalTrials.gov) (U.S. National Library of Medicine, Bethesda)

	group study		more for measures of respiratory function						
Minocycline NINDS NCT00047723	Multicentre, double-blinded, placebo controlled, randomised parallel-group study	NOV-DEC 2003-2005 (n=412) 30 centres in 22 American states	- ALS definite/probable - onset <3yrs - stable dose Riluzole - FVC ≥75% - 21-85yrs	Administered orally in escalating doses of up to 400mg daily for a period of 9mnths	ALSFRS-R	Muscle strength, respiratory function, quality of life and time to death	Minocycline worsened the clinical course of ALS with some neurological & GI related adverse events recorded	Anti-apoptotic and anti-inflammatory compound used in the treatment of bacterial infections. Inhibits iNOS and caspase activation.	Phase III (Gordon et al 2007)
BDNF Study Group	Multicentre, double-blinded, placebo controlled, randomised parallel-group study	Pre-1999 (n=1,135)	- N/A	Subcutaneous injection 25 or 100mg /kg daily for a period of 9mnths	Time to death and rate of decline FVC	ALSFRS-R, syllable repetition and walking speed over 15ft	Safe and well tolerated but no significant improvement in survival or ALSFRS-R	Potent survival factor for MN’s	Phase III (BDNF 1999)

Abbreviations: Ab - antibody, ALS - Amyotrophic Lateral Sclerosis, BDNF - brain derived neurotrophic factor, FRS-R - Functional Rating Scale Revised, FVC - forced vital capacity, GI - gastrointestinal, iNOS - inducible nitric oxide synthase, LiC - lithium carbonate, MN - motor neuron, MND - Motor Neurone Disease, MS - Multiple Sclerosis, N/A - not available, NINDS - National Institute of Neurological Disorders and Stroke, PK - pharmacokinetics and SVC - slow vital capacity.

Table B5: Clinical Information Relating to Control LCL's in the ECACC Replication Cohort

ID	ECACC	Sex	Age	ID	ECACC	Sex	Age	ID	ECACC	Sex	Age	ID	ECACC	Sex	Age	ID	ECACC	Sex	Age
C101	LNh0053	M	51	C121	SC3734	F	40	C141	LC0414	M	35	C161	BC6084	F	57	C181	BC6162	F	77
C102	SNc0201	F	52	C122	LPo0087	M	47	C142	LRo0025	M	38	C162	BLi0198	M	61	C182	SC3754	M	44
C103	LC0162	M	59	C123	LRo0009	F	48	C143	SC3117	M	54	C163	SMa0054	F	48	C183	BC6416	M	51
C104	SPr0016	M	73	C124	SMa0227	M	52	C144	SNc0078	F	56	C164	SC3571	M	50	C184	LC0290	M	56
C105	LC0538	F	74	C125	LPy0011	F	55	C145	SC3425	M	57	C165	LC0095	F	71	C185	BLi0240	M	58
C106	BC6048	M	77	C126	SC3386	M	57	C146	SNc0167	M	60	C166	SC3142	M	72	C186	LC0220	F	58
C107	BC6434	F	80	C127	BM6403	F	59	C147	BC6043	F	61	C167	SMa0203	M	75	C187	SC3175	M	61
C108	BC6428	M	62	C128	LC0441	M	60	C148	BLi0259	M	63	C168	BC6426	M	80	C188	BLi0074	M	64
C109	SNc0158	F	63	C129	LC0521	M	62	C149	LC0045	M	65	C169	BC6274	F	63	C189	LCa0093	F	66
C110	BOx0008	M	64	C130	BLi0105	F	65	C150	BBr0020	F	66	C170	SMa0232	M	63	C190	LCa0134	M	66
C111	SMa0096	M	56	C131	SC3097	M	64	C151	SMa0050	F	67	C171	SMa0133	M	65	C191	LC0241	M	69
C112	SC3170	F	58	C132	SC3141	M	67	C152	SC3533	M	69	C172	BC6511	F	66	C192	LC0394	M	70
C113	LC0370	M	69	C133	SMa0009	F	67	C153	BBe0002	F	71	C173	LRf0012	M	68	C193	SC3178	M	71
C114	SC3403	F	69	C134	LNh0073	M	69	C154	BC6067	M	71	C174	BC6525	M	70	C194	SMa0013	M	73
C115	LC0459	M	70	C135	SNc0125	F	69	C155	LC0478	M	72	C175	BLi0021	M	71	C195	BLi0204	F	73
C116	SC3305	M	71	C136	SC3780	M	70	C156	SC3248	M	75	C176	LC0329	F	52	C196	BC6196	M	76
C117	BLi0224	F	36	C137	BC6238	M	72	C157	SNc0015	F	75	C177	SNt0075	M	57	C197	SDu0009	F	79
C118	LC0466	M	46	C138	BC6170	M	74	C158	SC3040	M	78	C178	SC3283	M	41	C198	BC6200	F	69
C119	LPo0059	M	66	C139	SMa0188	F	74	C159	LC0457	M	49	C179	LC0514	M	55	C199	SC3343	M	83
C120	SDu0007	F	66	C140	BC6156	M	78	C160	BLi0032	M	68	C180	BC6145	F	69	C200	SC3479	F	63

Table B6: Clinical Information Relating to Sporadic LCL's in the ECACC Replication Cohort

ID	ECACC	Sex	Age	EEC	Diagnosis	Genotype	Survival	Presentation	ALSFRS-R	Riluzole	Meds Other	Supplements	Smoking
S250	SP3375	M	46	Probable	ALS	Unknown	Unknown	Limb	46	Y	None	Vitamin C/E	N
S251	LP0077	M	47	Probable	ALS	Unknown	28	Limb	46	N	None	None	?
S252	BP6185	M	49	Probable	ALS	Unknown	Unknown	Limb	Unknown	Y	None	Multivitamin	?
S253	BP6180	F	50	Probable	ALS	Unknown	24	Limb	Unknown	Y	Minocycline	Vitamin E	?
S254	LP0036	M	51	Definite	ALS	Unknown	32	Bulbar	38	Y	None	None	?
S255	SP3388	F	51	Probable	ALS	Unknown	Unknown	Limb	34	Y	None	None	N
S256	LP0244	M	56	Definite	ALS	Unknown	34	Limb	42	Y	None	None	?
S257	SP3394	M	56	Probable	ALS	Unknown	45	Mixed	32	Y	None	Vitamin C/E	Y
S258	BP6230	F	58	Definite	ALS	Unknown	21	Limb	Unknown	Y	None	Vitamin E	?
S259	LNh0062	M	59	Probable	ALS	Unknown	Unknown	Bulbar	45	Y	None	None	?
S260	SP3161	M	58	Probable	ALS	Unknown	32	Bulbar	27	discontd	None	Vitamin C/E	?
S261	BP6163	F	60	Probable	ALS	Unknown	109	Limb	Unknown	Y	None	None	?
S262	BP6273	M	61	Probable	ALS	Unknown	66	Limb	Unknown	Y	None	None	?
S263	LP0407	F	73	Probable	ALS	Unknown	58	Limb	42	Y	None	None	?
S264	LNh0049	M	75	Definite	ALS	Unknown	45	Limb	40	Y	None	None	?
S265	BP6226	M	77	Definite	ALS	Unknown	74	Limb	Unknown	Y	None	None	?
S266	BP6155	F	78	Probable	ALS	Unknown	40	Bulbar	Unknown	N	None	Vitamin C	?
S267	SP3100	F	61	Probable	ALS	Unknown	Unknown	Limb	46	Y	None	None	?
S268	BP6107	M	62	Probable	ALS	*C9ORF72*	21	Limb	Unknown	Y	None	Multivitamin	?
S269	BP6262	M	61	Probable	ALS	Unknown	42	Limb	Unknown	Y	None	Vitamin E	?
S270	SP3350	M	61	Probable	ALS	Unknown	95	Limb	32	N	None	None	N
S271	BP6345	F	64	Probable	ALS	Unknown	34	Bulbar	Unknown	Y	None	None	?
S272	SP3253	M	52	PBP	PBP	Unknown	Unknown	Bulbar	37	Y	None	None	N
S273	LP0401	M	53	Probable	ALS	Unknown	66	Limb	0	Y	None	None	?
S274	SNt0008	M	52	Definite	ALS	Unknown	Unknown	Limb	45	Y	None	None	?
S275	LP0067	F	55	Definite	ALS	Unknown	24	Limb	43	Y	None	None	?
S276	LP0066	F	56	Definite	ALS	Unknown	40	Limb	43	N	None	None	?
S277	SP3267	M	55	Probable	ALS	Unknown	67	Limb	42	Y	None	None	Y
S278	BP6159	F	69	Probable	ALS	Unknown	Unknown	Limb	Unknown	Y	None	Vitamin C/E	?
S279	BP6079	M	69	Definite	ALS	Unknown	25	Limb	Unknown	Y	None	None	?
S280	BP6291	M	69	Probable	ALS	Unknown	13	Mixed	Unknown	Y	None	None	?
S281	LP0482	M	70	Probable	ALS	Unknown	Alive	Limb	44	Y	None	None	?

Table B6: Clinical Information Relating to Sporadic LCL’s in the ECACC Replication Cohort

S282	LP0439	F	35	Probable	ALS	Unknown	76	Limb	38	Y	None	None	?
S283	BP6096	M	35	Definite	ALS	Unknown	59	Limb	Unknown	Y	None	Vitamin C/E	?
S284	SP3069	M	38	Probable	ALS	Unknown	Unknown	Limb	46	Y	None	Vitamin C/E	N
S285	LP0221	M	42	Definite	ALS	Unknown	72	Bulbar	41	Y	None	Vitamin C/E	?
S286	SP3435	M	43	Definite	ALS	Unknown	Unknown	Limb	43	Y	None	None	Y
S287	BP6208	F	46	Definite	ALS	*C9ORF72*	36	Bulbar	Unknown	Y	None	None	?
S288	LP0323	F	63	Probable	ALS	Unknown	57	Limb	45	N	None	Multivitamin	?
S289	LPo0003	M	63	Definite	ALS	Unknown	41	Limb	19	N	None	None	?
S290	LNh0040	M	65	Probable	ALS	*C9ORF72*	43	Limb	36	N	None	None	?
S291	BP6098	M	66	Definite	ALS	*C9ORF72*	36	Limb	Unknown	Y	None	None	?
S292	BP6361	M	66	Probable	ALS	Unknown	29	Limb	Unknown	Y	None	None	?
S293	SP3302	M	67	Probable	ALS	Unknown	79	Limb	43	N	None	None	N
S294	BP6285	M	67	Definite	ALS	Unknown	38	Limb	Unknown	Y	None	Multivitamin	?
S295	BP6357	M	75	Probable	ALS	Unknown	31	Limb	Unknown	Y	None	None	?
S296	BP6369	F	67	Definite	ALS	Unknown	23	Bulbar	Unknown	discontd	None	None	?
S297	LP0448	M	58	Definite	ALS	Unknown	22	Bulbar	29	Y	None	Vitamin E	?
S298	LPo0001	M	72	Probable	ALS	Unknown	Alive	Limb	0	Y	None	None	?
S299	SNc0028	F	73	PBP	PBP	Unknown	91	Bulbar	44	Y	None	Vitamin C/E	?
S300	LNh0020	M	31	Probable	ALS	Unknown	Alive	Limb	Unknown	Y	None	Vitamin C	?
S301	SP3402	F	32	PLS	PLS	Unknown	Unknown	Limb	15	Y	None	Vitamin E	N
S302	LP0260	M	39	Definite	ALS	Unknown	32	Limb	40	Y	None	None	?
S303	BP6181	M	43	Definite	ALS	Unknown	94	Limb	Unknown	Y	None	Vitamin C/E	?
S304	LP0400	M	42	Probable	ALS	Unknown	Alive	Limb	42	Y	None	None	?
S305	SNc0043	F	45	Definite	ALS	Unknown	83	Limb	41	discontd	None	Vitamin C/E	?
S306	SP3439	M	46	Definite	ALS	Unknown	Unknown	Limb	41	Y	None	None	N
S307	LNh0048	M	48	Definite	ALS	Unknown	28	Limb	16	Y	None	None	?
S308	BP6328	M	50	PBP	PBP	Unknown	Unknown	Bulbar	Unknown	Y	None	None	?
S309	BP6363	F	50	Probable	ALS	*C9ORF72*	45	Limb	Unknown	Y	None	Vitamin E	?
S310	LNh0018	F	51	Definite	ALS	Unknown	20	Mixed	Unknown	Y	None	None	?
S311	LP0086	M	52	Probable	ALS	Unknown	Alive	Limb	48	Y	None	Vitamin E	?
S312	LP0199	M	52	Definite	ALS	Unknown	17	Limb	46	Y	None	None	?
S313	BP6236	M	53	Definite	ALS	Unknown	Unknown	Bulbar	Unknown	Y	None	None	?
S314	LP0269	M	53	Definite	ALS	Unknown	84	Limb	30	Y	None	Multivitamin	?

Table B6: Clinical Information Relating to Sporadic LCL's in the ECACC Replication Cohort

S315	LP0403	F	53	Probable	ALS	Unknown	56	Bulbar	42	Y	None	None	?
S316	SP3332	M	53	Probable	ALS	Unknown	60	Limb	46	Y	None	Vitamin C/E	N
S317	LP0132	M	54	Probable	ALS	Unknown	28	Limb	27	Y	None	Vitamin E	?
S318	LP0522	M	56	Probable	ALS	Unknown	28	Mixed	2	Y	None	None	?
S319	LP0203	F	57	Definite	ALS	*C9ORF72*	24	Bulbar	44	Y	None	Multivitamin	?
S320	BP6171	F	58	Probable	ALS	Unknown	46	Mixed	Unknown	Y	None	None	?
S321	LP0003	M	59	Probable	ALS	Unknown	Alive	Limb	37	Y	None	Multivitamin	?
S322	LSh0002	M	58	Probable	ALS	*C9ORF72*	30	Limb	39	Y	None	None	?
S323	LP0308	M	59	Definite	ALS	Unknown	18	Bulbar	32	Y	None	None	?
S324	SP3421	M	59	Probable	ALS+EL	Unknown	Unknown	Bulbar	45	Y	None	None	Y
S325	LP0248	F	61	Definite	ALS	*C9ORF72*	25	Bulbar	36	Y	None	None	?
S326	LSh0016	F	60	Probable	ALS	Unknown	Alive	Bulbar	39	Y	None	None	?
S327	SDu0001	M	62	Probable	ALS	Unknown	53	Limb	39	Y	None	Vitamin C	?
S328	BP6070	M	63	Definite	ALS	Unknown	37	Bulbar	Unknown	Y	None	Vitamin E	?
S329	BP6256	M	65	Probable	ALS	Unknown	44	Unknown	Unknown	Y	None	None	?
S330	SP3311	F	63	Definite	ALS	Unknown	Unknown	Bulbar	45	Y	None	None	N
S331	BP6268	M	65	Definite	ALS	Unknown	19	Limb	Unknown	Y	None	None	?
S332	BP6305	M	65	Probable	ALS	Unknown	110	Limb	Unknown	Y	None	None	?
S333	LP0432	F	66	Probable	ALS	Unknown	29	Respiratory	45	Y	Copaxone®	Vitamin E	?
S334	LP0442	M	65	Definite	ALS	Unknown	Alive	Limb	44	Y	None	None	?
S335	SP3387	M	65	Definite	ALS	Unknown	Unknown	Limb	26	Y	None	Vitamin C/E	N
S336	BP6116	M	66	Probable	ALS	Unknown	57	Limb	Unknown	N	None	None	?
S337	LP0012	M	67	Probable	ALS	Unknown	42	Limb	0	Y	None	None	?
S338	LP0338	F	68	Probable	ALS	Unknown	39	Bulbar	48	discontd	None	None	?
S339	BP6294	M	69	Definite	ALS	Unknown	18	Limb	Unknown	Y	None	None	?
S340	LP0458	F	69	Probable	ALS	Unknown	24	Bulbar	43	Y	None	None	?
S341	BP6175	M	70	Definite	ALS	Unknown	19	Bulbar	Unknown	Y	None	None	?
S342	BP6275	M	71	Probable	ALS	Unknown	Unknown	Limb	Unknown	Y	None	Multivitamin	?
S343	LP0330	F	71	Probable	ALS	Unknown	30	Mixed	22	Y	None	None	?
S344	LNh0065	M	73	Definite	ALS	Unknown	55	Bulbar	37	Y	None	None	?
S345	BP6320	M	75	Probable	ALS	Unknown	90	Limb	Unknown	Y	None	None	?
S346	LPo0016	M	75	Definite	ALS	Unknown	45	Limb	32	Y	None	Multivitamin	?
S347	BP6169	F	75	Definite	ALS	Unknown	47	Bulbar	Unknown	Y	None	Multivitamin	?

Table B6: Clinical Information Relating to Sporadic LCL's in the ECACC Replication Cohort

S348	BP6177	F	82	Definite	ALS	Unknown	23	Bulbar	Unknown	N	None	None	?
S349	BP6100	M	70	PBP	PBP	Unknown	82	Bulbar	Unknown	Y	None	None	?
S350	LP0210	M	35	Probable	ALS	Unknown	33	Limb	41	Y	None	None	?
S351	LP0451	M	37	Definite	ALS	Unknown	Alive	Limb	31	Y	None	None	?
S352	SP3484	F	37	Probable	ALS	*C9ORF72-TARDBP*	57	Limb	42	Y	None	Vitamin E	N
S353	BP6075	M	43	Probable	ALS	Unknown	70	Limb	Unknown	Y	None	Vitamin C	?
S354	BP6215	M	45	Probable	ALS	Unknown	51	Limb	Unknown	Y	None	Vitamin C/E	?
S355	SP3031	F	47	Definite	ALS	Unknown	Unknown	Bulbar	38	Y	None	None	N
S356	LP0413	M	46	Probable	ALS	Unknown	54	Limb	44	N	None	Multivitamin	?
S357	LP0331	M	48	Definite	ALS	Unknown	47	Bulbar	42	discontd	None	None	?
S358	LP0321	M	50	Definite	ALS	Unknown	105	Mixed	26	Y	None	None	?
S359	SNt0012	F	49	PBP	PBP	Unknown	Unknown	Bulbar	35	N	None	Multivitamin	?
S360	BP6136	M	52	Probable	ALS	Unknown	27	Limb	Unknown	Y	None	Vitamin C/E	?
S361	BP6266	M	52	Probable	ALS	Unknown	60	Limb	Unknown	Y	None	None	?
S362	LPo0019	F	53	Probable	ALS	Unknown	27	Limb	36	discontd	None	None	?
S363	BP6355	M	52	Definite	ALS	Unknown	34	Limb	Unknown	Y	None	None	?
S364	LP0373	M	52	Definite	ALS	Unknown	37	Limb	40	N	None	None	?
S365	BP6348	M	55	Probable	ALS	Unknown	Unknown	Limb	Unknown	N	None	None	?
S366	LP0427	F	55	Probable	ALS	Unknown	54	Limb	44	N	None	None	?
S367	BP6233	F	56	Probable	ALS	Unknown	62	Limb	Unknown	Y	None	None	?
S368	LP0454	M	56	Probable	ALS	*C9ORF72*	28	Bulbar	43	Y	None	None	?
S369	BP6197	F	58	Probable	ALS	Unknown	18	Bulbar	Unknown	Y	None	Vitamin C/E	?
S370	LP0350	M	59	Definite	ALS	Unknown	26	Mixed	39	Y	None	None	?
S371	BP6087	M	60	Probable	ALS	Unknown	44	Limb	Unknown	Y	None	None	?
S372	LP0339	F	60	Probable	ALS	Unknown	43	Bulbar	43	Y	None	None	?
S373	LP0359	M	61	Probable	ALS	*C9ORF72*	47	Mixed	35	Y	None	None	?
S374	LP0395	M	62	Definite	ALS	Unknown	44	Limb	39	Y	None	Multivitamin	?
S375	BP6120	F	64	Probable	ALS	Unknown	21	Limb	Unknown	N	None	None	?
S376	BP6131	M	63	Probable	ALS	Unknown	67	Limb	Unknown	Y	None	Multivitamin	?
S377	BP6289	M	64	Probable	ALS	Unknown	19	Limb	Unknown	Y	None	None	?
S378	LP0280	M	64	Probable	ALS	Unknown	45	Limb	0	Y	None	None	?
S379	SP3212	F	64	Definite	ALS	Unknown	Unknown	Limb	0	N	None	None	N
S380	SNc0049	M	65	Probable	ALS	Unknown	Unknown	Limb	42	Y	None	Vitamin C/E	?

Table B6: Clinical Information Relating to Sporadic LCL's in the ECACC Replication Cohort

S381	BP6240	M	87	Probable	ALS	Unknown	59	Limb	Unknown	Y	None	Vitamin C/E	?
S382	LP0062	F	66	Probable	ALS	Unknown	38	Limb	42	Y	None	None	?
S383	LPo0018	F	67	Definite	ALS	Unknown	39	Limb	37	Y	None	None	?
S384	BP6343	M	68	Definite	ALS	Unknown	27	Bulbar	Unknown	Y	None	None	?
S385	LP0063	M	68	Definite	ALS	Unknown	29	Respiratory	28	Y	None	None	?
S386	LP0131	M	68	Probable	ALS	Unknown	30	Limb	31	N	None	Multivitamin	?
S387	BP6224	M	69	Probable	ALS	Unknown	17	Mixed	Unknown	Y	None	None	?
S388	BP6199	M	72	Probable	ALS	Unknown	31	Limb	Unknown	Unknown	Unknown	Unknown	?
S389	BP6137	F	72	Definite	ALS	Unknown	24	Bulbar	Unknown	Y	None	None	?
S390	LP0431	F	75	Probable	ALS	Unknown	49	Mixed	32	Y	None	None	?
S391	BP6161	M	76	Probable	ALS	Unknown	Unknown	Limb	Unknown	Y	None	None	?
S392	BP6324	M	81	Probable	ALS	Unknown	Unknown	Limb	Unknown	Y	None	None	?
S393	BP6250	F	83	Probable	ALS	Unknown	28	Bulbar	Unknown	Y	None	None	?
S394	LPo0009	M	57	Definite	ALS	Unknown	12	Limb	46	Y	None	None	?
S395	LP0109	M	59	Probable	ALS	Unknown	Alive	Unknown	44	Y	None	None	?
S396	BP6259	M	69	Probable	ALS	Unknown	37	Limb	Unknown	Y	None	None	?
S397	LPo0047	F	68	Probable	ALS	Unknown	33	Bulbar	31	Y	None	None	?
S398	BP6202	M	70	Probable	ALS	Unknown	52	Unknown	Unknown	Y	None	None	?
S399	LP0040	M	76	Probable	ALS	Unknown	48	Limb	43	Y	None	None	?
S400	BP6083	M	56	Probable	ALS	Unknown	78	Limb	Unknown	Y	None	None	?
S401	BP6184	M	56	Probable	ALS	Unknown	36	Limb	Unknown	Y	None	Multivitamin	?
S402	BP6307	F	58	Probable	ALS	Unknown	18	Bulbar	Unknown	N	None	None	?
S403	BP6331	M	58	Probable	ALS	Unknown	32	Bulbar	Unknown	Y	None	None	?
S404	LP0173	M	59	Definite	ALS	Unknown	71	Limb	45	Y	None	None	?
S405	LSh0028	M	59	Probable	ALS	Unknown	45	Limb	41	Y	None	None	?
S406	BP6153	F	62	Probable	ALS	Unknown	13	Mixed	Unknown	Y	None	None	?
S407	SNt0042	M	35	Definite	ALS	Unknown	17	Limb	29	N	None	None	?
S408	LP0082	M	40	Probable	ALS	Unknown	70	Limb	41	N	None	None	?
S409	LP0227	F	44	Definite	ALS	Unknown	65	Limb	40	Y	None	None	?
S410	BP6088	M	44	Probable	ALS	Unknown	29	Limb	Unknown	Y	None	Vitamin C/E	?
S411	LP0281	M	44	Probable	ALS	Unknown	30	Limb	40	Y	None	None	?
S412	SP3147	F	47	Probable	ALS	*TARDBP*	115	Limb	31	Y	None	None	N
S413	LP0019	M	70	Probable	ALS	*C9ORF72*	44	Limb	41	N	ONO-trial	None	?

Table B6: Clinical Information Relating to Sporadic LCL's in the ECACC Replication Cohort

S414	LP0313	M	70	Definite	ALS	Unknown	61	Limb	40	Y	None	Multivitamin	?
S415	BP6283	M	72	Definite	ALS	Unknown	69	Limb	Unknown	Y	None	None	?
S416	LP0028	F	83	Definite	ALS	Unknown	32	Bulbar	33	N	None	None	?
S417	BP6064	M	62	Probable	ALS	Unknown	Unknown	Limb	Unknown	Y	None	None	?
S418	SP3194	M	64	Probable	ALS+EL	Unknown	Unknown	Limb	21	Y	None	None	Ex-Smoker
S419	LP0206	F	64	Definite	ALS	Unknown	5	Bulbar	44	Y	None	None	?
S420	SNc0057	M	65	Definite	ALS	Unknown	123	Limb	41	Y	None	Vitamin C/E	?
S421	BP6314	M	66	Definite	ALS	Unknown	24	Limb	Unknown	Y	None	None	?
S422	LP0071	F	66	Probable	ALS	Unknown	29	Mixed	0	Y	None	None	?
S423	LP0384	M	67	Probable	ALS	Unknown	50	Limb	36	Y	None	None	?
S424	BP6174	F	69	Probable	ALS	Unknown	Unknown	Limb	Unknown	Y	None	None	?
S425	BP6228	M	70	Probable	ALS	Unknown	22	Unknown	Unknown	Unknown	Unknown	Unknown	?
S426	BP6279	M	51	Definite	ALS	Unknown	24	Limb	Unknown	Y	None	None	?
S427	SNt0021	F	51	Probable	ALS	Unknown	17	Limb	40	Y	None	None	?
S428	BP6299	F	54	Probable	ALS	Unknown	20	Limb	Unknown	Y	None	Vitamin E	?
S429	LPo0039	M	53	Probable	ALS	Unknown	17	Mixed	34	Y	None	None	?
S430	BP6270	M	54	Probable	ALS	Unknown	Unknown	Limb	Unknown	Y	None	Vitamin C/E	?
S431	BP6190	M	55	Definite	ALS	Unknown	16	Bulbar	Unknown	Y	None	Vitamin C/E	?
S432	BBe0015	M	45	Probable	ALS	Unknown	Unknown	Limb	Unknown	Y	None	None	?
S433	BP6353	M	46	Probable	ALS	Unknown	70	Limb	Unknown	Y	None	Vitamin C	?
S434	BP6306	M	51	Probable	ALS	Unknown	Unknown	Limb	Unknown	Y	None	None	?
S435	BP6349	F	56	Probable	ALS	Unknown	25	Bulbar	Unknown	Y	None	None	?
S436	BP6142	M	60	Probable	ALS	Unknown	28	Mixed	Unknown	Y	None	Multivitamin	?
S437	LP0355	F	61	Definite	ALS	Unknown	Unknown	Limb	40	Y	None	None	?
S438	LP0411	M	62	Probable	ALS	*C9ORF72*	12	Limb	34	Y	None	None	?
S439	BP6090	M	64	Probable	ALS	Unknown	117	Unknown	Unknown	N	None	None	?
S440	BP6297	M	65	Definite	ALS	*C9ORF72*	15	Limb	Unknown	discontd	None	None	?
S441	LP0119	F	64	Definite	ALS	Unknown	29	Bulbar	30	N	None	None	?
S442	SP3261	M	66	Probable	ALS	Unknown	Unknown	Limb	35	Y	None	None	N
S443	BP6239	F	67	Definite	ALS	Unknown	38	Limb	Unknown	Y	None	None	?
S444	LP0349	M	68	Probable	ALS	Unknown	78	Limb	17	Y	None	Vitamin C/E	?
S445	SP3407	M	69	Probable	ALS	Unknown	64	Limb	43	Y	None	None	N
S446	SPr0005	F	73	Probable	ALS	Unknown	67	Bulbar	37	Y	None	None	?

Table B6: Clinical Information Relating to Sporadic LCL's in the ECACC Replication Cohort

S447	BP6347	M	76	Probable	ALS	Unknown	19	Limb	Unknown	Y	None	None	?
S448	LP0078	F	78	Probable	ALS	Unknown	31	Bulbar	38	N	None	None	?
S449	BP6352	M	81	Probable	ALS	Unknown	Unknown	Respiratory	Unknown	N	None	None	?
S450	LP0014	M	31	Probable	ALS	Unknown	40	Limb	Unknown	Y	Novartis-trial	None	?
S451	BP6134	M	37	Definite	ALS	Unknown	55	Limb	Unknown	Y	None	Vitamin C/E	?
S452	LP0195	M	41	Probable	ALS	Unknown	Alive	Limb	0	Y	None	None	?
S453	LP0380	M	43	Probable	ALS	Unknown	Alive	Limb	43	Y	None	None	?
S454	LP0364	M	44	Probable	ALS	Unknown	Alive	Limb	43	Y	None	None	?
S455	BP6152	F	45	Definite	ALS+PD	Unknown	27	Mixed	Unknown	Y	None	None	?
S456	SPr0001	M	49	Definite	ALS	Unknown	49	Bulbar	32	Y	ONO-trial	Vitamin E	?
S457	LNh0016	M	50	Probable	ALS	Unknown	72	Limb	Unknown	Y	None	None	?
S458	BP6085	F	50	Probable	ALS	Unknown	56	Limb	Unknown	Y	None	Vitamin C	?
S459	BP6364	M	50	Probable	ALS	Unknown	53	Limb	Unknown	Y	None	None	?
S460	BP6167	F	51	Probable	ALS	Unknown	27	Bulbar	Unknown	Y	None	None	?
S461	SP3107	M	51	Probable	ALS	*TARDBP*	77	Limb	43	Y	None	Vitamin C/E	Y
S462	BP6094	F	54	Probable	ALS	*C9ORF72*	31	Limb	Unknown	Y	None	Vitamin C/E	?
S463	SNt0013	F	54	Probable	ALS	Unknown	77	Bulbar	42	Y	None	Vitamin C/E	?
S464	SNt0040	M	55	Definite	ALS	Unknown	38	Mixed	38	Y	None	None	?
S465	SP3226	M	55	Probable	ALS	Unknown	33	Limb	0	N	None	None	?
S466	SNc0020	M	55	Probable	ALS	Unknown	98	Bulbar	35	N	None	None	?
S467	SP3198	M	56	Probable	ALS-FA	Unknown	Unknown	Limb	0	Y	None	None	Ex-Smoker
S468	BP6360	M	57	Probable	ALS	Unknown	31	Limb	Unknown	Y	None	None	?
S469	BP6277	M	59	Definite	ALS	Unknown	35	Limb	Unknown	Y	None	Vitamin C/E	?
S470	BP6122	M	60	Probable	ALS	Unknown	55	Bulbar	Unknown	Y	None	None	?
S471	LP0382	M	59	Probable	ALS	Unknown	68	Limb	46	Y	None	None	?
S472	BP6310	M	61	Probable	ALS	Unknown	81	Limb	Unknown	Y	None	None	?
S473	LSh0004	M	61	Definite	ALS	Unknown	73	Bulbar	36	Y	None	None	?
S474	LP0366	F	61	Definite	ALS	Unknown	53	Mixed	0	N	None	None	?
S475	BP6264	F	63	Probable	ALS	Unknown	41	Limb	Unknown	Y	None	None	?
S476	SDu0005	M	64	Probable	ALS	Unknown	18	Bulbar	36	Y	None	None	?
S477	LP0208	F	65	Probable	ALS	Unknown	38	Limb	30	Y	None	None	?
S478	LP0126	M	66	Definite	ALS	Unknown	17	Mixed	42	Y	None	None	?
S479	BP6069	M	66	Probable	ALS	Unknown	53	Limb	Unknown	N	None	None	?

Table B6: Clinical Information Relating to Sporadic LCL's in the ECACC Replication Cohort

S480	BP6278	M	67	Probable	ALS	Unknown	90	Limb	Unknown	Y	None	None	?
S481	BP6292	M	66	Probable	ALS	Unknown	95	Limb	Unknown	Y	None	None	?
S482	SP3367	M	67	Definite	ALS	Unknown	Unknown	Limb	37	N	None	None	N
S483	BP6252	M	68	Probable	ALS	Unknown	27	Respiratory	Unknown	Y	None	None	?
S484	BP6269	F	67	Probable	ALS	Unknown	25	Mixed	Unknown	Y	None	None	?
S485	LPo0005	M	68	Probable	ALS	*C9ORF72*	47	Bulbar	0	Y	None	None	?
S486	SP3229	M	68	Probable	ALS	Unknown	Unknown	Limb	22	Y	None	None	?
S487	LP0398	M	70	Probable	ALS	Unknown	20	Bulbar	41	N	None	None	?
S488	BP6191	F	72	Probable	ALS	Unknown	23	Limb	Unknown	Y	None	Vitamin C	?
S489	LPo0017	M	74	Probable	ALS	Unknown	17	Limb	34	Y	None	None	?
S490	LP0312	F	75	Probable	ALS	Unknown	61	Limb	27	N	None	None	?
S491	SP3344	M	75	Definite	ALS	Unknown	69	Limb	38	Y	None	None	N
S492	SNt0019	M	76	Definite	ALS	Unknown	106	Bulbar	30	Y	None	None	?
S493	BP6321	M	82	Probable	ALS	Unknown	17	Bulbar	Unknown	Y	None	None	?
S494	BP6172	F	59	Probable	ALS	Unknown	40	Bulbar	Unknown	Y	None	None	?
S495	BP6316	M	66	Probable	ALS	Unknown	39	Limb	Unknown	N	None	Multivitamin	?
S496	BP6350	F	68	Probable	ALS	Unknown	34	Limb	Unknown	Y	None	None	?
S497	SP3234	F	79	PLS	PLS	Unknown	16	Limb	0	Y	None	None	N
S498	BP6326	M	53	Probable	ALS	Unknown	13	Bulbar	Unknown	Y	None	None	?
S499	BP6272	F	59	Probable	ALS	Unknown	17	Limb	Unknown	discontd	None	None	?

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

Sample	Collection	Extraction	260/280	260/230	RNA (ng/μl)	RIN	Amplification	as-cRNA (ng/μl)	ss-cDNA (ng/μl)	Frag/Lab	Scan Date	GeneChip®
C001	13/06/08	29/11/11	2.02	1.12	203.21	9.2	13/03/13	1049.94	278.81	03/04/13	23/04/13	LOT4188786
C002	21/12/10	01/12/11	2.02	1.43	120.40	8.7	07/12/12	1710.48	331.49	08/04/13	30/04/13	LOT4187458
C003	13/10/10	02/12/11	2.03	0.42	121.96	poor	26/03/13	2280.46	300.88	24/07/13	15/08/13	LOT4205079
C004	25/04/07	02/12/11	2.08	0.74	150.47	9.9	26/10/12	896.68	211.87	?	16/01/13	LOT4181223
C005	22/05/07	05/12/11	2.02	1.74	103.67	9.4	15/11/12	1446.52	262.65	?	29/01/13	LOT4181223
C006	17/04/07	05/12/11	1.99	1.85	112.12	8.5	16/03/12	1007.90	237.31	25/04/12	02/05/12	LOT4156426
C007	17/05/06	06/12/11	2.03	2.33	152.45	OK	24/10/12	724.60	218.01	?	30/01/13	LOT4184161
C008	28/01/09	06/12/11	2.00	2.33	150.16	poor	26/10/12	1249.30	245.70	?	30/01/13	LOT4184161
C009	04/04/08	06/12/11	1.91	2.00	48.85	6.5	20/03/13	1585.73	283.33	05/06/13	31/07/13	LOT4205079
C010	28/05/08	07/12/11	2.01	1.07	117.04	7.7	25/04/13	2560.20	286.43	27/04/13	22/05/13	LOT4181871
C011	15/06/06	07/12/11	2.05	2.00	91.10	9.3	07/12/12	2243.90	282.64	02/04/13	23/04/13	LOT4188786
C012	02/04/08	07/12/11	1.84	0.60	30.76	7.0	22/03/13	1337.98	245.98	11/06/13	18/07/13	LOT4188786
C013	06/02/09	08/12/11	2.01	1.86	141.51	7.0	19/03/13	1744.27	268.43	20/03/13	10/04/13	LOT4181871
C014	06/03/07	08/12/11	2.06	0.56	160.91	9.1	07/05/13	2267.51	265.04	14/05/13	18/07/13	LOT4188786
C015	10/06/09	08/12/11	1.98	0.83	67.52	8.3	30/04/13	1559.62	267.09	17/06/13	30/07/13	LOT4181223
C016	06/03/08	08/12/11	2.02	1.96	195.38	7.5	15/11/12	1370.07	266.72	?	29/01/13	LOT4181223
C017	25/01/07	09/12/11	1.98	2.42	164.98	7.2	05/12/12	1411.07	255.17	02/04/13	24/04/13	LOT4187458
C018	26/02/08	09/12/11	2.06	0.97	106.69	8.9	13/03/13	2198.64	274.72	03/04/13	24/04/13	LOT4187458
C019	17/04/08	09/12/11	2.03	1.60	113.88	9.8	05/12/12	2343.48	275.36	26/03/13	12/04/13	LOT4181871
C020	27/10/07	18/04/12	2.00	2.15	167.74	7.0	07/11/12	747.17	215.39	?	06/02/13	LOT4181871
C021	03/11/08	13/12/11	2.01	2.49	173.37	8.3	03/04/12	2156.61	311.82	26/04/12	03/05/12	LOT4156426
C022	10/12/10	13/12/11	1.97	2.70	81.46	7.0	28/11/12	949.07	370.68	26/03/13	25/04/13	LOT4187458
C023	17/07/10	14/12/11	1.97	1.60	148.86	7.8	22/03/13	2697.84	301.09	05/06/13	31/07/13	LOT4205079
C024	14/07/05	14/12/11	2.06	2.09	158.63	9.7	14/03/13	2124.93	285.46	26/03/13	24/04/13	LOT4187458
C025	17/02/11	15/12/11	2.02	2.56	149.47	9.3	20/03/13	2990.10	296.13	17/06/13	23/07/13	LOT4188786
C026	23/05/07	15/12/11	2.03	1.79	223.37	9.4	03/04/12	2541.23	267.16	25/04/12	02/05/12	LOT4156426
C027	28/10/05	16/12/11	1.95	1.76	183.78	9.5	28/11/12	2125.91	286.02	03/04/13	23/04/13	-
C028	08/11/07	16/12/11	2.04	2.35	112.66	9.3	22/03/13	2290.58	277.15	17/06/13	02/07/13	LOT4181871
C029	25/05/05	19/12/11	2.02	1.47	171.39	9.6	28/11/12	2238.83	277.64	26/03/13	23/04/13	LOT4188786
C030	29/07/09	19/12/11	2.03	1.21	143.87	9.3	26/03/13	2463.98	288.94	29/07/13	15/08/13	LOT4205079
C031	06/11/10	19/12/11	1.99	1.95	118.13	9.7	23/03/12	1142.49	221.59	26/04/12	01/05/12	LOT4153111
C032	18/03/08	20/12/11	2.03	2.51	138.58	9.5	13/03/13	1818.47	286.36	25/03/13	10/04/13	LOT4181871

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

C033	21/01/11	20/12/11	2.00	0.71	64.94	5.2	22/03/13	1841.56	244.33	------------------- FAILED -------------------		
C034	26/08/05	20/12/11	2.01	3.15	62.10	9.4	16/04/13	1974.66	270.30	24/04/13	22/05/13	LOT4181871
C035	22/01/04	20/12/11	2.01	1.18	151.19	8.9	26/10/12	1023.09	243.60	?	05/02/13	LOT4184161
C036	22/02/10	21/12/11	2.04	1.81	153.13	9.5	09/03/12	682.30	226.04	25/04/12	01/05/12	LOT4153111
C037	19/02/09	21/12/11	2.05	0.95	138.30	9.6	12/04/12	868.78	249.42	25/04/12	09/05/12	LOT4158373
C038	13/09/07	21/12/11	2.01	1.95	127.38	2.9	22/03/13	2937.83	272.05	12/06/13	16/07/13	LOT4181871
C039	15/10/09	21/12/11	2.04	2.04	122.22	9.8	23/03/12	1125.91	217.39	26/04/12	02/05/12	LOT4156426
C040	08/11/08	21/12/11	2.04	2.30	163.49	9.8	14/03/13	2429.54	281.56	08/04/13	01/05/13	LOT4187458
C041	26/06/08	09/01/12	2.06	1.93	213.12	3.9	20/02/13	2606.84	269.00	25/03/13	11/04/13	LOT4188786
C042	07/04/06	09/01/12	2.02	2.13	141.28	9.3	16/04/13	1602.42	257.86	24/04/13	22/05/13	LOT4181871
C043	19/08/06	10/01/12	2.03	1.35	174.61	8.8	20/02/13	773.23	246.01	25/03/13	11/04/13	LOT4188786
C044	15/06/06	10/01/12	2.09	1.85	206.00	8.8	30/08/12	611.13	214.29	?	27/10/12	LOT4179034
C045	05/07/07	11/01/12	2.05	1.59	244.71	9.5	02/03/12	477.79	203.49	25/04/12	09/05/12	LOT4158373
C046	25/09/07	11/01/12	2.06	1.87	173.56	9.3	17/04/13	1664.34	263.85	17/06/13	24/07/13	LOT4181223
C047	11/12/08	11/01/12	2.10	1.77	73.99	8.3	27/03/13	2603.59	293.78	31/07/13	06/08/13	LOT4205911
C048	17/02/05	11/01/12	2.05	1.15	172.09	9.7	20/02/13	1877.06	263.63	02/04/13	25/04/13	LOT4187458
C049	18/06/04	11/01/12	2.04	1.99	116.56	9.3	06/08/12	674.92	212.53	?	26/10/12	LOT4174114
C050	19/09/05	09/01/12	2.03	1.88	105.05	8.9	12/04/13	1464.91	284.22	20/03/13	10/04/13	LOT4181871
C051	10/06/07	12/01/12	2.03	1.81	114.78	9.0	27/03/13	3498.70	298.36	24/07/13	13/08/13	LOT4205911
C052	26/08/09	12/01/12	1.99	1.82	90.79	8.0	26/03/13	2800.67	432.64	29/07/13	15/08/13	LOT4205079
C053	06/10/09	12/01/12	2.06	2.18	194.05	9.2	27/02/13	2194.73	282.66	02/04/13	23/04/13	LOT4188786
C054	25/03/07	26/01/12	2.07	2.22	137.07	9.0	12/04/13	2515.20	292.41	------------------- FAILED -------------------		
C055	19/08/06	12/01/12	2.05	2.05	134.87	9.1	16/04/13	2397.82	271.77	24/04/13	18/07/13	-
C056	13/01/06	12/01/12	2.07	1.12	185.85	10	12/04/13	2311.03	276.93	05/06/13	31/07/13	LOT4205079
C057	25/10/07	12/01/12	2.05	1.66	134.50	9.2	27/03/13	2715.58	294.45	31/07/13	06/08/13	LOT4205911
C058	02/06/06	13/01/12	2.09	2.14	192.79	10	04/09/12	1051.20	196.83	?	25/10/12	LOT4174114
C059	06/04/06	13/01/12	2.03	1.60	128.20	8.7	27/02/13	1895.96	262.85	26/03/13	30/04/13	LOT4187458
C060	21/05/10	13/01/12	2.08	1.79	157.79	8.9	02/11/12	943.31	237.41	?	30/01/13	LOT4184161
C061	26/08/05	16/01/12	2.08	2.25	117.80	8.0	12/04/12	2666.64	252.83	25/04/12	03/05/12	LOT4156426
C062	26/02/05	23/04/12	2.05	1.57	308.32	8.1	01/05/13	2283.50	289.81	17/06/13	24/07/13	LOT4181223
C063	08/08/06	23/04/12	2.04	1.20	238.11	OK	25/04/13	1947.96	263.69	14/05/13	18/07/13	-
C064	09/10/10	23/04/12	2.08	0.75	162.01	10	02/05/13	1709.54	285.75	15/05/13	30/07/13	LOT4181223
C065	05/05/09	17/01/12	2.04	1.99	170.27	9.2	17/04/13	2042.11	271.05	15/05/13	23/07/13	LOT4188786

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

C066	13/01/06	17/01/12	2.05	0.98	182.55	10	18/04/13	3004.21	308.73	17/06/13	24/07/13	LOT4181223
C067	11/04/08	17/01/12	2.03	1.51	146.34	poor	28/09/12	793.89	222.89	?	29/01/13	LOT4181223
C068	17/11/08	19/01/12	2.09	0.73	91.23	4.1	16/04/13	2920.08	283.83	03/06/13	09/07/13	-
C069	13/10/06	19/01/12	1.97	1.77	117.27	8.9	17/04/13	2504.95	282.99	03/06/13	09/07/13	LOT4187458
C070	24/11/06	19/01/12	2.07	1.40	133.21	9.1	08/05/13	1985.57	269.82	12/06/13	16/07/13	LOT4188786
C071	29/04/08	19/01/12	2.04	1.03	142.94	9.3	19/04/13	2604.87	242.17	12/06/13	16/07/13	LOT4188786
C072	26/01/09	19/01/12	2.05	2.20	181.69	9.5	02/05/13	3050.58	293.85	17/06/13	17/07/13	LOT4188786
C073	12/05/05	20/01/12	2.08	1.90	283.45	3.0	02/11/12	2051.99	251.97	------------------- FAILED -------------------		
C074	25/02/10	20/01/12	2.03	1.07	63.81	9.6	18/04/13	2195.63	297.27	17/06/13	31/07/13	LOT4205079
C075	21/04/06	20/01/12	2.05	2.22	151.01	9.7	28/09/12	578.21	221.99	?	05/02/13	LOT4184161
C076	24/04/08	20/01/12	2.05	0.97	121.32	3.3	18/04/13	2906.02	306.38	17/06/13	17/07/13	LOT4188786
C077	25/07/08	20/01/12	2.05	1.64	105.89	OK	03/05/13	2536.71	347.58	11/06/13	31/07/13	LOT4205079
C078	06/03/08	23/01/12	1.99	1.50	106.92	7.8	19/04/13	2130.91	299.15	12/06/13	24/07/13	LOT4188786
C079	13/06/06	26/01/12	2.06	1.25	57.39	4.0	16/04/13	1838.20	280.91	24/04/13	02/07/13	LOT4181871
C080	06/08/07	25/01/12	2.02	2.13	163.88	8.5	15/03/13	2449.40	279.63	08/04/13	25/04/13	LOT4187458
C081	19/02/11	23/01/12	1.95	1.50	128.88	6.3	07/05/13	2045.19	293.28	12/06/13	31/07/13	LOT4205079
C082	05/11/09	23/01/12	1.98	0.55	111.39	7.3	19/04/13	1526.32	279.38	05/06/13	31/07/13	LOT4205079
C083	12/03/11	19/04/12	2.02	2.17	220.37	9.6	01/05/13	2537.44	294.92	11/06/13	30/07/13	LOT4181223
C084	28/07/09	24/01/12	1.99	2.07	91.90	OK	14/02/13	866.27	262.10	02/04/13	30/04/13	LOT4187458
C085	17/05/06	24/01/12	2.06	1.94	170.90	7.2	01/05/13	2342.98	294.67	12/06/13	31/07/13	LOT4205079
C086	07/08/10	24/01/12	2.00	2.12	193.39	7.6	02/05/13	2016.99	284.69	------------------- FAILED -------------------		
C087	02/12/05	25/01/12	2.02	1.23	107.79	2.6	02/05/13	3140.04	286.58	17/06/13	17/07/13	LOT4188786
C088	30/08/07	27/01/12	2.10	2.22	201.12	10	11/09/12	1082.94	224.58	?	26/10/12	LOT4174114
C089	02/05/09	26/01/12	2.05	2.04	220.86	8.8	03/05/13	2319.70	278.72	17/06/13	17/07/13	LOT4188786
C090	03/02/11	31/01/12	2.00	2.06	145.08	7.4	01/05/13	2655.29	292.81	17/06/13	02/07/13	LOT4181871
C091	25/02/11	26/01/12	2.09	2.12	124.77	poor	08/05/13	2714.89	281.39	11/06/13	09/07/13	LOT4188786
C092	07/10/10	31/01/12	2.08	2.21	203.36	9.1	07/05/13	1105.14	247.41	------------------- FAILED -------------------		
C093	07/03/10	01/02/12	2.06	2.02	206.06	9.6	09/04/13	2050.72	265.54	17/06/13	16/07/13	LOT4188786
C094	16/10/10	01/02/12	2.02	2.16	155.96	6.8	24/10/12	732.81	197.58	?	16/01/13	LOT4181223
C095	11/07/07	26/01/12	2.03	2.21	147.12	8.2	08/05/13	1675.19	275.87	12/06/13	17/07/13	LOT4188786
C096	28/10/09	26/01/12	2.06	1.90	136.21	8.5	30/04/13	1696.15	275.01	29/07/13	15/08/13	LOT4205079
C097	02/09/08	26/01/12	2.04	2.28	153.24	8.9	24/10/12	704.59	203.66	?	16/01/13	LOT4181223
C098	19/08/06	27/01/12	2.02	2.08	137.96	8.4	04/09/12	815.39	251.56	?	25/10/12	LOT4174114

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

C099	08/06/06	27/01/12	2.04	2.19	182.49	9.6	03/04/12	2090.20	264.17	26/04/12	01/05/12	LOT4153111
C100	07/03/08	13/03/12	2.04	1.86	101.83	8.3	09/04/13	3181.44	270.62	31/07/13	06/08/13	LOT4205911
F001	21/05/05	29/11/11	2.03	1.46	267.27	9.9	15/11/12	1508.44	283.67	?	16/01/13	LOT4181223
F002	17/11/08	01/12/11	2.05	1.88	160.47	8.6	07/12/12	1995.32	271.67	20/03/13	10/04/13	LOT4181871
F003	02/10/04	02/12/11	2.28	0.09	34.31	7.4	22/03/13	923.13	245.97	29/07/13	15/08/13	LOT4205079
F004	22/08/08	02/12/11	2.01	0.60	145.30	8.2	05/12/12	1598.97	253.32	26/03/13	12/04/13	LOT4181871
F005	12/11/05	02/12/11	2.10	0.18	77.32	7.7	07/11/12	528.08	205.64	?	05/02/13	LOT4184161
F006	01/06/06	05/12/11	2.04	1.86	207.82	8.4	22/03/13	2178.68	244.95	01/07/13	30/07/13	LOT4181223
F007	23/10/06	05/12/11	2.01	1.83	305.28	9.4	15/11/12	1279.09	243.87	?	05/02/13	LOT4184161
F008	17/03/05	05/12/11	2.04	2.25	166.78	6.9	15/11/12	1494.11	272.62	?	29/01/13	LOT4184161
F009	10/02/05	05/12/11	2.06	2.04	131.10	9.8	07/12/12	2122.76	284.80	25/03/13	11/04/13	LOT4188786
F010	10/12/10	06/12/11	2.01	1.45	161.47	7.0	13/03/13	1545.54	278.71	26/03/13	23/04/13	LOT4188786
F011	04/02/09	06/12/11	1.99	0.97	60.08	8.8	18/09/12	632.75	237.18	?	26/10/12	LOT4174114
F012	30/01/08	06/12/11	2.06	1.13	107.63	9.1	05/12/12	2587.67	321.98	25/03/13	12/04/13	LOT4188786
F013	19/03/10	07/12/11	2.05	0.96	74.57	5.4	13/03/13	1790.06	285.99	02/04/13	25/04/13	LOT4187458
F014	05/03/09	07/12/11	2.04	1.24	55.96	4.8	20/03/13	1894.30	273.43	01/07/13	24/07/13	LOT4181223
F015	13/03/07	07/12/11	1.99	1.96	143.40	8.8	07/05/13	2687.48	274.18	31/07/13	06/08/13	LOT4205911
F016	19/06/06	07/12/11	1.97	1.88	106.93	7.7	07/11/12	1014.75	256.50	?	29/01/13	LOT4184161
F017	17/03/05	07/12/11	2.03	1.97	184.91	9.1	24/10/12	683.23	198.58	?	05/02/13	LOT4184161
F018	13/06/08	08/12/11	2.04	1.11	164.06	OK	07/11/12	1782.70	261.24	?	16/01/13	LOT4181223
F019	10/06/08	08/12/11	2.02	1.71	149.66	7.5	26/03/13	3089.85	287.98	29/07/13	13/08/13	LOT4205911
F020	24/09/10	09/12/11	1.97	1.42	149.47	7.6	07/12/12	1463.05	275.11	26/03/13	23/04/13	LOT4188786
F021	23/04/05	09/12/11	2.04	2.23	134.45	9.1	07/12/12	2143.96	289.11	26/03/13	30/04/13	LOT4187458
F022	06/03/06	09/12/11	1.99	1.88	157.47	9.5	22/03/13	2188.56	272.61	30/07/13	06/08/13	LOT4205911
F023	13/01/05	09/12/11	2.00	2.55	142.05	8.7	30/03/12	814.89	230.41	25/04/12	09/05/12	LOT4156426
F024	26/08/05	25/01/12	2.02	0.60	104.02	7.5	16/03/12	652.66	217.10	26/04/12	03/05/12	LOT4156426
F025	11/09/09	13/12/11	2.01	1.65	150.93	8.9	20/03/13	2008.51	285.02	20/03/13	10/04/13	LOT4181871
F026	11/05/09	14/12/11	2.07	2.38	168.50	9.3	26/10/12	1479.01	242.38	?	05/02/13	LOT4184161
F027	07/10/10	14/12/11	2.03	2.01	216.52	9.3	14/03/13	1428.03	253.58	02/04/13	25/04/13	LOT4187458
F028	23/05/08	14/12/11	1.99	1.09	79.51	8.8	27/03/13	2715.58	291.01	24/07/13	13/08/13	LOT4205911
F029	16/07/08	14/12/11	2.00	2.07	145.99	7.6	28/11/12	1814.48	282.77	25/03/13	11/04/13	LOT4188786
F030	22/04/07	15/12/11	2.03	2.33	208.65	9.3	20/03/13	1747.25	294.81	30/07/13	13/08/13	LOT4205911
F031	13/06/08	15/12/11	2.07	1.31	193.34	3.5	14/03/13	2095.91	262.79	02/04/13	25/04/13	LOT4187458

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

F032	06/11/10	15/12/11	2.01	1.31	138.80	9.2	22/03/13	2354.91	252.12	31/07/13	06/08/13	LOT4205911
F033	08/12/03	16/12/11	1.83	2.93	52.10	7.0	27/03/13	2159.92	293.47	30/07/13	06/08/13	LOT4205911
F034	22/05/10	16/12/11	1.94	2.27	206.95	9.8	22/03/13	2170.01	282.25	30/07/13	02/05/12	-
F035	17/04/09	16/12/11	1.94	2.47	157.19	9.3	12/04/13	2304.89	301.92	01/07/13	23/07/13	LOT4188786
F036	19/09/05	14/02/12	2.07	2.33	188.19	9.4	13/03/13	2022.43	294.77	02/04/13	01/05/13	LOT4187458
F037	06/10/07	16/12/11	2.07	2.31	222.14	4.8	26/03/13	3022.23	277.94	29/07/13	13/08/13	LOT4205911
F038	08/01/11	16/12/11	2.04	2.55	128.63	10	20/03/13	3097.12	314.56	29/07/13	14/08/13	LOT4205079
F039	19/02/09	19/12/11	2.03	2.48	164.71	8.9	14/03/13	1658.03	260.03	02/04/13	30/04/13	LOT4187458
F040	04/11/04	19/12/11	2.01	1.20	208.45	7.7	18/04/13	2471.95	300.23	30/07/13	06/08/13	LOT4205911
F041	07/08/07	19/12/11	2.01	1.36	131.62	8.8	12/04/13	2163.25	326.15	20/03/13	10/04/13	LOT4181871
F042	02/09/06	19/12/11	2.03	1.68	206.17	9.7	02/03/12	521.92	278.34	25/04/12	09/05/12	LOT4158373
F043	21/07/06	20/12/11	2.05	1.08	144.55	9.4	09/03/12	633.61	253.39	25/04/12	03/05/12	LOT4156426
F044	04/04/07	20/12/11	2.01	0.95	98.79	8.1	12/04/12	1743.77	231.77	25/04/12	01/05/12	LOT4181223
F045	08/01/11	20/12/11	1.98	2.42	180.17	7.8	12/04/13	2602.51	349.24	29/07/13	13/08/13	LOT4205911
F046	22/03/04	20/12/11	2.03	2.54	141.95	8.8	30/03/12	1247.74	259.22	25/04/12	01/05/12	LOT4153111
F047	14/05/10	21/12/11	2.04	0.30	86.67	4.6	28/11/12	1437.49	266.90	08/04/13	24/04/13	LOT4187458
F048	10/06/08	21/12/11	2.02	1.32	161.27	9.7	28/11/12	2172.48	279.21	20/03/13	10/04/13	LOT4181871
F049	01/08/07	09/01/12	2.02	2.05	138.63	9.5	17/04/13	2919.98	280.37	30/07/13	06/08/13	LOT4205911
F050	22/06/07	09/01/12	2.03	2.06	129.59	8.8	18/04/13	2222.23	303.80	30/07/13	06/08/13	LOT4205911
F051	13/04/06	10/01/12	2.07	1.13	129.05	8.7	27/02/13	2272.21	301.16	20/03/13	10/04/13	LOT4181871
F052	27/05/08	10/01/12	2.03	1.81	136.23	6.6	20/02/13	1913.20	261.05	03/04/13	24/04/13	LOT4187458
F053	29/08/09	10/01/12	2.06	2.00	174.91	7.7	24/10/12	480.70	192.97	?	16/01/13	LOT4181223
F054	10/06/04	11/01/12	2.06	2.15	171.37	9.4	09/03/12	467.77	254.34	25/04/12	02/05/12	LOT4156426
F055	12/09/09	11/01/12	2.04	1.29	188.70	8.7	16/04/13	2225.63	275.43	24/04/13	22/05/13	LOT4181871
F056	03/01/08	11/01/12	2.04	2.03	162.91	OK	26/03/13	2152.75	282.69	31/07/13	06/08/13	LOT4205911
F057	16/03/10	11/01/12	2.00	1.80	136.45	9.4	17/04/13	2086.50	281.52	08/04/13	31/07/13	LOT4205079
F058	20/03/07	11/01/12	2.03	0.79	119.32	8.6	16/04/13	2117.25	286.53	24/04/13	22/05/13	LOT4181871
F059	07/10/05	09/01/12	2.09	1.36	152.87	10	27/02/13	2121.25	289.81	08/04/13	01/05/13	LOT4187458
F060	27/06/08	09/01/12	2.07	0.77	78.96	9.8	20/02/13	1937.19	271.70	03/04/13	24/04/13	LOT4187458
F061	16/03/06	12/01/12	2.00	2.06	147.64	9.0	19/04/13	2857.14	309.61	15/05/13	18/07/13	LOT4188786
F062	25/05/05	12/01/12	2.08	2.14	142.68	8.8	18/04/13	2747.67	305.15	17/06/13	16/07/13	LOT4188786
F063	18/01/07	12/01/12	2.02	2.11	126.81	9.0	07/05/13	2628.46	269.28	03/06/13	30/07/13	LOT4181223
F064	23/09/06	12/01/12	2.04	1.39	129.96	9.1	23/03/12	1477.31	243.77	26/04/12	09/05/12	LOT4156426

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

F065	04/09/04	12/01/12	2.10	0.41	67.69	9.4	17/04/13	2387.06	275.53	12/06/13	02/07/13	LOT4181871
F066	03/07/10	13/01/12	2.07	0.90	177.55	9.5	24/10/12	779.18	202.58	?	06/02/13	LOT4181871
F067	08/03/07	13/01/12	2.06	2.05	159.03	7.4	27/03/13	3243.61	313.24	29/07/13	14/08/13	LOT4205079
F068	28/01/05	13/01/12	2.06	2.04	108.32	9.4	19/04/13	2133.06	284.08	17/06/13	17/07/13	LOT4188786
F069	10/06/05	13/01/12	2.05	2.02	138.80	9.1	03/05/13	2369.75	287.66	12/06/13	02/07/13	LOT4181871
F070	24/07/10	13/01/12	2.08	1.22	169.60	4.8	26/10/12	1159.85	234.36	?	16/01/13	LOT4181223
F071	29/03/06	13/01/12	2.03	1.12	81.92	8.8	12/04/12	854.84	241.28	25/04/12	03/05/12	LOT4156426
F072	10/01/11	13/01/12	2.10	2.06	96.67	8.6	16/04/13	2068.14	297.22	24/04/13	22/05/13	LOT4181871
F073	02/12/05	16/01/12	2.05	1.76	182.94	10	28/09/12	1425.80	245.62	?	29/01/13	LOT4181223
F074	19/03/11	16/01/12	2.06	1.87	260.55	7.1	25/04/13	2266.57	285.61	14/05/13	24/07/13	-
F075	02/12/10	16/01/12	2.04	1.55	148.39	10	01/05/13	2059.86	277.72	11/06/13	09/07/13	LOT4188786
F076	17/07/10	23/04/12	2.03	1.66	256.42	8.6	02/05/13	1897.40	295.05	05/06/13	30/07/13	LOT4181223
F077	27/02/07	17/01/12	2.06	2.12	172.65	8.7	28/09/12	1831.61	240.46	?	30/01/13	LOT4184161
F078	21/05/08	17/01/12	2.03	1.03	153.59	3.8	11/09/12	967.66	220.53	?	26/10/12	LOT4174114
F079	11/08/06	17/01/12	2.07	2.11	269.73	8.3	02/05/13	2727.61	298.97	-------------------	FAILED	-------------------
F080	18/04/08	17/01/12	2.06	1.91	97.14	3.3	01/05/13	3129.51	259.76	05/06/13	31/07/13	LOT4205079
F081	18/04/08	19/01/12	2.07	1.32	172.56	8.7	06/08/12	787.05	223.70	?	27/10/12	LOT4174114
F082	29/04/08	19/01/12	2.05	1.61	251.17	9.1	03/05/13	2179.55	272.63	17/06/13	17/07/13	LOT4188786
F083	31/05/09	19/01/12	2.08	1.60	146.00	8.9	19/04/13	2124.35	304.21	20/03/13	10/04/13	LOT4181871
F084	10/02/05	19/01/12	2.05	2.15	215.08	9.1	19/03/13	1953.99	258.41	20/03/13	10/04/13	LOT4181871
F085	17/05/04	19/01/12	2.01	2.12	159.24	4.2	03/05/13	2103.62	290.37	03/06/13	24/07/13	LOT4188786
F086	02/10/04	19/01/12	2.05	2.21	231.04	9.3	08/05/13	1810.39	280.43	17/06/13	02/07/13	LOT4181871
F087	07/02/06	19/01/12	2.09	2.02	162.87	2.9	01/05/13	2439.63	249.62	11/06/13	09/07/13	LOT4187458
F088	15/02/05	20/01/12	2.03	2.22	205.31	10	07/05/13	2193.17	276.36	11/06/13	18/07/13	-
F089	08/12/06	20/01/12	2.03	1.85	152.64	6.6	06/08/12	1735.60	236.44	?	25/10/12	LOT4174114
F090	27/08/04	20/01/12	2.05	1.83	194.74	9.3	01/05/13	2203.54	288.50	-------------------	FAILED	-------------------
F091	01/08/08	20/01/12	2.05	1.50	212.08	9.0	30/08/12	1184.40	237.32	?	27/10/12	LOT4174114
F092	01/09/05	20/01/12	2.01	1.79	154.16	9.0	02/05/13	2501.73	291.59	17/06/13	16/07/13	LOT4188786
F093	18/03/04	23/01/12	2.05	1.57	169.87	9.7	28/09/12	2155.02	245.04	?	30/01/13	LOT4184161
F094	21/12/10	23/01/12	2.06	1.50	214.23	5.2	25/04/13	2086.82	287.38	14/05/13	31/07/13	LOT4205079
F095	18/04/08	23/01/12	2.06	2.13	245.41	2.9	08/05/13	2088.15	273.67	17/06/13	18/07/13	LOT4188786
F096	28/03/07	12/04/12	2.06	1.73	179.77	7.7	19/09/12	770.48	230.45	?	25/10/12	LOT4174114
F097	02/06/06	23/01/12	2.05	1.64	267.54	10	02/11/12	751.76	216.98	?	06/02/13	-

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

F098	20/07/05	23/01/12	2.03	2.12	340.78	9.9	02/11/12	557.82	193.34	?	06/02/13	LOT4181871
F099	28/01/05	19/04/12	2.06	2.17	303.23	9.3	02/05/13	2085.13	295.28	05/06/13	31/07/13	LOT4205079
F100	17/11/04	19/04/12	2.04	2.25	313.03	2.9	19/09/12	745.23	218.94	?	26/10/12	LOT4174114
F101	14/07/08	24/01/12	2.06	2.13	288.81	8.2	03/05/13	2289.08	284.83	17/06/13	16/07/13	LOT4188786
F102	10/06/09	24/01/12	2.03	2.10	291.74	9.4	19/03/13	2076.06	276.29	20/03/13	10/04/13	LOT4181871
F103	12/03/11	25/01/12	2.07	2.03	271.11	8.7	30/04/13	1880.94	272.62	12/06/13	24/07/13	LOT4188786
F104	29/07/10	25/01/12	2.02	1.04	169.40	8.2	26/10/12	657.76	198.42	?	30/01/13	LOT4184161
F105	22/05/10	25/01/12	2.04	1.19	147.63	9.3	14/02/13	1433.23	259.47	03/04/13	30/04/13	LOT4187458
F106	15/10/04	26/01/12	2.04	0.82	187.66	8.2	03/04/12	2054.21	264.95	25/04/12	02/05/12	LOT4156426
F107	25/10/07	31/01/12	2.02	2.12	161.16	9.1	03/05/13	2030.45	289.93	15/05/13	09/07/13	LOT4181871
F108	02/05/09	27/01/12	2.07	2.05	196.40	9.4	30/04/13	2366.21	316.79	12/06/13	17/07/13	LOT4188786
F109	20/08/10	31/01/12	2.06	2.09	216.28	9.3	07/05/13	1977.93	285.68	17/06/13	16/07/13	LOT4188786
F110	14/02/05	31/01/12	2.05	2.09	250.15	8.8	25/04/13	2006.88	278.70	14/05/13	18/07/13	LOT4188786
F111	29/04/08	01/02/12	2.11	0.87	81.09	7.6	30/04/13	1548.27	276.66	------------------- FAILED -------------------		
F112	26/09/05	26/01/12	2.05	2.04	242.88	9.8	07/05/13	1705.33	273.91	11/06/13	02/07/13	LOT4181871
F113	04/11/06	26/01/12	2.07	1.30	192.71	9.0	09/04/13	2009.71	279.91	12/06/13	17/07/13	LOT4188786
F114	14/10/08	27/01/12	2.03	1.92	178.61	9.0	04/09/12	1005.40	206.38	?	27/10/12	LOT4174114
F115	27/05/05	27/01/12	2.04	2.23	219.45	8.4	03/04/12	2121.27	268.69	26/04/12	01/05/12	LOT4153111
F116	30/03/05	26/01/12	2.05	2.01	363.00	9.6	09/04/13	1528.37	290.66	------------------- FAILED -------------------		
F117	03/07/10	27/01/12	2.05	2.18	349.83	9.6	02/11/12	619.00	201.64	?	06/02/13	LOT4181871
F118	03/02/10	25/01/12	2.03	1.88	247.45	9.5	14/02/13	1523.96	270.12	26/03/13	23/04/13	LOT4188786
F119	03/02/05	27/01/12	2.04	1.67	245.51	9.0	03/04/12	2490.18	264.45	25/04/12	02/05/12	LOT4156426
F120	01/02/07	27/01/12	2.04	2.10	148.19	9.3	09/04/13	2489.04	290.10	05/06/13	31/07/13	LOT4205079
S001	15/12/04	29/11/11	1.99	1.58	154.16	OK	07/11/12	955.90	239.70	?	05/02/13	LOT4184161
S002	05/12/03	29/11/11	1.96	1.38	94.58	OK	12/04/12	1046.55	236.26	26/04/12	01/05/12	LOT4153111
S003	23/07/04	01/12/11	2.01	1.68	135.97	9.0	15/11/12	1253.41	271.19	?	05/02/13	LOT4184161
S004	01/03/08	01/12/11	2.03	1.77	120.80	8.8	07/11/12	1961.13	273.53	?	30/01/13	LOT4184161
S005	15/08/07	02/12/11	2.09	0.90	158.61	10	15/11/12	1736.32	259.96	?	29/01/13	LOT4181223
S006	27/08/04	02/12/11	2.41	0.05	23.19	poor	22/03/13	738.71	238.59	17/06/13	17/07/13	LOT4188786
S007	21/10/05	02/12/11	2.05	0.47	115.25	9.4	07/12/12	2134.28	293.89	26/03/13	12/04/13	LOT4188786
S008	11/05/05	02/12/11	2.10	0.31	93.58	7.9	15/11/12	1488.19	257.40	?	22/01/13	LOT4181223
S009	17/02/08	02/12/11	2.11	0.31	100.42	9.9	07/12/12	1880.84	265.98	02/04/13	23/04/13	LOT4188786
S010	04/06/06	05/12/11	2.03	1.65	137.79	3.5	20/03/13	3083.96	305.38	------------------- FAILED -------------------		

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

S011	10/02/05	05/12/11	2.06	1.80	200.56	9.6	19/03/13	1951.71	279.59	------------------- FAILED -------------------		
S012	27/05/05	05/12/11	2.03	1.48	222.92	9.7	07/11/12	1316.08	259.14	?	30/01/13	LOT4184161
S013	06/05/05	05/12/11	2.02	2.06	154.82	9.2	05/12/12	2259.23	289.16	08/04/13	01/05/13	LOT4187458
S014	27/08/04	05/12/11	2.07	1.97	188.06	8.4	28/09/12	1142.99	230.93	?	30/01/13	LOT4184161
S015	18/08/06	05/12/11	2.07	1.99	285.68	9.9	07/05/13	1946.25	277.64	05/06/13	18/07/13	-
S016	23/09/05	06/12/11	2.01	2.20	95.04	8.8	07/05/13	2002.05	272.44	05/06/13	18/07/13	LOT4188786
S017	30/09/05	06/12/11	2.05	2.24	228.11	9.5	05/12/12	2336.30	302.27	03/04/13	12/04/13	LOT4188786
S018	10/11/05	06/12/11	2.03	1.76	83.69	9.6	07/12/12	1979.80	282.58	08/04/13	30/04/13	LOT4187458
S019	06/10/05	06/12/11	2.02	1.98	188.43	8.4	30/03/12	566.15	229.86	26/04/12	02/05/12	LOT4156426
S020	20/08/04	06/12/11	2.03	0.66	120.47	7.9	20/03/13	2073.13	295.82	12/06/13	09/07/13	LOT4181871
S021	06/04/06	06/12/11	2.05	1.60	179.06	9.4	19/03/13	2107.41	287.73	03/04/13	12/04/13	LOT4188786
S022	21/05/04	06/12/11	2.05	2.14	194.44	9.7	19/03/13	2142.93	276.76	03/04/13	12/04/13	LOT4188786
S023	16/07/04	07/12/11	2.00	1.36	110.68	7.4	11/09/12	1003.06	237.00	?	25/10/12	LOT4174114
S024	05/02/05	07/12/11	2.07	1.88	264.48	9.7	19/03/13	1923.57	264.04	08/04/13	24/04/13	LOT4187458
S025	03/03/05	07/12/11	2.03	1.34	141.68	8.9	05/12/12	2035.98	309.03	26/03/13	30/04/13	LOT4187458
S026	30/01/04	07/12/11	2.07	0.79	106.37	9.0	12/04/12	938.51	285.72	25/04/12	01/05/12	LOT4156428
S027	19/08/05	07/12/11	2.02	1.07	153.80	9.2	07/12/12	2516.20	285.86	26/03/13	24/04/13	LOT4187458
S028	01/04/04	07/12/11	2.01	1.49	160.70	9.4	15/11/12	2422.41	266.67	?	22/01/13	LOT4181223
S029	26/11/04	07/12/11	2.00	0.79	92.56	8.7	07/05/13	1754.24	280.65	14/05/13	09/07/13	LOT4181871
S030	18/06/04	07/12/11	1.98	1.44	165.49	8.9	05/12/12	1934.41	277.91	08/04/13	25/04/13	LOT4187458
S031	05/05/05	08/12/11	2.07	1.54	191.96	9.9	24/10/12	794.36	202.31	?	29/01/13	LOT4181223
S032	17/05/07	08/12/11	2.06	1.85	230.34	9.8	03/04/12	2406.06	328.15	25/04/12	03/05/12	LOT4156426
S033	07/05/04	08/12/11	2.12	1.98	200.71	9.7	07/12/12	2057.15	293.74	03/04/13	12/04/13	LOT4188786
S034	23/03/07	08/12/11	1.76	0.69	174.57	9.0	22/03/13	2064.59	270.02	------------------- FAILED -------------------		
S035	27/04/06	08/12/11	2.03	2.28	213.90	9.5	15/11/12	1847.11	268.39	?	22/01/13	LOT4181223
S036	14/07/05	08/12/11	2.05	1.20	231.10	9.6	15/11/12	2246.07	278.74	?	29/01/13	LOT4181223
S037	21/05/04	08/12/11	2.03	1.98	215.97	9.4	05/12/12	2222.43	280.30	08/04/13	23/04/13	LOT4188786
S038	10/12/04	08/12/11	2.00	1.16	159.89	9.7	07/11/12	1794.18	253.68	?	29/01/13	LOT4181223
S039	28/11/03	08/12/11	2.03	1.30	217.06	8.9	03/04/12	2245.35	217.31	25/04/12	03/05/12	LOT4156426
S040	12/05/06	09/12/11	2.06	1.42	229.66	9.7	07/11/12	1330.06	269.86	?	30/01/13	LOT4184161
S041	16/02/05	09/12/11	2.07	1.77	202.29	9.3	05/12/12	2042.73	290.40	26/03/13	24/04/13	LOT4187458
S042	08/07/05	09/12/11	2.07	1.45	183.35	9.1	06/08/12	1850.81	236.23	?	26/10/12	LOT4174114
S043	14/10/05	09/12/11	2.05	1.85	181.43	9.9	13/03/13	2121.19	287.19	02/04/13	23/04/13	LOT4188786

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

S044	18/11/06	09/12/11	2.08	0.91	306.79	4.8	15/11/12	1845.13	282.64	?	22/01/13	LOT4181223
S045	04/07/06	09/12/11	2.03	1.37	156.00	8.8	13/03/13	2185.36	302.11	08/04/13	25/04/13	LOT4187458
S046	29/01/05	09/12/11	2.07	1.22	251.09	9.2	07/05/13	2036.52	290.69	05/06/13	18/07/13	-
S047	12/05/06	09/12/11	2.03	1.99	221.87	8.6	22/03/13	1987.72	273.39	11/06/13	30/07/13	LOT4181223
S048	27/10/04	09/12/11	2.03	1.87	190.44	9.3	24/10/12	807.40	206.84	?	05/02/13	LOT4184161
S049	02/07/05	25/01/12	2.04	1.36	135.14	9.3	07/11/12	1648.54	270.28	?	22/01/13	LOT4181223
S050	05/02/04	27/01/12	2.03	1.93	130.16	7.4	07/11/12	1812.26	284.12	?	29/01/13	LOT4181223
S051	08/09/07	13/12/11	2.00	1.20	147.55	8.9	22/03/13	2646.40	278.28	?	14/08/13	LOT4205079
S052	21/11/07	13/12/11	2.02	1.74	186.95	9.0	26/10/12	1999.49	266.59	?	29/01/13	LOT4181223
S053	08/03/07	13/12/11	2.03	1.15	132.87	9.5	22/03/13	2325.78	270.24	30/07/13	14/08/13	LOT4205079
S054	13/10/05	13/12/11	2.02	1.41	242.85	9.3	14/03/13	1731.47	266.93	03/04/13	25/04/13	LOT4187458
S055	18/08/06	13/12/11	2.05	1.38	188.31	9.9	28/09/12	2208.73	238.47	?	22/01/13	LOT4181223
S056	11/02/05	14/12/11	2.04	1.75	191.92	9.5	24/10/12	832.56	198.66	?	29/01/13	LOT4181223
S057	22/02/07	14/12/11	2.04	0.91	114.75	9.5	22/03/13	2614.14	292.49	30/07/13	06/08/13	LOT4205079
S058	09/08/07	14/12/11	2.07	2.14	392.49	8.6	28/11/12	2276.57	280.57	02/04/13	23/04/13	LOT4188786
S059	22/04/04	14/12/11	2.04	1.92	230.11	9.8	03/04/12	2624.19	258.43	25/04/12	02/05/12	LOT4156426
S060	22/12/06	14/12/11	2.08	1.39	144.34	9.7	20/03/13	2088.02	273.54	30/07/13	14/08/13	LOT4205079
S061	15/10/04	20/12/11	2.04	1.12	123.55	8.7	22/03/13	2607.22	293.65	29/07/13	13/08/13	LOT4205911
S062	18/08/06	14/12/11	2.07	2.43	181.61	10	26/10/12	795.58	212.80	?	06/02/13	LOT4181871
S063	01/07/05	14/12/11	2.06	0.93	218.09	9.5	20/03/13	1914.06	279.29	30/07/13	14/08/13	LOT4205079
S064	12/05/06	14/12/11	2.02	2.40	178.13	8.4	07/05/13	1898.51	272.46	29/07/13	13/08/13	LOT4205911
S065	23/05/07	15/12/11	2.07	2.09	339.50	9.9	03/04/12	2147.53	253.31	25/04/12	03/05/12	LOT4156426
S066	07/12/05	20/01/12	2.06	1.42	196.76	10	13/03/13	2435.44	293.76	25/03/13	11/04/13	LOT4188786
S067	12/11/05	15/12/11	2.01	2.32	153.15	9.4	26/03/13	2866.31	301.02	30/07/13	14/08/13	LOT4205079
S068	17/03/04	16/12/11	1.92	1.37	153.20	9.7	28/11/12	2655.00	265.67	26/03/13	23/04/13	LOT4188786
S069	25/02/06	16/12/11	1.95	2.26	254.78	8.9	14/03/13	2014.04	279.78	25/03/13	12/04/13	LOT4188786
S070	09/03/06	23/04/12	2.03	2.32	237.96	9.5	30/04/13	2329.43	277.95	29/07/13	15/08/13	LOT4205079
S071	10/09/04	23/04/12	2.04	2.12	267.82	9.4	25/04/13	1918.56	280.55	24/07/13	14/08/13	LOT4205079
S072	26/01/05	16/12/11	2.04	1.89	166.33	9.4	22/03/13	2092.88	268.55	31/07/13	15/08/13	LOT4205079
S073	23/12/04	16/12/11	2.01	1.96	131.46	8.8	13/03/13	1824.37	278.21	03/04/13	24/04/13	LOT4187458
S074	29/11/07	18/04/12	2.03	1.22	128.01	7.1	13/03/13	1712.30	308.64	08/04/13	30/04/13	LOT4187458
S075	14/07/05	16/12/11	2.04	1.39	201.88	9.8	20/03/13	2564.60	298.30	01/07/13	09/07/13	LOT4181871
S076	17/05/07	19/12/11	2.01	2.17	190.38	9.0	24/10/12	1119.00	232.85	?	05/02/12	LOT4184161

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

S077	15/06/06	19/12/11	2.05	1.51	136.13	10	22/03/13	2771.65	280.09	31/07/13	14/08/13	LOT4205079
S078	11/08/05	19/12/11	2.04	1.12	185.14	10	26/10/12	1592.67	261.81	?	06/02/13	LOT4181871
S079	03/06/05	19/12/11	2.06	1.49	194.97	4.4	14/03/13	2135.62	270.73	03/04/13	25/04/13	LOT4187458
S080	08/08/06	19/12/11	2.05	2.13	206.53	10	14/03/13	2258.33	277.57	26/03/13	01/05/13	LOT4187458
S081	01/02/07	19/12/11	2.03	2.17	188.99	7.2	28/09/12	2116.58	228.77	?	22/01/13	LOT4181223
S082	18/01/07	23/04/12	2.03	2.04	281.54	9.5	30/04/13	1505.78	269.64	01/07/13	16/07/13	LOT4188786
S083	15/02/07	23/04/12	2.04	2.19	267.04	10	25/04/13	1796.19	278.28	24/07/13	14/08/13	LOT4205079
S084	17/01/08	20/12/11	2.04	0.71	117.14	8.7	14/03/13	1958.79	258.91	02/04/13	23/04/13	LOT4188786
S085	11/11/04	20/12/11	2.05	1.25	190.15	1.9	28/09/12	2041.01	229.10	?	06/02/13	LOT4181871
S086	19/08/04	20/12/11	2.02	2.32	146.03	poor	13/03/13	2026.22	309.25	25/03/13	11/04/13	LOT4188786
S087	23/09/07	20/12/11	2.03	0.87	177.77	5.9	22/03/13	2644.11	271.97	31/07/13	15/08/13	LOT4205079
S088	09/11/06	20/12/11	2.08	2.31	266.16	6.5	27/03/13	3185.96	302.72	24/07/13	13/08/13	LOT4205911
S089	15/06/06	20/12/11	2.05	0.31	93.92	9.5	12/04/12	1987.11	262.27	25/04/12	09/05/12	LOT4158373
S090	13/09/06	20/12/11	2.04	0.79	157.12	9.8	07/05/13	2518.51	257.44	29/07/13	15/08/13	LOT4205079
S091	11/08/05	20/12/11	2.06	1.02	111.87	9.3	28/11/12	2323.34	271.92	02/04/13	30/04/13	LOT4187458
S092	22/09/06	21/12/11	2.03	0.95	140.15	8.6	26/03/13	3055.09	318.62	29/07/13	15/08/13	LOT4205079
S093	18/06/04	21/12/11	2.07	2.31	134.90	9.5	09/03/12	885.18	284.29	25/04/12	09/05/12	LOT4156426
S094	26/11/04	21/12/11	2.05	1.78	192.05	10	24/10/12	826.81	209.80	?	30/01/13	LOT4184161
S095	10/03/05	21/12/11	2.06	0.91	176.66	10	28/11/12	2052.47	329.36	08/04/13	25/04/13	LOT4187458
S096	10/02/05	21/12/11	2.06	2.50	143.36	9.4	22/03/13	2459.44	272.07	17/06/13	09/07/13	LOT4181871
S097	15/09/06	21/12/11	2.09	0.30	81.68	3.5	20/03/13	2568.65	290.34	12/06/13	09/07/13	LOT4181871
S098	19/09/07	21/12/11	2.05	1.78	176.61	9.7	26/03/13	2640.22	289.40	30/07/13	15/08/13	LOT4205079
S099	11/11/04	21/12/11	2.08	1.20	145.20	9.5	14/03/13	2200.19	312.91	03/04/13	24/04/13	LOT4187458
S100	25/02/05	21/12/11	2.06	0.69	124.65	8.8	22/03/13	2109.23	272.90	12/06/13	16/07/13	LOT4188786
S101	15/05/04	09/01/12	2.06	1.67	175.24	4.5	22/03/13	2659.45	267.66	------------------ FAILED ------------------		
S102	05/05/06	09/01/12	2.03	1.71	193.39	9.3	30/03/12	1432.11	240.09	25/04/12	02/05/12	LOT4156426
S103	15/09/05	09/01/12	2.03	1.91	158.18	9.0	20/02/13	1942.87	262.85	02/04/13	25/04/13	LOT4187458
S104	07/04/05	09/01/12	1.98	0.40	111.49	9.7	26/03/13	2425.84	284.51	31/07/13	13/08/13	LOT4205911
S105	27/04/05	10/01/12	2.10	0.94	202.97	9.9	20/02/13	2783.43	290.68	03/04/13	24/04/13	LOT4187458
S106	12/10/06	10/01/12	2.06	1.84	279.27	9.7	27/02/13	2202.53	320.92	03/04/13	24/04/13	LOT4187458
S107	23/01/07	10/01/12	2.07	2.08	319.61	8.5	02/11/12	667.15	220.05	?	30/01/13	LOT4184161
S108	31/03/07	11/01/12	2.06	1.07	176.77	3.2	26/03/13	3053.39	271.60	24/07/13	13/08/13	LOT4205911
S109	12/07/07	11/01/12	2.05	1.53	121.20	10	27/03/13	2518.69	292.77	24/07/13	14/08/13	LOT4205079

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

S110	02/09/06	11/01/12	2.03	1.35	201.66	9.1	12/04/12	1423.50	253.12	25/04/12	03/05/12	LOT4156426
S111	06/11/03	11/01/12	2.06	2.17	268.01	9.7	27/03/13	1672.81	285.77	30/07/13	06/08/13	LOT4205911
S112	22/02/07	11/01/12	2.08	1.56	162.68	3.4	27/03/13	2814.67	283.32	30/07/13	13/08/13	LOT4205911
S113	30/01/07	11/01/12	2.08	1.06	153.85	9.3	22/03/13	2267.01	300.11	11/06/13	30/07/13	LOT4181223
S114	09/02/07	11/01/12	2.06	0.34	98.14	9.2	12/04/12	1486.18	254.12	25/04/12	01/05/12	LOT4153111
S115	17/02/05	11/01/12	2.07	2.10	232.75	9.5	12/04/13	2215.33	313.29	11/06/13	30/07/13	LOT4181223
S116	01/02/07	11/01/12	2.09	1.41	120.47	8.8	23/03/12	528.06	195.56	26/04/12	03/05/12	LOT4156426
S117	03/02/05	11/01/12	2.01	1.58	141.14	8.8	12/04/13	2421.62	290.92	12/06/13	17/07/13	LOT4188786
S118	11/03/04	11/01/12	2.04	1.22	87.59	7.8	07/05/13	2522.19	267.79	------------------- FAILED -------------------		
S119	16/12/04	11/01/12	2.04	1.40	86.70	3.8	20/02/13	2697.62	259.26	03/04/13	24/04/13	LOT4187458
S120	09/07/07	11/01/12	2.04	0.75	54.55	9.5	27/03/13	2575.59	295.13	15/05/13	23/07/13	LOT4188786
S121	09/08/07	11/01/12	2.07	1.88	107.69	8.9	16/03/12	701.93	195.49	25/04/12	09/05/12	LOT4156426
S122	27/10/07	09/01/12	2.06	2.05	138.25	9.3	16/04/13	1904.39	269.12	24/04/13	22/05/13	LOT4181871
S123	23/09/04	09/01/12	2.07	1.03	185.14	2.7	19/09/12	854.39	231.38	?	25/10/12	LOT4174114
S124	20/08/04	12/01/12	2.04	2.04	193.46	9.6	26/03/13	2926.16	298.89	29/07/13	14/08/13	LOT4205079
S125	22/12/06	26/01/12	2.02	1.69	114.92	8.4	07/05/13	2490.64	289.30	05/06/13	30/07/13	-
S126	14/01/05	12/01/12	2.05	2.05	248.08	9.1	16/04/13	2082.28	290.35	24/04/13	22/05/13	LOT4181871
S127	28/10/05	12/01/12	2.00	2.04	125.53	9.8	27/02/13	2039.99	261.80	25/03/13	10/04/13	LOT4181871
S128	04/11/05	12/01/12	2.06	1.89	158.12	9.0	12/04/13	2292.95	304.59	------------------- FAILED -------------------		
S129	14/07/05	12/01/12	2.08	0.65	191.49	9.5	24/10/12	969.49	222.08	?	29/01/13	LOT4181223
S130	24/02/05	12/01/12	2.08	0.88	223.38	3.8	18/04/13	3107.25	294.05	11/06/13	30/07/13	LOT4181223
S131	04/02/06	12/01/12	2.11	0.24	82.05	8.9	20/02/13	1965.53	265.74	08/04/13	30/04/13	LOT4187458
S132	12/07/07	12/01/12	2.06	1.07	124.13	9.3	23/03/12	1845.94	222.69	26/04/12	09/05/12	LOT4156426
S133	05/01/08	12/01/12	2.04	0.79	135.78	9.5	23/03/12	603.05	200.72	26/04/12	09/05/12	LOT4156426
S134	12/05/06	12/01/12	2.08	0.51	86.28	9.4	16/04/13	1842.55	283.61	24/04/13	22/05/13	LOT4181871
S135	13/02/06	12/01/12	2.02	1.72	101.98	8.9	18/04/13	2332.22	300.03	------------------- FAILED -------------------		
S136	06/08/07	13/01/12	2.07	2.18	113.51	9.0	12/04/13	2174.75	285.07	------------------- FAILED -------------------		
S137	12/11/05	25/01/12	2.05	1.84	101.44	6.0	27/02/13	1837.41	282.65	08/04/13	30/04/13	LOT4187458
S138a	20/04/05	13/01/12	2.07	2.14	199.52	9.4	20/02/13	2653.52	272.39	02/04/13	01/05/13	LOT4187458
S138b	08/04/05	13/01/12	2.01	2.03	107.22	7.1	18/04/13	2621.71	291.70	------------------- FAILED -------------------		
S139	24/03/05	13/01/12	2.02	1.91	134.31	9.0	27/02/13	2861.15	282.68	26/03/13	25/04/13	LOT4187458
S140	29/04/05	13/01/12	2.01	2.01	126.86	9.0	27/03/13	2431.47	292.40	24/07/13	15/08/13	LOT4205079
S141	14/07/06	13/01/12	2.02	0.96	120.39	8.9	17/04/13	2366.14	278.14	12/06/13	17/07/13	-

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

S142	08/01/04	13/01/12	2.10	0.78	94.41	9.5	16/04/13	2594.63	300.89	24/04/13	22/05/13	LOT4181871
S143	03/02/06	13/01/12	2.03	0.73	117.66	9.4	20/02/13	2610.71	284.17	26/03/13	12/04/13	LOT4181871
S144	02/03/06	13/01/12	2.05	1.92	151.66	4.9	12/04/13	2539.75	285.07	11/06/13	24/07/13	LOT4188786
S145	08/10/04	13/01/12	2.07	2.02	143.87	2.5	27/02/13	2127.97	288.90	03/04/13	24/04/13	LOT4187458
S146	08/04/05	13/01/12	2.12	1.15	116.90	8.6	12/04/13	2201.52	297.89	03/06/13	09/07/13	LOT4181871
S147	15/10/07	13/01/12	2.06	1.20	123.74	8.9	17/04/13	3023.54	288.38	05/06/13	24/07/13	LOT4181223
S148	02/03/07	13/01/12	2.11	0.63	96.55	9.0	16/04/13	1700.73	261.42	24/04/13	22/05/13	LOT4181871
S149	10/05/07	13/01/12	2.09	1.40	142.57	9.4	09/03/12	806.19	302.47	25/04/12	01/05/12	LOT4153111
S150	09/03/06	16/01/12	2.07	1.43	164.69	2.3	17/04/13	2205.00	267.96	15/05/13	23/07/13	LOT4188786
S151	30/01/08	16/01/12	2.07	1.77	245.61	9.5	03/04/12	2172.91	258.18	25/04/12	09/05/12	LOT4158373
S152	25/04/07	16/01/12	2.05	1.56	157.81	9.6	16/04/13	2317.23	297.40	24/04/13	22/05/13	LOT4181871
S153	09/08/07	23/04/12	2.05	2.16	313.11	3.0	30/04/13	1863.97	267.15	12/06/13	17/07/13	LOT4188786
S154	15/03/07	23/04/12	2.06	2.13	333.95	2.8	01/05/13	1820.78	237.97	------------------- FAILED -------------------		
S155	15/06/06	23/04/12	2.11	2.20	493.02	9.4	25/04/13	2305.79	290.14	14/05/13	30/07/13	LOT4181223
S156	23/03/06	23/04/12	2.04	1.59	399.34	7.6	25/04/13	1771.20	266.66	14/05/13	24/07/13	-
S157	24/06/04	17/01/12	2.03	0.76	189.15	9.9	28/09/12	1144.85	242.92	?	22/01/13	LOT4181223
S158	25/02/05	17/01/12	2.04	2.02	130.49	9.7	18/04/13	2740.18	314.93	------------------- FAILED -------------------		
S159	10/12/04	17/01/12	2.05	2.06	145.24	9.9	19/04/13	2442.12	306.76	12/06/13	17/07/13	LOT4188786
S160	02/12/04	17/01/12	2.03	0.98	145.92	4.4	17/04/13	2354.82	279.88	11/06/13	24/07/13	-
S161	06/10/05	17/01/12	2.05	1.74	287.17	2.5	17/04/13	2904.61	266.12	11/06/13	09/07/13	LOT4188786
S162	10/11/06	17/01/12	2.06	1.38	134.34	2.0	25/04/13	2673.10	268.44	14/05/13	23/07/13	LOT4188786
S163	20/10/05	17/01/12	2.10	1.84	234.04	poor	30/08/12	1586.62	221.49	?	26/10/12	LOT4174114
S164	19/10/04	17/01/12	2.10	1.42	262.64	9.7	17/04/13	2035.26	298.06	03/06/13	23/07/13	LOT4188786
S165	22/02/06	17/01/12	2.09	1.42	205.73	10	11/09/12	735.44	215.62	?	27/10/12	LOT4174114
S166	27/01/05	19/01/12	2.05	2.14	343.34	9.6	30/04/13	2165.92	296.69	17/06/13	17/07/13	LOT4188786
S167	29/11/06	19/01/12	2.07	1.56	287.71	10	08/05/13	1516.29	275.07	05/06/13	31/07/13	LOT4205079
S168	26/02/04	19/01/12	2.06	0.84	77.00	9.2	19/04/13	1826.81	299.64	11/06/13	24/07/13	-
S169	18/05/04	19/01/12	2.07	0.97	169.04	9.2	18/04/13	1695.88	289.32	17/06/13	16/07/13	LOT4188786
S170	20/04/04	19/01/12	2.06	2.11	204.14	9.2	30/03/12	994.31	227.59	26/04/12	02/05/12	LOT4156426
S171	16/07/04	19/01/12	2.03	1.24	112.30	9.5	06/08/12	664.21	221.15	?	26/10/12	LOT4174114
S172	29/10/04	19/01/12	2.05	2.01	237.67	7.5	02/11/12	651.73	239.45	?	06/02/13	-
S173	19/04/05	19/01/12	2.06	1.37	182.51	9.8	12/04/12	1899.85	245.80	25/04/12	02/05/12	LOT4156426
S174	22/03/04	19/01/12	2.06	2.04	144.00	8.0	18/04/13	2409.12	295.67	17/06/13	16/07/13	LOT4188786

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

S175	22/09/06	19/01/12	2.08	1.38	135.38	OK	30/04/13	2258.40	291.59	------------------- FAILED -------------------		
S176	19/04/07	19/01/12	2.07	1.38	104.88	9.7	28/03/12	395.64	194.04	26/04/12	03/05/12	LOT4156426
S177	13/12/04	19/01/12	2.05	1.31	149.07	3.0	25/04/13	3209.71	299.71	14/05/13	18/07/13	-
S178	18/08/05	20/01/12	2.08	1.31	233.92	4.4	02/11/12	1157.17	248.77	?	05/02/13	LOT4184161
S179	22/03/07	20/01/12	2.04	1.10	90.18	9.7	01/05/13	2326.04	281.85	31/07/13	13/08/13	LOT4205911
S180	15/10/04	20/01/12	2.07	0.46	165.24	2.4	19/04/13	2277.57	289.00	30/07/13	13/08/13	LOT4205911
S181	27/09/07	20/01/12	2.00	1.46	170.31	9.3	01/05/13	2260.42	292.53	29/07/13	14/08/13	LOT4205079
S182	01/03/05	20/01/12	2.05	2.19	254.44	9.4	19/04/13	2682.08	305.71	31/07/13	14/08/13	LOT4205079
S183	20/01/05	20/01/12	0.07	1.33	225.74	9.9	01/05/13	2067.72	294.80	01/07/13	09/07/13	LOT4181871
S184	15/04/06	20/01/12	2.07	1.65	268.59	10	25/04/13	1906.88	290.59	24/07/13	14/08/13	LOT4205079
S185	23/03/07	20/01/12	2.06	1.02	156.34	3.3	19/04/13	2631.04	293.84	29/07/13	13/08/13	LOT4205911
S186	06/09/07	20/01/12	2.04	0.73	105.53	8.5	16/03/12	885.01	233.57	25/04/12	01/05/12	LOT4156428
S187	04/03/05	20/01/12	2.03	2.06	174.87	9.5	02/05/13	2412.62	290.98	01/07/13	16/07/13	LOT4188786
S188	29/10/04	20/01/12	2.01	0.71	140.66	8.9	03/05/13	2429.15	289.25	31/07/13	15/08/13	LOT4205079
S189	25/02/05	20/01/12	1.98	0.72	73.19	9.3	19/04/13	2229.01	300.17	29/07/13	13/08/13	LOT4205911
S190	02/03/06	20/01/12	2.03	0.73	173.85	9.5	02/05/13	2648.59	285.96	29/07/13	15/08/13	LOT4205079
S191	27/04/04	23/01/12	2.07	1.26	266.01	10	06/03/13	2138.39	279.40	03/04/13	30/04/13	LOT4187458
S192	31/01/08	23/01/12	2.04	1.32	166.25	9.1	02/05/13	1763.91	281.78	01/07/13	17/07/13	LOT4188786
S193	26/08/05	23/01/12	2.06	1.74	228.80	9.4	03/05/13	1925.14	287.50	31/07/13	06/08/13	LOT4205079
S194	08/06/06	23/01/12	2.07	0.43	133.64	9.6	03/05/13	1977.24	285.60	01/07/13	16/07/13	LOT4188786
S195	10/11/06	25/01/12	2.01	0.78	84.63	OK	08/05/13	707.06	247.50	01/07/13	16/07/13	LOT4188786
S196	25/10/07	25/01/12	2.06	2.24	205.85	OK	30/04/13	2158.75	267.13	31/07/13	06/08/13	LOT4181223
S197	02/12/05	26/01/12	2.07	2.02	119.82	8.5	02/05/13	2675.95	287.44	05/06/13	30/07/13	LOT4181223
S198	07/04/05	26/01/12	2.03	2.18	182.46	8.3	26/10/12	1738.62	230.31	?	29/01/13	LOT4181223
S199	09/09/05	01/02/12	2.01	2.13	99.87	7.2	02/11/12	1394.56	272.97	?	30/01/13	LOT4184161
S200	27/03/06	23/01/12	2.02	2.12	232.99	9.2	03/05/13	2146.87	291.39	11/06/13	18/07/13	LOT4188786
S201	17/01/08	23/01/12	2.01	2.09	151.96	9.4	08/05/13	1544.26	274.67	15/05/13	23/07/13	LOT4188786
S202	15/01/05	23/01/12	2.00	1.32	194.21	7.4	04/09/12	1063.12	250.14	?	27/10/12	LOT4174114
S203	15/06/06	23/01/12	2.05	2.17	241.16	9.5	30/08/12	947.31	225.87	?	25/10/12	LOT4179034
S204	10/09/04	19/04/12	2.05	2.13	261.02	9.3	30/04/13	1267.09	281.71	30/07/13	14/08/13	LOT4205911
S205	06/09/07	19/04/12	2.04	2.06	280.13	9.5	11/09/12	1301.20	234.57	?	27/10/12	LOT4179034
S206	25/01/08	19/04/12	2.06	2.29	256.74	9.3	03/05/13	1994.19	266.68	11/06/13	18/07/13	LOT4188786
S207	21/01/04	19/04/12	2.03	2.22	333.41	9.1	10/05/13	1867.19	273.47	05/06/13	30/07/13	LOT4181223

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

S208	13/01/05	19/04/12	2.03	1.49	258.08	9.1	10/05/13	1652.51	250.13	------------------- FAILED -------------------		
S209	25/02/05	24/01/12	2.04	1.89	199.98	9.4	10/05/13	2102.08	277.92	05/06/13	24/07/13	-
S210	04/12/04	24/01/12	2.06	1.13	188.41	9.4	28/09/12	1345.72	232.30	?	06/02/13	LOT4181871
S211	13/01/05	24/01/12	2.08	0.59	88.66	2.7	10/05/13	2123.93	274.16	------------------- FAILED -------------------		
S212	29/01/05	25/01/12	2.01	0.94	118.66	7.3	10/05/13	1951.42	296.12	05/06/13	18/07/13	LOT4188786
S213	07/10/05	25/01/12	2.00	0.91	152.36	8.9	18/09/12	545.93	232.57	?	26/10/12	LOT4174114
S214	10/04/04	25/01/12	2.06	0.72	142.00	poor	15/03/13	2166.61	258.90	08/04/13	30/04/13	LOT4187458
S215	03/11/05	31/01/12	2.00	2.09	140.19	3.9	10/05/13	2097.93	280.88	11/06/13	24/07/13	-
S216	15/06/06	31/01/12	2.02	2.16	187.75	8.5	28/09/12	1866.10	258.48	?	30/01/13	-
S217	15/10/04	27/01/12	2.03	1.96	198.12	7.4	10/05/13	1307.94	279.91	03/06/13	31/07/13	LOT4205079
S218	23/03/07	27/01/12	2.03	2.12	182.03	9.1	26/10/12	1906.36	266.75	?	30/01/13	LOT4184161
S219	22/09/05	26/01/12	2.08	1.50	185.32	9.9	26/10/12	1177.26	238.29	?	06/02/13	LOT4181871
S220	29/04/05	26/01/12	2.06	1.59	98.70	poor	09/04/13	2919.29	276.62	12/06/13	17/07/13	LOT4188786
S221	14/12/04	26/01/12	2.02	1.91	157.71	8.6	10/05/13	1656.25	275.76	03/06/13	30/07/13	LOT4181223
S222	03/01/08	26/01/12	2.05	2.10	246.65	9.3	09/04/13	2570.63	285.68	------------------- FAILED -------------------		
S223	26/02/08	31/01/12	2.06	2.02	216.87	8.4	09/04/13	2449.39	283.88	15/05/13	31/07/13	LOT4205079
S224	15/05/04	31/01/12	2.05	2.01	283.46	9.2	02/11/12	1126.74	256.13	?	29/01/13	LOT4181223
S225	09/07/07	27/01/12	2.08	2.11	256.90	9.5	15/03/13	1966.03	270.31	08/04/13	01/05/13	LOT4187458
S226	29/04/05	26/01/12	2.05	2.03	177.99	5.2	09/04/13	2024.22	251.87	05/06/13	18/07/13	LOT4188786
S227	06/05/04	26/01/12	2.09	2.02	219.29	2.4	14/02/13	2211.91	281.03	08/04/13	30/04/13	LOT4187458
S228	11/11/04	31/01/12	2.03	1.93	282.32	8.9	09/04/13	2299.09	278.55	15/05/13	09/07/13	LOT4181871
S229	15/08/06	31/01/12	2.05	1.99	411.28	8.5	02/11/12	978.14	235.77	?	05/02/13	LOT4184161
S230	15/09/05	31/01/12	2.07	1.97	317.31	9.6	02/11/12	668.92	229.33	?	30/01/13	LOT4184161
S231	24/11/06	01/02/12	2.04	2.18	212.11	8.5	15/03/13	2046.53	268.01	26/03/13	01/05/13	LOT4187458
S232	15/06/06	01/02/12	2.04	2.26	284.99	10	09/04/13	2258.55	276.43	------------------- FAILED -------------------		
S233	21/05/05	01/02/12	2.06	1.94	199.76	9.2	09/04/13	2149.72	276.43	15/05/13	02/07/13	LOT4181871
S234	20/08/04	26/01/12	2.01	2.00	185.56	8.8	12/04/12	2049.73	306.49	25/04/12	02/05/12	LOT4156426
S235	04/04/06	26/01/12	2.03	2.02	166.20	7.7	07/05/13	1828.61	282.75	------------------- FAILED -------------------		
S236	15/06/06	26/01/12	2.05	2.02	210.24	7.2	30/03/12	582.87	222.95	26/04/12	03/05/12	LOT4156426
S237	15/05/04	27/01/12	2.02	2.10	263.97	7.6	14/02/13	1280.58	274.03	26/03/13	25/04/13	LOT4187458
S238	12/12/05	27/01/12	2.02	2.03	199.26	9.5	10/05/13	1279.63	269.87	11/06/13	30/07/13	LOT4181223
S239	30/12/04	26/01/12	2.09	2.13	296.96	8.1	15/03/13	1880.88	263.49	03/04/13	30/04/13	LOT4187458
S240	14/07/05	27/01/12	2.05	1.40	166.22	9.4	14/02/13	1821.56	272.16	02/04/13	25/04/13	LOT4187458

Table B7: ECACC LCL QIAGEN Extraction and Ambion® RNA Amplification Data for Exon 1.0ST Expression Arrays

S241	11/06/04	27/01/12	2.06	2.18	229.92	8.6	14/02/13	1640.17	272.77	03/04/13	25/04/13	LOT4187458
S242	30/08/07	25/01/12	2.05	2.11	251.82	9.3	03/04/12	2374.99	279.17	25/04/12	01/05/12	LOT4158373
S243	20/12/03	25/01/12	2.04	2.08	222.00	9.1	15/03/13	1803.93	260.74	25/03/13	10/04/13	LOT4181871
S244	05/01/05	25/01/12	2.02	2.06	168.29	1.9	14/02/13	2391.92	259.21	02/04/13	23/04/13	LOT4188786
S245	08/04/05	18/04/12	2.01	2.17	208.92	9.8	14/02/13	1778.67	293.96	25/03/13	10/04/13	LOT4181871
S246	22/05/07	25/01/12	2.04	1.86	145.57	9.4	15/03/13	2420.68	278.54	08/04/13	01/05/13	LOT4187458
S247	01/02/07	31/01/12	1.98	0.42	126.77	7.9	15/03/13	1721.38	261.67	02/04/13	23/04/13	LOT4188786
S248	06/08/07	------------------------------ SAMPLE NOT RECEIVED FROM ECACC ------------------------------										
S249	01/07/04	31/01/12	2.39	2.14	78.32	8.0	14/02/13	1751.73	268.03	08/04/13	24/04/13	LOT4187458
S268	08/04/05	03/02/12	2.02	1.95	165.61	9.1	30/08/12	996.88	241.23	?	26/10/12	LOT4174114
S319	03/10/05	09/02/12	2.06	1.86	196.36	9.4	18/09/12	1232.66	257.00	?	26/10/12	LOT4174114
S352	28/02/08	14/02/12	2.02	0.12	47.96	4.8	11/09/12	1492.86	221.79	?	25/10/12	LOT4179034
S368	17/04/07	15/02/12	2.07	2.09	136.00	8.6	06/03/13	2160.88	271.99	20/03/13	10/04/13	LOT4181871
S373	06/09/06	15/02/12	2.09	1.84	154.03	8.9	18/09/12	915.91	286.97	?	26/10/12	LOT4174114
S438	12/01/07	13/03/12	1.99	2.18	167.39	6.2	06/03/13	2255.68	298.73	20/03/13	10/04/13	LOT4181871
S440	06/06/07	15/03/12	2.01	2.13	151.77	6.9	30/08/12	1696.08	264.04	?	27/10/12	LOT4174114

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

RefSeq #	Transcript	Symbol	Gene Name	Fold	p-value
Apoptosis					
NM_012138	3719362	AATF	apoptosis antagonizing transcription factor	⇧ 1.21	3.19E-04
NM_032306	3818395	ALKBH7	alkB, alkylation repair homolog 7 (*E. coli*)	⇧ 1.28	0.020
NM_001188	2950753	BAK1	BCL2-antagonist/killer 1	⇧ 1.28	0.001
NM_003824	3338424	FADD	Fas (TNFRSF6)-associated via death domain	⇧ 1.20	0.012
NM_005256	3323891	GAS2	growth arrest-specific 2	⇩ 1.42	0.044
NM_014320	2927722	HEBP2	heme binding protein 2	⇧ 1.28	0.001
NM_003897	2948630	IER3	immediate early response 3	⇧ 1.31	0.010
NM_018622	2708229	PARL	presenilin associated, rhomboid-like	⇧ 1.21	0.002
NM_007350	3462816	PHLDA1	pleckstrin homology-like domain, family A, member 1	⇩ 1.22	0.027
NM_019006	3603884	ZFAND6	zinc finger, AN1-type domain 6	⇧ 1.29	0.001
Autophagy					
NM_003766	3758157	BECN1	beclin 1, autophagy related	⇧ 1.25	8.27E-04
NM_017983	3768474	WIPI1	WD repeat domain, phosphoinositide interacting 1	⇧ 1.20	0.034
Cell Adhesion/Extracellular Matrix					
NM_058172	2774971	ANTXR2	anthrax toxin receptor 2	⇩ 1.28	0.009
NM_006614	2607568	CHL1	cell adhesion molecule with homology to L1CAM (close homolog of L1)	⇩ 1.80	0.016
NM_004273	3251298	CHST3	carbohydrate (chondroitin 6) sulfotransferase 3	⇩ 1.21	0.019
NM_001858	2912649	COL19A1	collagen, type XIX, alpha 1	⇩ 1.22	0.038
NM_017549	2997907	EPDR1	ependymin related protein 1 (zebrafish)	⇩ 1.20	0.034
NM_000885	2518272	ITGA4	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	⇩ 1.25	0.007
NM_002205	3456732	ITGA5	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)	⇩ 1.34	0.032
NM_002211	3284188	ITGB1	integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12)	⇩ 1.24	0.019
NM_021219	3916527	JAM2	junctional adhesion molecule 2	⇩ 1.27	0.028
NM_004994	3887210	MMP9	matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)	⇩ 1.31	0.038
NM_001142864	3704376	PIEZO1	piezo-type mechanosensitive ion channel component 1	⇩ 1.24	6.41E-04
NM_000302	2320581	PLOD1	procollagen-lysine 1, 2-oxoglutarate 5-dioxygenase 1	⇩ 1.25	0.002
NM_021111	3168309	RECK	reversion-inducing-cysteine-rich protein with kazal motifs	⇩ 1.21	0.016
NR_028076	3740432	SCARF1	scavenger receptor class F, member 1	⇩ 1.23	0.020
NM_003118	2882098	SPARC	secreted protein, acidic, cysteine-rich (osteonectin)	⇩ 1.33	0.040

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_014000	3252071	VCL	vinculin	⇩	1.39	0.007

Cellular Response to Stress

NM_015696	2336439	GPX7	glutathione peroxidase 7	⇧	1.36	0.043
NM_001540	3009399	HSPB1	heat shock 27kDa protein 1	⇧	1.24	0.046
NM_016126	2413519	HSPB11	heat shock protein family B (small), member 11	⇧	1.21	0.020
NM_000305	3061997	PON2	paraoxonase 2	⇩	1.39	0.038
NM_003330	3429460	TXNRD1	thioredoxin reductase 1	⇧	1.21	5.48E-04

Cytoskeleton

NM_005720	3014714	ARPC1B	actin related protein 2/3 complex, subunit 1B, 41kDa	⇧	1.22	0.002
NM_018462	2662581	BRK1	BRICK1, SCAR/WAVE actin-nucleating complex subunit	⇧	1.51	0.026
NM_020240	2828146	CDC42SE2	CDC42 small effector 2	⇧	1.25	6.72E-06
NM_001011546	3878025	DSTN	destrin (actin depolymerizing factor)	⇧	1.20	0.038
NM_000259	3624607	MYO5A	myosin VA (heavy chain 12, myoxin)	⇩	1.20	0.015
NM_001142287	4051226	SEMA4D	sema domain, immunoglobin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain, (semaphoring) 4D	⇩	1.31	3.25E-05
NM_020846	2726323	SLAIN2	SLAIN motif family, member 2	⇧	1.20	0.001
NM_006088	4050485	TUBB2C	tubulin, beta 2C	⇧	1.20	0.001
NM_006087	3847959	TUBB4	tubulin, beta 4	⇧	1.27	0.020

Development

NM_031443	3000167	CCM2	cerebral cavernous malformation 2	⇧	1.26	5.76E-04
NM_130468	3589972	CHST14	carbohydrate (N-acetylgalactosamine 4-0) sulfotransferase 14	⇩	1.24	0.002
NM_005618	2986350	DLL1	delta-like 1 (Drosophila)	⇩	1.24	0.003
NM_000138	3623031	FBN1	fibrillin 1	⇩	1.53	0.001
NM_018972	3103607	GDAP1	ganglioside-induced differentiation-associated protein 1	⇧	1.21	0.013
NM_001448	4022370	GPC4	glypican 4	⇩	1.86	0.001
NM_019590	3238962	KIAA1217	KIAA1217	⇩	1.28	0.023
NM_013349	2379068	NENF	neuron derived neurotrophic factor	⇧	1.26	1.78E-04
NM_017617	3230141	NOTCH1	notch 1	⇩	1.30	6.87E-05
NM_002586	2949859	PBX2	B-cell leukemia homeobox 2	⇩	1.20	0.023
NM_015068	3013255	PEG10	paternally expressed 10	⇩	1.31	0.017
NM_024299	3893458	PPDPF	pancreatic progenitor cell differentiation and proliferation factor homolog (Zebrafish)	⇧	1.33	5.63E-04

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_013441	2325479	RCAN3	RCAN family member 3	⇧	1.40	1.41E-04
NM_001122752	2651165	SERPINI1	serpin peptidase inhibitor, clade I (neuroserpin), member 1	⇩	1.34	0.004
NM_005841	2742224	SPRY1	sprout homolog 1, antagonist of FGF signalling (*Drosophila*)	⇩	1.37	0.008

DNA Damage & Repair

NM_000465	2598099	BARD1	BRCA1 associated RING domain 1	⇧	1.21	0.001
NM_152266	3829160	C19orf40	chromosome 19 open reading frame 40	⇧	1.26	1.47E-04
NM_022774	2331959	DEM1	defects in morphology 1 homolog (*S. cerevisiae*)	⇧	1.23	2.04E-04
NM_023015	2359817	INTS3	integrator complex subunit 3	⇩	1.21	6.25E-06
NM_001174084	3303870	POLL	polymerase (DNA directed), lambda	⇩	1.21	4.01E-04
NM_006515	2608419	SETMAR	SET domain and mariner transposase fusion gene	⇧	1.28	0.001
NM_003211	3429365	TDG	thymine-DNA glycosylase	⇧	1.21	0.004

DNA Replication & the Cell Cycle

NR_024400	2696379	ANAPC13	anaphase promoting complex subunit 13	⇧	1.25	0.011
NM_173473	3251353	ANAPC16	anaphase promoting complex subunit 16	⇧	1.29	0.002
NM_021178	3555300	CCNB1IP1	cyclin B1 interacting protein 1	⇧	1.25	0.018
NM_032436	3503119	CHAMP1	chromosome alignment maintaining phosphoprotein 1	⇧	1.26	6.63E-04
NM_001177611	3580319	CINP	cyclin-dependent kinase 2 interacting protein	⇧	1.20	0.019
NM_052951	3887017	DNTTIP1	deoxynucleotidyltransferase, terminal, interacting protein 1	⇧	1.28	2.81E-04
NM_022731	2452637	NUCKS1	nuclear casein kinase and cyclin-dependent kinase substrate 1	⇧	1.20	8.75E-04
NM_032346	3829751	PDCD2L	programmed cell death 2-like	⇧	1.23	3.74E-04
NM_001130475	3067644	THAP5	THAP domain containing 5	⇧	1.21	0.004
NM_175866	2364155	UHMK1	U2AF homology motif (UHM) kinase 1	⇧	1.25	9.64E-05
NM_016478	3072368	ZC3HC1	zinc finger, C3HC-type containing 1	⇧	1.23	8.56E-05

Hormone Function

NM_015893	2534324	PRLH	prolactin releasing hormone	⇧	1.25	0.018

Immune Response & Inflammation

NM_001178098	3655109	CD19	CD19 molecule	⇩	1.24	0.005
NM_001782	3204648	CD72	CD72 molecule	⇩	1.27	0.023
NM_000651	2377332	CR1	complement component (3b/4b) receptor 1 (Knops blood group)	⇩	1.56	0.007
NR_024548	3005332	CRCP	CGRP receptor component	⇧	1.20	0.003

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_018284	2421843	GBP3	guanylate binding protein 3	⇧	1.24	0.020
NM_130759	3031544	GIMAP1	GTPase, IMAP family member 1	⇧	1.32	0.016
NM_012483	2491745	GNLY	granulysin	⇧	1.32	0.019
NM_024503	2408681	HIVEP3	human immunodeficiency virus type I enhancer binding protein 3	⇩	1.23	0.007
NM_002125	4048241	HLA-DRB5	major histocompatibility complex, class II, DR beta 5	⇩	3.61	0.027
NM_024013	3164825	IFNA1	interferon, alpha 1	⇩	1.34	0.012
NM_001551	3980455	IGBP1	immunoglobulin (CD79A) binding protein 1	⇧	1.31	0.011
NM_002201	3607275	ISG20	interferon stimuluated exonuclease gene 20kDa	⇧	1.21	0.012
NM_000575	2571483	IL1A	interleukin 1, alpha	⇧	1.46	0.041
NM_000880	3141589	IL7	interleukin 7	⇩	1.29	0.045
NM_007360	3444086	KLRK1	killer cell lectin-like receptor subfamily K, member 1	⇧	1.41	0.008
NM_005565	2886595	LCP2	lymphocyte cytosolic protein 2 (SH2 domain containing leukocyte protein of 76kDa)	⇩	1.27	0.045
NM_001531	2370317	MR1	Mov10, Moloney leukemia virus 10, homolog (mouse)	⇩	1.20	0.008
NM_032322	3716993	RNF135	ring finger protein 135	⇧	1.22	0.001
NM_022136	3925473	SAMSN1	SAM domain, SH3 domain and nuclear localization signals 1	⇧	1.24	0.046
NM_003037	2440327	SLAMF1	signalling lymphocytic activation molecule family member 1	⇩	1.21	1.28E-04
NM_001104587	3753500	SLFN11	schlafen family member 11	⇩	1.28	0.009
NM_001030288	3655574	SPN	sialophorin	⇩	1.24	6.75E-05
NM_001077238	3816424	SPPL2B	signal peptide peptidase-like 2B	⇩	1.24	3.22E-05

Ion Binding

NM_017623	2494749	CNNM3	cyclin M3	⇩	1.29	5.21E-05
NM_005950	3692999	MT1G	metallothionein 1G	⇧	1.82	0.001
NM_005951	3662201	MT1H	metallothionein 1H	⇧	1.54	0.007

Membrane Trafficking

NM_000443	3060117	ABCB4	ATP-binding cassette, sub-family B (MDR/TAP), member 4	⇩	1.21	0.032
NM_004996	3649890	ABCC1	ATP-binding cassette, sub-family C (CFTR/MRP), member 1	⇩	1.22	2.33E-04
NM_005845	3521174	ABCC4	ATP-binding cassette, sub-family C (CFTR/MRP), member 4	⇩	1.25	0.005
NM_005050	3571810	ABCD4	ATP-binding cassette, sub-family D (ALD), member 4	⇩	1.24	1.83E-07
NM_002940	2746024	ABCE1	ATP-binding cassette, sub-family E (OABP), member 1	⇧	1.29	0.003
NM_020980	3595594	AQP9	aquaporin 9	⇩	1.39	0.016
NM_022089	2398736	ATP13A2	ATPase type 13A2	⇩	1.23	0.005
NM_001679	2645764	ATP1B3	ATPase, Na+/K+ transporting, beta 3 polypeptide	⇩	1.29	0.009

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_001001323	3464983	ATP2B1	ATPase, Ca++ transporting, plasma membrane 1	⇩	1.20	0.002
NM_014382	2642325	ATP2C1	ATPase, Ca++ transporting, type 2C, member 1	⇩	1.24	5.19E-05
NM_006095	2767378	ATP8A1	ATPase, aminophospholipid transporter (APLT), class I, type 8A, member 1	⇩	1.20	0.002
NM_001048210	2426791	CLCC1	chloride channel CLIC-like 1	⇩	1.24	7.24E-04
NM_013943	2325593	CLIC4	chloride intracellular channel 4	⇧	1.24	0.012
NM_001293	3382948	CLNS1A	chloride channel, nucleotide-sensitive, 1A	⇧	1.20	0.007
NM_020897	2360818	HCN3	hyperpolarization activated cyclic nucleotide-gated potassium channel 3	⇩	1.20	0.003
NM_012281	3021009	KCND2	potassium voltage-gated channel, Shal-related subfamily, member 2	⇩	1.39	0.021
NM_001160133	2913277	KCNQ5	potassium voltage-gated channel, KQT-like subfamily, member 5	⇩	1.21	3.74E-04
NM_153259	2420642	MCOLN2	mucolipin 2	⇩	1.21	0.002
NM_198887	2979056	NUP43	SAM domain, SH3 domain and nuclear localization signals 1	⇧	1.21	9.11E-05
NM_032790	3434888	ORAI1	ORAI calcium release-activated calcium modulator 1	⇩	1.21	0.011
NM_006598	2845699	SLC12A7	solute carrier family 12 (potassium/chloride transporters), member 7	⇩	1.37	0.020
NM_201566	3708245	SLC16A13	solute carrier family 16, member 13 (monocarboxylic acid transporter 13)	⇩	1.27	0.004
NM_004170	3160658	SLC1A1	solute carrier family 1 (neuronal/epithelial high affinity glutamate transporter, system xag), member 1	⇩	1.30	0.016
NM_001040454	2673547	SLC26A6	solute carrier family 26, member 6	⇩	1.31	1.58E-05
NM_001532	3378244	SLC29A2	solute carrier organic anion transporter family, member 2B1	⇩	1.22	0.004
NM_021194	2454378	SLC30A1	solute carrier family 30 (zinc transporter), member 1	⇩	1.20	0.013
NM_198277	3354443	SLC37A2	solute carrier family 37 (glycerol-3-phosphate transporter), member 2	⇩	1.29	0.035
NM_003627	3373893	SLC43A1	solute carrier family 43, member 1	⇩	1.24	0.015
NM_080669	3750685	SLC46A1	solute carrier family 46 (folate transporter), member 1	⇩	1.20	0.012
NM_033262	3570373	SLC8A3	solute carrier family 8 (sodium/calcium exchanger), member 3	⇩	1.45	0.006
NM_007256	3340449	SLCO2B1	solute carrier organic anion transporter family, member 2B1	⇩	1.24	0.010
NM_152468	3736162	TMC8	transmembrane channel-like 8	⇩	1.24	2.90E-04

Metabolism

NM_006821	3543673	ACOT2	acyl-CoA thioesterase 2	⇧	1.22	0.030
NM_025149	3726406	ACSF2	acyl-CoA synthetase family member 2	⇩	1.23	0.013
NR_023318	3632298	ADPGK	ADP-dependent glucokinase	⇩	1.20	0.011
NM_000687	3903361	AHCY	adenosylhomocysteinase	⇧	1.30	0.002
NM_006995	2899340	BTN2A2	butyrophilin, subfamily 2, member A2	⇩	1.22	0.002
NM_006090	2351632	CEPT1	choline/ethanolamine phosphotransferase 1	⇩	1.20	0.008
NM_183075	2738697	CYP2U1	cytochrome P450, family 2, subfamily U, polypeptide 1	⇩	1.30	5.77E-04

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_024090	2781813	ELOVL6	ELOVL family member 6, elongation of long chain fatty acids (FEN1/Elo2, SUR4/Elo3-like, yeast)	⇩	1.26	0.020
NM_005670	2977949	EPM2A	epilepsy, progressive myoclonus type 2A, Lafora disease (laforin)	⇧	1.20	1.44E-04
NM_018638	3408018	ETNK1	ethanolamine kinase 1	⇩	1.29	2.10E-06
NM_207122	3328389	EXT2	exostosin 2	⇩	1.20	0.012
NM_004265	3333247	FADS2	fatty acid desaturase 2	⇩	1.24	0.002
NM_021727	3375582	FADS3	fatty acid desaturase 3	⇩	1.20	0.002
NM_017423	2751936	GALNT7	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 7 (GalNAc-T7)	⇩	1.26	0.010
NM_000155	3167511	GALT	galactose-1-phosphate uridylyltransferase	⇩	1.20	6.30E-04
NM_021996	3228523	GBGT1	globoside alpha-1,3-N-acetylgalactosaminyltransferase 1	⇩	1.34	0.014
NM_002061	2423625	GCLM	glutamate-cysteine ligase, modifier subunit	⇧	1.24	3.37E-06
NM_001128227	3205108	GNE	glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosamine kinase	⇧	1.20	0.001
NM_000190	3351841	HMBS	hydroxymethylbilane synthase	⇧	1.36	0.011
NM_000859	2815965	HNGCR	3-hydroxy-3-methylglutaryl-CoA reductase	⇩	1.24	3.55E-04
NM_012262	2345196	HS2ST1	heparin sulfate 2-O-sulfotransferase 1	⇩	1.21	0.004
NM_016142	3328069	HSD17B12	hydroxysteroid (17-beta) dehydrogenase 12	⇩	1.24	0.013
NM_024552	3819401	LASS4	LAG1 homolog, ceramide synthase 4	⇩	1.24	1.32E-05
NM_000527	3821015	LDLR	low density lipoprotein receptor	⇩	1.23	7.82E-04
NM_153613	3617412	LPCAT4	lysophosphatidylcholine acyltransferase 4	⇩	1.27	7.79E-05
NM_145693	2469910	LPIN1	lipin 1	⇧	1.21	0.032
NM_205834	3830246	LSR	lipolysis stimulated lipoprotein receptor	⇩	1.25	4.87E-04
NM_013283	2838688	MAT2B	methionine adenosyltransferase II, beta	⇧	1.27	6.51E-04
NM_001080480	2944491	MBOAT1	membrane bound O-acyltransferase domain containing 1	⇩	1.22	4.72E-04
NM_138799	2539607	MBOAT2	membrane bound O-acyltransferase domain containing 2	⇩	1.57	0.008
NM_002413	2744734	MGST2	microsomal glutathione S-transferase 2	⇩	1.37	0.008
NM_001018137	3726960	NME2	non-metastatic cells 2, protein (NM23B) expressed in	⇧	1.20	0.003
NM_005793	2673136	NME6	NME/NM23 nucleoside diphosphate kinase 6	⇧	1.25	0.001
NM_002537	3629206	OAZ2	ornithine decarboxylase antizyme 2	⇧	1.21	0.003
NM_018425	3259978	PI4K2A	phosphatidylinositol 4-kinase type 2 alpha	⇧	1.36	0.002
NM_018323	2721777	PI4K2B	phosphatidylinositol 4-kinase type 2 beta	⇧	1.24	0.001
NM_006556	2436920	PMVK	phosphomevalonate kinase	⇧	1.22	3.28E-06
NM_001136113	3192171	POMT1	protein-O-mannosyltransferase 1	⇩	1.20	1.30E-05
NM_017750	2562233	RETSAT	retinol saturase (all-trans-retinol 13,14-reductase)	⇩	1.21	0.010
NM_012235	2672712	SCAP	SREBF chaperone	⇩	1.26	7.58E-05

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_005505	3476665	SCARB1	scavenger receptor class F, member 1	⇩	1.29	3.77E-06
NM_005063	3260586	SCD	stearoyl-CoA desaturase (delta-9-desaturase)	⇩	1.21	4.41E-04
NM_001037582	2775735	SCD5	stearoyl-CoA desaturase 5	⇩	1.30	0.026
NM_152386	2529421	SGPP2	sphingosine-1-phosphate phosphatase 2	⇩	1.25	3.68E-06
NM_003101	2369557	SOAT1	sterol O-acyltransferase 1	⇩	1.21	0.016
NM_006415	3214582	SPTLC1	serine palmitoyltransferase, long chain base subunit 1	⇩	1.22	0.005
NM_000351	3967689	STS	steroid sulfatase (microsomal), isozyme S	⇩	1.24	0.043
NM_003129	3114832	SQLE	squalene epoxidase	⇩	1.27	8.78E-04
NM_003358	3185063	UGCG	UDP-glucose ceramide glucosyltransferase	⇩	1.21	0.006
NM_022167	3726325	XYLT2	xylosyltransferase II	⇩	1.22	6.76E-04

Mitochondrion & the Respiratory Electron Transport Chain

NM_001190329	2588127	ATP5G3	ATP synthase, H+ transporting, mitochondrial Fo complex, subunit C3 (subunit 9)	⇧	1.22	0.003
NM_006012	3818376	CLPP	ClpP caseinolytic peptidase, ATP-dependent, proteolytic subunit homolog (*E. coli*)	⇧	1.21	2.95E-04
NM_001040431	3758148	COA3	cytochrome c oxidase assembly factor 3	⇧	1.24	8.76E-04
NR_029466	2961300	COX7A2	cytochrome c oxidase subunit VIIa polypeptide 2 (liver)	⇧	1.29	0.013
NM_152783	2536800	D2HGDH	D-2-hydroxyglutarate dehydrogenase	⇩	1.21	0.014
NM_001985	3868963	ETFB	electron-transfer-flavoprotein, beta polypeptide	⇧	1.31	9.96E-06
NM_001085411	2853388	NADKD1	NAD kinase domain containing 1	⇧	1.20	6.68E-04
NM_004541	3988987	NDUFA1	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 1, 7.5kDa	⇧	1.31	0.011
NM_005000	3070658	NDUFA5	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 5, 13kDa	⇧	1.31	0.038
NM_004546	3027538	NDUFB2	NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 2, 8kDa	⇧	1.20	0.021
NM_003000	2398789	SDHB	succinate dehydrogenase complex, subunit B, iron sulphur (Ip)	⇧	1.27	0.001
NM_001024465	2982319	SOD2	s⇧eroxide dismutase 2, mitochondrial	⇧	1.26	0.001
NM_013442	3204534	STOML2	stomatin (EPB72)-like 2	⇧	1.28	7.01E-05
NM_003355	3381817	UCP2	unco⇧ling protein 2 (mitochondrial, proton carrier)	⇧	1.24	2.19E-04
NM_006830	3845352	UQCR11	ubiquinol-cytochrome c reductase, complex III subunit XI	⇧	1.27	0.026

Neurotransmission

NM_001114	3659966	ADCY7	adenylate cyclase 7	⇩	1.25	1.05E-05
NM_001009566	2395890	CLSTN1	calsyntenin 1	⇩	1.22	6.03E-04
NM_014718	3403244	CLSTN3	calsyntenin 3	⇩	1.38	4.58E-05
NM_003632	3721989	CNTNAP1	contactin associated protein 1	⇩	1.52	9.81E-04
NM_001184796	3417371	ESYT1	extended synaptotagmin-like protein 1	⇩	1.25	0.002

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_007278	3743486	GABARAP	GABA(A) receptor-associated protein	⇧	1.21	4.72E-04
NM_012428	3632492	NPTN	neuroplastin	⇩	1.24	0.001
NM_004782	3937755	SNAP29	synaptosomal-associated protein, 29kDa	⇧	1.48	1.45E-06

Nucleosome

NM_032482	3816264	DOT1L	DOT1-like, histone H3 methyltransferase (*S. cerevisiae*)	⇩	1.20	0.004
NM_153757	2777447	NAP1L5	nucleosome assembly protein 1-like 5	⇧	1.24	2.03E-04
NM_021062	2946225	HIST1H2BB	histone cluster 1, H2bb	⇧	1.57	0.024
NM_003527	2900116	HIST1H2BO	histone cluster 1, H2bo	⇧	1.34	3.10E-04
NM_003539	2946319	HIST1H4D	histone cluster 1, H4d	⇧	1.40	0.002
NM_003540	2899243	HIST1H4F	histone cluster 1, H4f	⇧	1.23	0.010

Protein Processing

NM_024105	3965393	ALG12	asparagine-linked glycosylation 12, alpha-1,6-mannosyltransferase	⇩	1.20	0.001
NM_003917	3557614	AP1G2	adaptor-related protein complex 1, gamma 2 subunit	⇩	1.20	0.001
NM_001039569	2601287	APS3	adaptor-related protein complex 1, sigma 3 subunit	⇧	1.21	0.010
NM_014570	3962587	ARFGAP3	ADP-ribosylation factor GTPase activating protein	⇧	1.24	0.001
NM_024095	3453036	ASB8	ankyrin repeat and SOCS box-containing 8	⇧	1.36	0.020
NM_001139457	4026669	BCAP31	B-cell receptor-associated protein 31	⇩	1.31	1.27E-05
NM_024814	3018652	CBLL1	Cas-Br-M (murine) ecotropic retroviral transforming sequence-like 1	⇧	1.25	2.64E-06
NM_005776	3565303	CNIH	cornichon homolog (*Drosophila*)	⇩	1.20	5.18E-04
NM_007263	3855324	COPE	coatomer protein complex, subunit epsilon	⇧	1.24	0.002
NM_024050	3824212	DDA1	DET1 and DDB1 associated 1	⇧	1.27	0.031
NM_206831	2664607	DPH3	DPH3, KTI11 homolog (*S. cerevisiae*)	⇧	1.25	0.016
NM_013234	3832616	EIF3K	eukaryotic translation initiation factor 3, subunit K	⇧	1.33	1.68E-04
NM_001417	3455946	EIF4B	eukaryotic translation initiation factor 4B	⇧	1.45	0.011
NM_004846	2532422	EIF4E2	eukaryotic translation initiation factor 4E family member 2	⇧	1.23	0.011
NM_183004	3553607	EIF5	eukaryotic translation initiation factor 5	⇧	1.20	0.001
NM_033644	2886977	FBXW11	F-box and WD repeat domain containing 11	⇧	1.22	1.02E-04
NM_000801	3894601	FKBP1A	FK506 binding protein 1A, 12kDa	⇩	1.23	0.006
NM_015949	2986906	GET4	golgi to ER traffic protein 4 homolog (*S. cerevisiae*)	⇧	1.24	0.002
NM_022130	2852237	GOLPH3	golgi phosphoprotein 3 (coat-protein)	⇧	1.20	0.002
NM_014761	3667766	IST1	increased sodium tolerance 1 homolog (yeast)	⇧	1.20	0.008
NM_016475	3538324	JKAMP	JNK1/MAPK8-associated membrane protein	⇩	1.26	9.14E-04

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NR_033646	3675462	LMF1	lipase maturation factor 1	⇩	1.21	0.015
NM_005358	3494137	LMO7	LIM domain 7	⇩	1.28	0.025
NM_022149	2708610	MAGEF1	melanoma antigen family F, 1	⇧	1.20	0.007
NM_032868	3817464	MPND	MPN domain containing	⇧	1.22	1.86E-04
NM_145255	3760945	MRPL10	mitochondrial ribosomal protein L10	⇧	1.21	0.037
NM_014175	3098454	MRPL15	mitochondrial ribosomal protein L15	⇧	1.27	1.83E-04
NM_017840	3374856	MRPL16	mitochondrial ribosomal protein L16	⇧	1.20	0.022
NM_014763	2489806	MRPL19	mitochondrial ribosomal protein L19	⇧	1.22	0.012
NM_181515	3379708	MRPL21	mitochondrial ribosomal protein L21	⇧	1.32	0.003
NM_145212	2495806	MRPL30	mitochondrial ribosomal protein L30	⇧	1.20	0.014
NM_023937	3824197	MRPL34	mitochondrial ribosomal protein L34	⇧	1.33	6.39E-05
NM_146388	3820414	MRPL4	mitochondrial ribosomal protein L4	⇧	1.21	0.002
NM_003776	3936887	MRPL40	mitochondrial ribosomal protein L40	⇧	1.22	0.023
NM_053050	2560141	MRPL53	mitochondrial ribosomal protein L53	⇧	1.22	3.77E-04
NM_031420	2435195	MRPL9	mitochondrial ribosomal protein L9	⇧	1.21	0.007
NM_022839	3607183	MRPS11	mitochondrial ribosomal protein S11	⇧	1.33	1.60E-05
NM_021107	3832777	MRPS12	mitochondrial ribosomal protein S12	⇧	1.29	1.89E-05
NM_016065	3294348	MRPS16	mitochondrial ribosomal protein S16	⇧	1.21	1.83E-04
NM_016034	3193900	MRPS2	mitochondrial ribosomal protein S2	⇧	1.26	0.001
NM_016100	3878934	NAA20	N(alpha)-acetyltransferase 20, NatB catalytic subunit	⇧	1.22	0.002
NM_015678	3485292	NBEA	neurobeachin	⇩	1.27	0.014
NM_006812	3418436	OS9	osteosarcoma amplified 9, endoplasmic reticulum lectin	⇩	1.20	0.007
NM_000287	2954280	PEX6	peroxisomal biogenesis factor 6	⇩	1.25	1.61E-04
NM_012394	2440612	PFDN2	prefoldin subunit 2	⇧	1.20	0.003
NM_176787	3811086	PIGN	phosphatidylinositol glycan anchor biosynthesis, class N	⇩	1.26	9.66E-04
NM_032634	3204496	PIGO	phosphatidylinositol glycan anchor biosynthesis, class O	⇩	1.26	0.010
NM_006221	3820177	PIN1	peptidylprolyl cis/trans isomerase, NIMA-interacting 1	⇧	1.37	1.52E-05
NM_012388	3592484	PLDN	pallidin homolog (mouse)	⇧	1.30	6.86E-04
NM_017958	2505957	PLEKHB2	pleckstrin homology domain containing, family B (evectins) member 2	⇧	1.21	0.008
NM_005817	3847005	PLIN3	perilipin 3	⇧	1.20	0.004
NM_152329	3534785	PPIL5	peptidylprolyl isomerase (cyclophilin)-like 5	⇧	1.24	0.002
NM_002792	3912861	PSMA7	proteasome (prosome, macropain) subunit, alpha type, 7	⇧	1.28	5.44E-05
NM_002800	2903285	PSMB9	proteasome (prosome, macropain) subunit, beta type, 9 (large multifunctional peptidase 2)	⇧	1.22	0.001

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_002814	4017519	PSMD10	proteasome (prosome, macropain) 26S subunit, non-ATPase, 10	⇧	1.22	7.62E-05
NM_031296	2744674	RAB33B	RAB33B, member RAS oncogene family	⇧	1.27	0.004
NM_014372	2335986	RNF11	ring finger protein 11	⇧	1.23	0.004
NM_015528	3707352	RNF167	ring finger protein 167	⇩	1.23	2.12E-05
NM_017763	3764399	RNF43	ringer finger protein 43	⇩	1.20	0.007
NM_000975	2325192	RPL11	ribosomal protein L11	⇧	1.25	0.035
NM_000983	2394558	RPL22	ribosomal protein L22	⇧	1.40	1.06E-04
NM_052969	2709606	RPL39L	ribosomal protein L39-like	⇧	1.35	0.007
NM_021104	3717034	RPL41	ribosomal protein L41	⇧	1.32	0.003
NM_001024921	2766419	RPL9	ribosomal protein L9	⇧	1.24	0.014
NM_001019	3683018	RPS15A	ribosomal protein S15a	⇧	1.27	0.039
NM_002952	3676300	RPS2	ribosomal protein S2	⇧	1.49	0.003
NM_001042576	3899173	RRBP1	ribosome binding protein 1 homolog 180kDa (dog)	⇩	1.26	0.009
NM_005619	3865422	RTN2	reticulon 2	⇩	1.23	4.12E-05
NM_013346	4011768	SNX12	sorting nexin 12	⇧	1.20	0.002
NM_003134	3619165	SRP14	signal recognition particle 14kDa (homologous Alu RNA binding protein)	⇧	1.34	0.002
NM_152713	3354764	STT3A	STT3, subunit of the oligosaccharyltransferase complex, homolog A (*S. cerevisiae*)	⇩	1.21	0.009
NM_004853	3744800	STX8	syntaxin 8	⇧	1.22	0.013
NM_006936	3934669	SUMO3	SMT3 suppressor of mif two 3 homolog 3 (*S. cerevisiae*)	⇧	1.32	5.38E-04
NR_028383	3391234	TIMM8B	translocase of inner mitochondrial membrane 8 homolog B (yeast)	⇧	1.20	0.015
NM_014506	3191147	TOR1B	torsin family 1, member B (torsin B)	⇩	1.20	0.006
NM_003338	3247757	UBE2D1	ubiquitin-conjugating enzyme E2D 1 (UBC4/5 homolog, yeast)	⇧	1.21	0.001
NM_015983	2999640	UBE2D4	ubiquitin-conjugating enzyme E2D 4 (putative)	⇧	1.30	1.32E-04
NM_003342	3742067	UBE2G1	ubiquitin-conjugating enzyme E2G 1 (UBC7 homolog, yeast)	⇧	1.22	0.004
NM_005339	2766532	UBE2K	ubiquitin-conjugating enzyme E2K (UBC1 homolog, yeast)	⇧	1.38	0.009
NM_015853	3376023	UBXN1	UBX domain protein 1	⇧	1.21	0.015
NM_006634	2491676	VAMP5	vesicle-associated membrane protein 5 (myobrevin)	⇧	1.24	0.040
NM_006555	2999816	YKT6	YKT6 v-SNARE homolog (*S. cerevisiae*)	⇧	1.28	5.00E-05

RNA Processing

NM_001002252	3435681	ARL6IP4	ADP-ribosylation-like factor 6 interacting protein 4	⇧	1.26	8.01E-05
NM_018696	3788270	ELAC1	elaC homolog 1 (*E. coli*)	⇧	1.24	0.001
NM_019037	3120008	EXOSC4	exosome component 4	⇧	1.27	2.04E-04

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_032288	2659887	FYTTD1	forty-two-three domain containing 1	⇧	1.33	1.59E-04
NM_203505	2773756	G3BP2	GTPase activating protein (SH3 domain) binding protein 2	⇧	1.24	4.20E-05
NM_018983	2739242	GAR1	GAR1 ribonucleoprotein homolog (yeast)	⇧	1.31	6.95E-05
NM_002047	2995420	GARS	glycyl-tRNA synthetase	⇧	1.24	0.004
NM_024775	2477980	GEMIN6	gem (nuclear organelle) associated protein 6	⇧	1.29	1.16E-04
NM_004966	3286286	HNRNPF	heterogeneous nuclear ribonucleoprotein F	⇧	1.22	6.15E-04
NM_015155	3273484	LARP4B	La ribonucleoprotein domain family, member 4B	⇧	1.20	0.025
NM_016648	2740005	LARP7	La ribonucleoprotein domain family, member 7	⇧	1.20	0.022
NM_139242	3629378	MTFMT	mitochondrial methionyl-tRNA formyltransferase	⇧	1.24	0.007
NM_007362	2713074	NCBP2	nuclear cap binding protein subunit 2, 20kDa	⇧	1.20	0.010
NM_007006	3692895	NUDT21	nudix (nucleoside diphosphate linked moiety X)-type motif 21	⇧	1.20	6.68E-05
NM_005008	3962054	NHP2L1	NHP2 non-histone chromosome protein 2-like 1 (*S. cerevisiae*)	⇧	1.22	4.57E-04
NM_001127460	3457696	PAN2	PAN2 poly(A) specific ribonuclease subunit homolog (*S. cerevisiae*)	⇩	1.21	2.09E-05
NM_020528	3924254	PCBP3	poly(rC) binding protein 3	⇧	1.23	0.025
NM_032758	3961955	PHF5A	PHD finger protein 5A	⇧	1.21	0.020
NM_004805	2575134	POLR2D	polymerase (RNA) II (DNA directed) polypeptide D	⇧	1.22	0.010
NM_021974	3945133	POLR2F	polymerase (RNA) II (DNA directed) polypeptide F	⇧	1.22	0.020
NM_002696	3333622	POLR2G	polymerase (RNA) II (DNA directed) polypeptide G	⇧	1.24	3.80E-04
NM_006627	3828032	POP4	processing of precursor 4, ribonuclease P/MRP subunit (*S. cerevisiae*)	⇧	1.20	0.022
NM_016059	2952065	PPIL1	peptidylprolyl isomerase (cyclophilin)-like 1	⇧	1.22	0.017
NM_006743	3976519	RBM3	RNA binding motif (RNP1, RRM) protein 3	⇧	1.22	9.22E-05
NM_053043	3033397	RBM33	RNA binding motif protein 33	⇩	1.20	4.75E-04
NM_001098783	2626141	RPP14	ribonuclease P/MRP 14kDa subunit	⇧	1.37	0.001
NM_014502	3375049	PRPF19	PSO4 pre-mRNA processing factor 19 homolog (*S. cerevisiae*)	⇧	1.21	2.24E-04
NM_024839	2901552	RPP21	ribonuclease P/MRP 21kDa subunit	⇧	1.23	0.005
NM_183005	3236538	RPP38	ribonuclease P/MRP 38kDa subunit	⇧	1.34	0.011
NM_016047	2544179	SF3B14	splicing factor 3B, 14kDa subunit	⇧	1.21	0.002
NM_005850	2434159	SF3B4	splicing factor 3b, subunit 4, 49kDa	⇧	1.20	0.019
NM_019108	3864597	SMG9	Smg-9 homolog, nonsense mediated mRNA decay factor (*C. elegans*)	⇩	1.24	6.65E-05
NM_177542	3865568	SNRPD2	small nuclear ribonucleoprotein D2 polypeptide 16.5kDa	⇧	1.23	0.012
NM_014188	2391647	SSU72	SSU72 RNA polymerase II CTD phosphatase homolog (*S. cerevisiae*)	⇧	1.25	1.64E-04
NM_007178	3406421	STRAP	serine/threonine kinase receptor associated protein	⇧	1.20	0.001
NM_005646	2461473	TARBP1	TAR (HIV-1) RNA binding protein 1	⇩	1.22	0.002

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NR_027962	2342391	TYW3	tRNA-yW synthesizing protein 3 homolog (*S. cerevisiae*)	⇧	1.24	0.010
NM_007187	3486807	WBP4	WW domain binding protein 4 (formin binding protein 21)	⇧	1.20	0.002
NM_033114	3451318	ZCRB1	zinc finger CCHC-type and RNA binding motif 1	⇧	1.26	7.15E-05

Sensory Perception

NM_001001963	2390253	OR2L8	olfactory receptor, family 2, subfamily L, member 8	⇧	1.34	0.032
NM_001005278	2439508	OR6N2	olfactory receptor, family 6, subfamily N, member 2	⇧	1.34	0.032

Signal Transduction

NM_001040196	2320411	AGTRAP	angiotensin II receptor-associated protein	⇩	1.22	0.006
NM_130847	3345222	AMOTL1	angiomotin like 1	⇩	1.20	0.036
NM_018287	3283920	ARHGAP19	Rho GTPase activating protein 12	⇩	1.20	0.007
NM_032900	3302177	ARHGAP19	Rho GTPase activating protein 19	⇧	1.22	0.042
NM_012106	3662650	ARL2BP	ADP-ribosylation factor-like 2 binding protein	⇧	1.20	0.022
NM_016289	2531522	CAB39	calcium binding protein 39	⇧	1.25	7.76E-04
NM_030925	3513752	CAB39L	calcium binding protein 39-like	⇧	1.27	0.007
NM_005795	2591367	CALCRL	calcitonin receptor-like	⇩	1.33	0.037
NM_006833	3015216	COPS6	COP9 constitutive photomorphogenic homolog subunit 6 (*Arabidopsis*)	⇧	1.22	0.004
NM_001130048	3522398	DOCK9	dedicator of cytokinesis 9	⇩	1.39	0.033
NM_000118	3226097	ENG	endoglin	⇩	1.31	0.002
NM_004447	3445908	EPS8	epidermal growth factor receptor pathway substrate 8	⇧	1.51	0.035
NM_004101	2863363	F2RL2	coagulation factor II (thrombin) receptor-like 2	⇩	1.20	0.002
NM_004112	3708644	FGF11	fibroblast growth factor 11	⇩	1.33	0.005
NM_001174064	3132016	FGFR1	fibroblast growth factor receptor 1	⇩	1.73	6.68E-04
NM_213647	2842911	FGFR4	fibroblast growth factor receptor 4	⇩	1.21	0.001
NM_138445	2986999	GPR146	G protein-coupled receptor 146	⇧	1.55	0.003
NM_014181	2485406	HSPC159	galectin-related protein	⇩	1.34	0.011
NM_002224	2903782	ITPR3	inositol 1,4,5-triphosphate receptor, type 3	⇩	1.22	7.81E-04
NM_017907	3380980	LAMTOR1	late endosomal/lysosomal adaptor, MAPK and mTOR activator 1	⇩	1.29	6.93E-04
NM_002309	3957160	LIF	leukemia inhibitory factor (cholinergic differentiation factor)	⇧	1.23	0.013
NM_001040056	3687494	MAPK3	mitogen-activated protein kinase 3	⇩	1.32	0.001
NM_001142633	3744680	PIK3R5	phosphoinositide-3-kinase, regulatory subunit 5	⇧	1.25	0.014
NM_021959	2901352	PPP1R11	protein phosphatase 1, regulatory (inhibitor) subunit 11	⇧	1.21	0.002
NM_001009552	3130211	PPP2CB	protein phosphatase 2, catalytic subunit, beta isozyme	⇧	1.32	4.81E-04

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_001033582	2316245	PRKCZ	protein kinase C, zeta	⇩	1.26	8.50E-04
NM_000956	3535780	PTGER2	prostaglandin E receptor 2 (subtype EP2), 53kDa	⇩	1.23	6.53E-04
NM_002838	2373842	PTPRC	protein tyrosine phosphatase, receptor type, C	⇧	1.24	0.011
NM_014990	3561110	RALGAPA1	Ral GTPase activating protein, alpha subunit 1 (catalytic)	⇧	1.20	0.023
NM_001010935	2351872	RAP1A	RAP1A, member of RAS oncogene family	⇩	1.20	0.004
NM_002886	2648378	RAP2B	RAP2B, member of RAS oncogene family	⇧	1.24	1.87E-04
NM_024599	3771602	RHBDF2	rhomboid 5 homolog 2 (*Drosophila*)	⇧	1.28	4.45E-05
NM_022157	2407729	RRAGC	Ras-related GTP binding C	⇧	1.25	6.98E-04
NM_021244	2964231	RRAGD	Ras-related GTP binding D	⇧	1.71	0.004
NM_174919	3759824	SH3D20	SH3 domain containing 20	⇩	1.20	0.027
NM_054114	2982076	TAGAP	T-cell activation Rho GTPase activating protein	⇧	1.22	0.007
NM_014604	3741528	TAX1BP3	Tax1 (human T-cell leukemia virus type I) binding protein 3	⇧	1.24	0.036
NM_003839	3791254	TNFRSF11A	tumor necrosis factor receptor superfamily, member 11a, NFKB activator	⇩	1.36	0.034
NM_002546	3150455	TNFRSF11B	tumor necrosis factor receptor superfamily 11b	⇩	1.34	0.027
NM_014452	2956052	TNFRSF21	tumor necrosis factor receptor superfamily, member 21	⇩	1.28	0.039
NM_001243	2320683	TNFRSF8	tumor necrosis factor receptor superfamily, member 8	⇩	1.22	0.003
NM_005981	3418492	TSPAN31	tetraspanin 31	⇩	1.25	0.005
NM_003353	2545645	UCN	urocortin	⇧	1.20	0.003
NM_003904	3392871	ZNF259	zinc finger protein 259	⇧	1.21	0.002
Transcription						
NM_001129	2999755	AEBP1	AE binding protein 1	⇩	1.25	0.020
NM_007021	3286776	C10orf10	chromosome 10 open reading frame 10	⇩	1.26	0.005
NM_005760	2548459	CEBPZ	CCAAT/enhancer binding protein (C/EBP), zeta	⇧	1.20	0.015
NM_001127192	2694644	CNBP	CCHC-type zinc finger, nucleic acid binding protein	⇧	1.21	0.008
NM_014335	3593261	EID1	interacting inhibitor of differentiation 1	⇧	1.23	0.005
NM_032377	3851055	ELOF1	elongation factor 1 homolog (*S. cerevisiae*)	⇧	1.21	0.022
NM_002095	3130113	GTF2E2	general transcription factor IIE, polypeptide 2, beta 34kDa	⇧	1.23	0.002
NM_001516	3435946	GTF2H3	general transcription factor IIH, polypeptide 3, 34kDa	⇧	1.20	0.003
NM_012259	2924492	HEY2	hairy/enhancer-of-split related with YRPW motif 2	⇧	1.27	0.003
NM_001080424	3709153	KDM6B	lysine (K)-specific demethylase 6B	⇩	1.20	0.004
NM_199072	3019981	MDFIC	MyoD family inhibitor domain containing	⇧	1.20	0.010
NM_020963	2352275	MOV10	Mov10, Moloney leukemia virus 10, homolog (mouse)	⇩	1.20	0.002

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_018270	3892918	MRGBP	MRG/MORF4L binding protein	⇧	1.21	0.010
NM_030759	3248897	NRBF2	nuclear receptor binding factor 2	⇧	1.24	2.93E-05
NM_013388	2545509	PREB	prolactin regulatory element binding	⇧	1.21	7.15E-04
NM_005859	2831567	PURA	purine-rich element binding protein A	⇧	1.20	1.39E-05
NM_152501	2362351	PYHIN1	pyrin and HIN domain family, member 1	⇧	1.49	0.010
NM_002904	2948713	RDBP	RNA binding protein	⇧	1.21	0.002
NM_134428	3196842	RFX3	regulatory factor X, 3 (influences HLA class II expression)	⇩	1.20	0.006
NM_001134338	3895795	RNF24	ring finger protein 24	⇩	1.21	0.002
NM_001035235	2878347	SRA1	steroid receptor RNA activator 1	⇧	1.21	8.68E-04
NM_004599	3947123	SREBF2	sterol regulatory element binding transcription factor 2	⇩	1.21	2.29E-06
NM_003935	3954331	TOP3B	topoisomerase (DNA) III beta	⇩	1.24	3.93E-05
NM_020368	2730531	UTP3	UTP3, small subunit (SSU) processome component, homolog (*S. cerevisiae*)	⇧	1.24	0.002
NM_153477	4007216	UXT	ubiquitously-expressed transcript	⇧	1.25	0.035
NM_016535	3842301	ZNF581	zinc finger protein 581	⇧	1.21	0.034
NM_152457	3677612	ZNF597	zinc finger protein 597	⇧	1.27	2.12E-04
NM_001082480	3119735	ZNF623	zinc finger protein 623	⇧	1.20	0.002
NM_016331	2653902	ZNF639	zinc finger protein 639	⇧	1.32	2.20E-04
NM_001159293	3856184	ZNF737	zinc finger protein 737	⇧	1.20	0.047
NM_170783	2901333	ZNRD1	zinc ribbon domain containing 1	⇧	1.24	0.002
NM_017580	3269373	ZRANB1	zinc finger, RAN-binding domain containing 1	⇧	1.29	0.039

Miscellaneous

NM_133174	2878368	APBB3	amyloid beta (A4) precursor protein-binding, family B, member 3	⇩	1.23	4.07E-04
NM_001034850	2849992	FAM134B	family with sequence similarity 134, member B	⇩	1.33	0.043
NM_014053	2379280	FLVCR1	feline leukemia virus subgroup C cellular receptor 1	⇩	1.22	0.012
NM_173794	4006416	FUNDC1	FUN14 domain containing 1	⇧	1.27	0.004
NM_198682	2787902	GYPE	glycophorin E (MNS blood group)	⇧	1.26	0.043
NM_198527	3639007	HDDC3	HD domain containing 3	⇧	1.22	3.63E-04
NM_001005405	3380769	KRTAP5-11	keratin associated protein 5-11	⇧	1.27	6.69E-04
NM_018368	2960010	LMBRD1	LMBR1 domain containing 1	⇩	1.20	0.012
NM_014623	2954324	MEA1	male-enhanced antigen 1	⇧	1.31	0.001
NM_001161	3167383	NUDT2	nudix (nucleoside diphosphate linked moiety X)-type motif 2	⇧	1.29	0.005
NM_016422	3362795	RNF141	ring finger protein 167	⇧	1.23	0.005

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_016104	2922756	RWDD1	RWD domain containing 1	⇧	1.26	2.93E-04
NM_170601	3396003	SIAE	sialic acid acetylesterase	⇩	1.32	0.005
NM_145251	3535922	STYX	serine/threonine/tyrosine interacting protein	⇧	1.20	0.004
NM_022152	2599371	TMBIM1	transmembrane BAX inhibitor motif containing 1	⇩	1.20	0.004
NM_199360	3893760	TPD52L2	tumor protein D52-like 2	⇧	1.20	0.007

Unknown Function

NM_019048	2519860	ASNSD1	asparagine synthetase domain containing 1	⇧	1.20	0.009
NM_173694	4024160	ATP11C	ATPase, class VI, type 11C	⇩	1.24	0.001
NM_003910	3014742	BUD31	BUD31 homolog (*S. cerevisiae*)	⇧	1.21	0.005
NM_024099	3375999	C11orf48	chromosome 11 open reading frame 48	⇧	1.27	0.049
NM_014267	3322048	C11orf58	chromosome 11 open reading frame 58	⇧	1.20	7.36E-04
NM_013300	3431553	C12orf24	chromosome 12 open reading frame 24	⇩	1.20	0.049
NM_025113	3512948	C13orf18	chromosome 13 open reading frame 18	⇧	1.47	0.034
NM_017799	3537264	C14orf101	chromosome 14 open reading frame 101	⇩	1.27	3.37E-06
BC030270	3743734	C17orf61	chromosome 17 open reading frame 61	⇧	1.22	0.021
NM_001162530	2330393	C1orf113	chromosome 1 open reading frame 113	⇩	1.21	0.006
NM_020362	2325274	C1orf128	chromosome 1 open reading frame 128	⇧	1.26	7.02E-05
NM_001136494	2460325	C1orf198	chromosome 1 open reading frame 198	⇧	1.22	0.001
BC001508	2332767	C1orf50	chromosome 1 open reading frame 50	⇧	1.29	0.002
NR_026761	2378710	C1orf97	chromosome 1 open reading frame 97	⇧	1.24	0.010
NR_026562	388397	C20orf24	chromosome 20 open reading frame 24	⇧	1.23	0.004
NM_015500	3933331	C2CD2	C2 calcium-dependent domain containing 2	⇩	1.27	4.14E-05
NM_032319	2559494	C2orf7	chromosome 2 open reading frame 7	⇧	1.28	0.017
NM_016474	2611981	C3orf19	chromosome 3 open reading frame 19	⇧	1.21	0.022
NM_018356	2805176	C5orf22	chromosome 5 open reading frame 22	⇧	1.28	0.001
NM_001048249	2858793	C5orf43	chromosome 5 open reading frame 43	⇧	1.27	5.44E-05
NM_199184	2954489	C6orf108	chromosome 6 open reading frame 108	⇧	1.34	3.28E-04
NM_001135674	3096271	C8orf40	chromosome 8 open reading frame 40	⇧	1.26	8.96E-04
NM_033428	3198289	C9orf123	chromosome 9 open reading frame 123	⇧	1.24	0.003
NM_032357	2575980	CCDC115	coiled-coil domain containing 115	⇧	1.21	0.012
NM_015510	3714659	DHRS7B	dehydrogenase/reductase (SDR family) member 7B	⇩	1.20	0.007
NM_207325	3828949	DPY19L3	dpy-19-like 3 (*C. elegans*)	⇩	1.23	0.002

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_024693	3235255	ECHDC3	enoyl CoA hydratase domain containing 3	⇧	1.21	0.002
NM_001015045	2777487	FAM13A	family with sequence similarity 13, member A	⇩	1.30	0.028
NM_018999	3255402	FAM190B	family with sequence similarity 190, member B	⇧	1.20	0.019
NM_030797	2541699	FAM49A	family with sequence similarity 49, member A	⇧	1.33	0.003
NM_004699	3996430	FAM50A	family with sequence similarity 50, member A	⇧	1.22	8.57E-04
AK127183	3110055	FLJ45248	FLJ45248 protein	⇧	1.23	0.001
NR_002188	2437205	GBAP1	glucosidase, beta, acid pseudogene 1	⇩	1.34	0.014
NR_002830	2422227	GEMIN8P4	gem (nuclear organelle) associated protein 8 pseudogene 4	⇧	1.25	0.014
NM_022343	3168385	GLIPR2	GLI pathogenesis-related 2	⇧	1.21	0.018
NM_001001413	3583541	GOLGA6L1	golgin A6 family-like 1	⇧	1.20	0.011
NM_001036645	2341645	HHLA3	HERV-H LTR-associating 3	⇧	1.26	0.014
BC034589	2399620	KIAA0090	KIAA0090	⇩	1.21	0.007
NM_014734	3542145	KIAA0247	KIAA0247	⇩	1.20	0.004
NM_033426	3545311	KIAA1737	KIAA1737	⇧	1.22	0.001
NM_020803	2776998	KLHL8	kelch-like 8 (*Drosophila*)	⇧	1.27	1.94E-06
NM_006014	4027345	LAGE3	L antigen family, member 3	⇧	1.24	3.69E-07
NR_036496	2555252	LOC339803	hypothetical LOC339803	⇧	1.26	0.011
NR_015341	3717452	LRRC37BP1	leucine rich repeat containing 37B pseudogene 1	⇩	1.22	0.001
NM_052940	2336913	LRRC42	leucine rich repeat containing 42	⇧	1.26	3.59E-05
NM_001168465	4002081	MAP7D2	MAP7 domain containing 2	⇩	1.39	0.025
NM_018349	3609592	MCTP2	multiple C2 domains, transmembrane 2	⇩	1.20	0.013
NR_027345	3433466	NCRNA00173	non-protein coding RNA 173	⇩	1.35	0.031
NM_004337	3106276	OSGIN2	oxidative stress induced growth inhibitor family member 2	⇧	1.22	0.035
NM_207351	2662473	PRRT3	proline-rich transmembrane protein 3	⇩	1.25	0.002
NM_017699	2636483	SIDT1	SID1 transmembrane family, member 1	⇩	1.26	2.04E-04
NM_018225	3203382	SMU1	smu-1 suppressor of mec-8 and unc-52 homolog (*C. elegans*)	⇧	1.32	0.011
NM_139015	3474697	SPPL3	signal peptide peptidase 3	⇩	1.20	9.51E-04
NM_003731	3195296	SSNA1	Sjogren syndrome nuclear autoantigen 1	⇧	1.25	0.015
NM_001163436	2780734	TBCK	TBC1 domain containing kinase	⇩	1.23	8.60E-04
NM_198563	2676471	TMEM110	transmembrane protein 110	⇩	1.20	0.011
NM_032928	3194613	TMEM141	transmembrane protein 141	⇧	1.21	0.005
NM_018342	2749380	TMEM144	transmembrane protein 144	⇩	1.28	0.039
NM_017854	3866339	TMEM160	transmembrane protein 160	⇧	1.20	0.007

Table B8: *C9ORF72* Specific Gene List (n=501) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_018004	2633691	TMEM45A	transmembrane protein 45A	⇩	1.30	0.019
NM_014698	2458513	TMEM63A	transmembrane protein 63A	⇩	1.33	8.31E-07
NM_032824	2500615	TMEM87B	transmembrane protein 87B	⇩	1.22	4.61E-04
NM_001193451	3449068	TMTC1	transmembrane and tetratricopeptide repeat containing 1	⇩	1.49	0.034
NM_01167942	3817602	TNFAIP8L1	tumor necrosis factor, alpha-induced protein 8-like 1	⇧	1.27	4.07E-05
NM_182752	2317434	TPRG1L	tumor protein p63 regulated 1-like	⇧	1.21	0.015
NM_181713	2472914	UBXN2A	UBX domain protein 2A	⇧	1.33	8.80E-05
NM_020945	3245783	WDFY4	WDFY family member 4	⇩	1.22	1.44E-04
NM_018268	2863535	WDR41	WD repeat domain 41	⇧	1.22	1.50E-04
NM_018471	2519140	ZC3H15	zinc finger CCCH-type containing 15	⇧	1.20	3.26E-04
NM_153251	3504691	ZDHHC20	zinc finger, DHHC-type containing 20	⇩	1.22	0.002
NM_001011657	4016001	ZMAT1	zinc finger, amtrin-type 1	⇩	1.40	0.018
NM_019103	3956984	ZMAT5	zinc finger, matrin-type 5	⇧	1.26	2.98E-04
NM_005649	2889753	ZNF354A	zinc finger protein 354A	⇧	1.24	0.006

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

RefSeq #	**Transcript**	**Symbol**	**Gene Name**	**Fold**	**p-value**	**Fold**	**p-value**
				C9ORF72		**SALS**	
Apoptosis							
NM_006305	3630912	ANP32A	acidic (leucine-rich) nuclear phosphoprotein 32 family, member A	⇧ 1.26	1.91E-04	⇧ 1.23	2.77E-04
NM_000484	3927226	APP	amyloid beta (A4) precursor protein	⇩ 1.36	0.005	⇩ 1.39	0.001
NM_001114735	3635198	BCL2A1	BCL2-related protein A1	⇧ 1.34	0.007	⇧ 1.26	0.020
NM_001168	3736290	BIRC5	baculoviral IAP repeat-containing 5	⇧ 1.21	0.003	⇧ 1.31	8.64E-06
NM_145018	3342426	C11orf82	chromosome 11 open reading frame 82	⇧ 1.25	0.024	⇧ 1.64	2.72E-07
NM_004346	2796484	CASP3	caspase 3	⇧ 1.42	4.50E-05	⇧ 1.30	8.42E-04
NM_001226	2781693	CASP6	caspase 6	⇧ 1.21	0.011	⇧ 1.32	1.15E-04
AF151902	3823613	FAM32A	family with sequence similarity 32, member A	⇧ 1.25	0.004	⇧ 1.34	6.12E-05
NM_002342	3402444	LTBR	lymphotoxin beta receptor (TNFR superfamily, member 3)	⇩ 1.21	0.037	⇩ 1.20	0.030
NM_003804	2892341	RIPK1	receptor (TNFRSF)-interacting serine-threonine kinase 1	⇧ 1.27	0.003	⇧ 1.21	0.008
NM_024787	3130850	RNF122	ring finger protein 122	⇩ 1.38	7.97E-04	⇩ 1.23	0.016
NM_053055	2435347	THEM4	thioesterase superfamily member 4	⇧ 1.23	0.042	⇧ 1.20	0.045
NM_032027	2415728	TM2D1	TM2 domain containing 1	⇩ 1.25	8.03E-04	⇩ 1.28	8.08E-05
NM_003842	3127703	TNFRSF10B	tumor necrosis factor receptor superfamily, member 10b	⇩ 1.32	1.64E-04	⇩ 1.25	0.001
Autophagy							
NM_052936	3986672	ATG4A	ATG4 autophagy related 4 homolog A (*S. cerevisiae*)	⇧ 1.24	3.02E-04	⇧ 1.24	9.89E-05
NM_001077198	2599955	ATG9A	ATG9 autophagy related 9 homolog A (*S. cerevisiae*)	⇩ 1.28	6.35E-06	⇩ 1.26	8.27E-06
Cell Adhesion/Extracellular Matrix							
NM_001110	3626555	ADAM10	ADAM metallopeptidase domain 10	⇩ 1.22	3.91E-04	⇩ 1.23	6.52E-05
NM_003183	2539821	ADAM17	ADAM metallopeptidase domain 17	⇩ 1.26	0.001	⇩ 1.32	2.72E-05
NM_021723	3011492	ADAM22	ADAM metallopeptidase domain 22	⇩ 1.47	1.39E-05	⇩ 1.32	6.61E-04
NM_007002	3892607	ADRM1	adhesion regulating molecule 1	⇧ 1.24	2.48E-05	⇧ 1.20	9.75E-05
NM_022842	2671728	CDCP1	CUB domain containing protein 1	⇩ 1.66	4.81E-04	⇩ 1.53	0.001
NM_001185072	3012019	CLDN12	claudin 12	⇩ 1.22	0.039	⇩ 1.40	1.75E-04
NM_003798	3219621	CTNNAL1	catenin (cadherin-associated protein), alpha-like 1	⇧ 1.30	0.004	⇧ 1.41	4.76E-05
NM_016938	3377933	EFEMP2	EGF-containing fibulin-like extracellular matrix protein 2	⇩ 1.33	0.002	⇩ 1.35	5.51E-04
NM_138961	3396107	ESAM	endothelial cell adhesion molecule	⇩ 1.35	0.003	⇩ 1.24	0.021

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_001099786	3766621	ICAM2	intracellular adhesion molecule 2	⇩	1.21	0.016	⇩	1.22	0.006
NM_002210	2519229	ITGAV	integrin, alpha V (vitronectin receptor, alpha polypeptide, antigen CD51)	⇩	1.20	0.001	⇩	1.28	7.71E-06
NM_004763	2539765	ITGB1BP1	integrin beta 1 binding protein 1	⇧	1.20	0.016	⇧	1.33	7.71E-06
NM_000212	3724545	ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	⇩	1.52	0.005	⇩	1.53	0.003
NM_002293	2371065	LAMC1	laminin, gamma 1 (formerly LAMB2)	⇩	1.34	0.003	⇩	1.31	0.003
NM_022356	2409004	LEPRE1	leucine proline-enriched proteoglycan (leprecan) 1	⇩	1.30	8.39E-05	⇩	1.29	4.00E-05
NM_002428	3663074	MMP15	matrix metallopeptidase 15 (membrane-inserted)	⇩	1.23	0.043	⇧	1.57	6.22E-06
NM_002508	2462160	NID1	nidogen 1	⇩	1.45	0.009	⇩	1.34	0.027
NM_000285	3859026	PEPD	peptidase D	⇧	1.20	0.008	⇧	1.29	8.90E-05
NM_182943	2699564	PLOD2	procollagen-lysine 1, 2-oxoglutarate 5-dioxygenase 2	⇩	1.69	0.006	⇩	1.57	0.010
NM_001084	3064541	PLOD3	procollagen-lysine 1, 2-oxoglutarate 5-dioxygenase 3	⇩	1.25	6.22E-05	⇩	1.32	1.62E-07
NM_002855	3394488	PVRL1	poliovirus receptor-related 1 (herpesvirus entry mediator C)	⇩	1.23	0.004	⇩	1.21	0.004
NM_001235	3340589	SERPINH1	serpin peptidase inhibitor, clade H (heat shock protein 47), member 1 (collagen binding protein 1)	⇩	1.40	2.90E-04	⇩	1.21	0.024
NM_001099401	3061805	SGCE	sarcoglycan, epsilon	⇩	1.48	1.15E-04	⇩	1.33	0.002

Cellular Response to Stress

NM_000637	3130161	GSR	glutathione reductase	⇧	1.36	2.29E-04	⇧	1.23	0.006
NM_006948	3925439	HSPA13	heat shock protein 70kDa family, member 13	⇩	1.21	0.048	⇩	1.39	3.64E-04
NM_020677	3678147	NMRAL1	NmrA-like family domain containing 1	⇧	1.23	0.007	⇧	1.21	0.006
NM_007262	2318736	PARK7	Parkinson disease (autosomal recessive, early onset) 7	⇧	1.25	6.36E-05	⇧	1.20	3.54E-04
NM_001012961	2333168	SZT2	seizure threshold 2 homolog (mouse)	⇩	1.22	8.40E-04	⇩	1.20	9.92E-04
NM_032731	3707990	TXNDC17	thioredoxin domain containing 7	⇧	1.22	0.019	⇧	1.29	0.001

Cytoskeleton

NM_002313	3307939	ABLIM1	acting binding LIM protein 1	⇧	1.32	3.10E-04	⇧	1.40	3.55E-06
NM_001613	3299504	ACTA2	actin, alpha 2, smooth muscle, aorta	⇧	1.26	0.027	⇧	1.27	0.016
NM_013427	3999568	ARHGAP6	Rho GTPase activating protein 6	⇩	1.25	0.032	⇩	1.32	0.005
NM_005717	2447454	ARPC5	actin related protein 2/3 complex, subunit 5, 16kDa	⇧	1.20	0.009	⇧	1.22	0.003
NM_030978	3188993	ARPC5L	actin related protein 2/3 complex, subunit 5-like	⇧	1.31	3.22E-04	⇧	1.29	2.53E-04
NM_004368	3815399	CNN2	calponin 2	⇧	1.34	0.002	⇧	1.50	6.63E-06
NM_021149	3702547	COTL1	coactosin-like 1 (Dictylostelium)	⇧	1.25	0.044	⇧	1.51	9.13E-05
NM_144666	3318844	DNHD1	dynein heavy chain domain 1	⇩	1.25	3.31E-04	⇩	1.20	0.002
NM_001037494	3434393	DYNLL1	dynein, light chain, LC8-type 1	⇧	1.26	0.020	⇧	1.23	0.023

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_080677	3728509	DYNLL2	dynein, light chain, LC8-type 2	⇧	1.29	8.27E-07	⇧	1.25	4.32E-06
NM_006520	4004819	DYNLT3	dynein, light chain, Tctex-type 3	⇧	1.25	0.024	⇧	1.20	0.041
NM_005103	3396593	FEZ1	fasciculation and elongation protein zeta 1 (zygin I)	⇧	1.59	0.008	⇧	1.49	0.016
NM_201274	3712363	MPRIP	myosin phosphatase Rho interacting protein	⇩	1.20	0.034	⇩	1.22	0.015
NM_032242	2640579	PLXNA1	plexin A1	⇩	1.22	0.007	⇩	1.40	2.30E-06
NM_203401	2402459	STMN1	stathmin 1	⇧	1.21	0.034	⇧	1.42	3.02E-05
NM_001039141	3944922	TRIOBP	TRIO and F-actin binding protein	⇧	1.20	0.003	⇧	1.21	0.001
NM_001070	3721926	TUBG1	tubulin, gamma 1	⇧	1.29	0.005	⇧	1.37	2.68E-04

Development

NM_014913	3795501	ADNP2	ADNP homeobox 2	⇧	1.36	1.02E-04	⇧	1.26	0.001
AY358167	2494579	ARID5A	AT rich interactive domain 5A	⇩	1.25	3.26E-04	⇩	1.22	5.55E-04
NM_004078	2450865	CSRP1	cysteine and glycine-rich protein 1	⇧	1.22	0.008	⇧	1.31	1.20E-04
NM_019074	3590239	DLL4	delta-like 4 (*Drosophil*a)	⇩	1.32	0.012	⇩	1.33	0.006
NM_001197293	3091077	DPYSL2	dihydropyrimidinase-like 2	⇧	1.29	0.042	⇧	1.40	0.004
NM_021783	4011096	EDA2R	ectodysplasin A2 receptor	⇩	1.33	0.003	⇩	1.30	0.003
NM_002146	3761313	HOXB3	homeobox B3	⇩	1.38	3.38E-06	⇩	1.23	0.001
NM_024019	2782267	NEUROG2	neurogenin 2	⇩	1.40	0.009	⇩	1.52	5.26E-04
NM_024408	2431112	NOTCH2	notch 2	⇩	1.28	0.044	⇩	1.42	0.002
NM_020796	2872047	SEMA6A	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6A	⇩	1.52	8.13E-04	⇩	1.33	0.013
NM_000346	3733590	SOX9	SRY (sex determining region Y)-box 9	⇩	1.30	0.008	⇩	1.27	0.009
NM_181642	3590164	SPINT1	serine peptidase inhibitor, Kunitz type 1	⇩	1.37	0.001	⇩	1.26	0.008
NM_001025366	2908179	VEGFA	vascular endothelial growth factor A	⇩	1.28	0.002	⇩	1.29	8.93E-04
NM_025216	2528159	WNT10A	wingless-type MMTV integration site family, member 10A	⇩	1.30	0.008	⇩	1.22	0.027

DNA Damage & Repair

NM_015251	3670668	ATMIN	ATM interactor	⇧	1.45	3.82E-07	⇧	1.24	0.001
NM_020375	3401756	C12orf5	chromosome 12 open reading frame 5	⇧	1.47	0.004	⇧	1.51	0.001
NM_022836	2352743	DCLRE1B	DNA cross-link repair 1B	⇧	1.22	6.15E-04	⇧	1.27	1.96E-05
NM_024086	3687789	DCTPP1	dCTP pyrophosphatase 1	⇧	1.30	4.82E-04	⇧	1.27	7.24E-04
NM_138287	2638962	DTX3L	deltex 3-like (*Drosophila*)	⇧	1.22	0.039	⇧	1.31	0.003
NM_006482	3420854	DYRK2	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 2	⇧	1.33	0.003	⇧	1.22	0.022
NM_005236	3648995	ERCC4	excision repair cross-complementing rodent repair deficiency,	⇧	1.22	0.018	⇧	1.28	0.001

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

			complementation group 4						
NM_130398	2388219	EXO1	exonuclease 1	⇧	1.21	0.027	⇧	1.49	1.85E-06
NM_004111	3333226	FEN1	flap structure-specific endonuclease 1	⇧	1.25	0.007	⇧	1.33	2.25E-04
NM_021218	3221135	INIP	INTS3 and NAPB interacting protein	⇧	1.23	6.79E-04	⇧	1.28	2.71E-05
NM_007349	3080843	PAXIP1	PAX interacting (with transcription-activation domain) protein 1	⇧	1.20	3.03E-04	⇧	1.24	3.99E-06
NM_002592	3896200	PCNA	proliferating cell nuclear antigen	⇧	1.30	2.11E-04	⇧	1.46	3.91E-08
NM_015584	3750625	POLDIP2	polymerase (DNA-directed), delta interacting protein 2	⇧	1.21	4.02E-04	⇧	1.22	4.91E-05
NM_002692	3563395	POLE2	polymerase (DNA directed), epsilon 2 (p59 subunit)	⇧	1.20	0.024	⇧	1.44	2.03E-06
NM_002875	3590086	RAD51	RAD51 homolog (RecA homolog, *E. coli*) (*S. cerevisiae*)	⇧	1.23	0.007	⇧	1.45	8.04E-07
NM_002894	3781429	RBBP8	retinoblastoma binding protein 8	⇧	1.24	0.002	⇧	1.34	1.03E-05
NM_018124	3699044	RFWD3	ring finger and WD repeat domain 3	⇧	1.25	1.22E-04	⇧	1.30	1.95E-06
NM_152308	3648247	RMI2	RMI2, RecQ mediated genome instability 2, homolog (*S. cerevisiae*)	⇧	1.30	0.003	⇧	1.39	7.20E-05
NM_002946	2403301	RPA2	replication protein A2, 32kDa	⇧	1.32	3.35E-04	⇧	1.26	0.001
NM_001010984	2385258	SPRTN	SprT-like N-terminal domain	⇧	1.28	6.47E-04	⇧	1.23	0.002
NM_016614	2945645	TDP2	tyrosyl-DNA phosphodiesterase 2	⇧	1.28	0.003	⇧	1.32	3.53E-04
NM_017858	3630099	TIPIN	TIMELESS interacting protein	⇧	1.22	0.009	⇧	1.50	5.93E-08

DNA Replication & the Cell Cycle

NM_014042	3380996	ANAPC15	anaphase promoting complex subunit 15	⇧	1.32	0.006	⇧	1.38	6.01E-04
NM_006401	3181417	ANP32B	acidic (leucine-rich) nuclear phosphoprotein 32 family, member B	⇧	1.32	0.032	⇧	1.27	0.048
NM_024037	2402416	AUNIP	aurora kinase A and ninein interacting protein	⇧	1.20	1.20E-04	⇧	1.20	3.69E-05
NM_001238	3828112	CCNE1	cyclin E1	⇧	1.30	0.003	⇧	1.40	4.06E-05
NM_001789	2673085	CDC25A	cell division cycle 25 homolog A (*S. pombe*)	⇧	1.24	0.004	⇧	1.35	2.93E-05
NM_080668	3377423	CDCA5	cell division cycle associated 5	⇧	1.20	0.035	⇧	1.47	2.85E-06
NM_001786	3248289	CDK1	cyclin-dependent kinase 1	⇧	1.24	0.039	⇧	1.31	0.005
NM_004642	3476097	CDK2AP1	cyclin-dependent kinase 2 associated protein 1	⇧	1.24	0.013	⇧	1.29	0.002
NM_001195132	3201437	CDKN2A	cyclin-dependent kinase inhibitor 2A (melanoma, p16, inhibits CDK4)	⇧	1.24	0.005	⇧	1.25	0.002
NM_022909	2813442	CENPH	centromere protein H	⇧	1.35	4.95E-04	⇧	1.45	5.06E-06
NM_001025248	3593147	DUT	deoxyuridine triphosphatase	⇧	1.30	0.031	⇧	1.51	3.35E-04
NM_032231	3628923	FAM96A	family with sequence similarity 96, member A	⇧	1.30	0.003	⇧	1.24	0.009
NM_023037	3484497	FRY	furry homolog (*Drosophila*)	⇩	1.33	0.048	⇩	1.44	0.008
NM_021067	3880827	GINS1	GINS complex subunit 1 (Psf1 homolog)	⇧	1.43	3.33E-04	⇧	1.57	1.66E-06
NM_016095	3703112	GINS2	GINS complex subunit 2 (Psf2 homolog)	⇧	1.29	0.006	⇧	1.36	4.25E-04

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_001126129	3663228	GINS3	GINS complex subunit 3 (PSf3 homolog)	⇧	1.28	6.47E-04	⇧	1.37	6.07E-06
NM_015895	2898597	GMNN	geminin, DNA replication inhibitor	⇧	1.21	0.034	⇧	1.20	0.028
NM_018097	3591044	HAUS2	HAUS augmin-like complex, subunit 2	⇧	1.25	3.35E-04	⇧	1.22	7.28E-04
NM_016073	3636522	HDGFRP3	hepatoma-derived growth factor, related protein 3	⇧	1.49	0.002	⇧	2.19	3.58E-10
NM_194282	2775858	LIN54	lin-54 homolog (*C. elegans*)	⇧	1.23	2.74E-04	⇧	1.25	2.19E-05
NM_001003690	2908144	MAD2L1BP	MAD2L1 binding protein	⇧	1.27	7.94E-05	⇧	1.25	8.38E-05
NM_005914	3097152	MCM4	minichromosome maintenance complex component 4	⇧	1.21	0.019	⇧	1.39	3.71E-05
NM_032485	3875195	MCM8	minichromosome maintenance complex component 8	⇧	1.29	1.93E-04	⇧	1.29	4.86E-05
NM_024039	3707759	MIS12	MIS12, MIND kinetochore complex component, homolog (*S. pombe*)	⇧	1.26	0.011	⇧	1.24	0.012
NM_024629	2796510	MLF1IP	MLF1 interacting protein	⇧	1.27	0.023	⇧	1.57	6.22E-06
NM_002480	2334404	NASP	nuclear autoantigenic sperm protein (histone-binding)	⇧	1.20	0.023	⇧	1.33	2.57E-04
NM_006600	2326799	NUDC	nuclear distribution gene C homolog (*A. nidulans*)	⇧	1.32	5.44E-04	⇧	1.39	1.49E-05
NM_018492	3129149	PBK	PDZ binding kinase	⇧	1.21	0.022	⇧	1.35	1.36E-04
NM_002764	3986514	PRPS1	phosphoribosyl pyrophosphate synthetase 1	⇧	1.23	0.013	⇧	1.36	9.54E-05
NM_001039091	3969047	PRPS2	phosphoribosyl pyrophosphate synthetase 2	⇧	1.26	9.64E-05	⇧	1.34	2.63E-07
NM_002895	3904747	RBL1	retinoblastoma-like 1 (p107)	⇧	1.20	0.008	⇧	1.26	4.76E-04
NM_181471	3056414	RFC2	replication factor C (activator 1) 2, 40kDa	⇧	1.28	8.26E-04	⇧	1.34	2.33E-05
NM_002915	3485074	RFC3	replication factor C (activator 1) 3, 38kDa	⇧	1.21	0.004	⇧	1.39	4.19E-07
NM_001165931	2469252	RRM2	ribonucleotide reductase M2	⇧	1.23	0.043	⇧	1.55	6.07E-06
NM_001039535	3788049	SKA1	spindle and kinetochore associated complex 1	⇧	1.24	0.029	⇧	1.33	0.002
NM_182513	3850660	SPC24	SPC24, NDC80 kinetochore complex component, homolog (*S. cerevisiae*)	⇧	1.31	0.011	⇧	1.53	2.98E-05
NM_005862	2696802	STAG1	stromal antigen 1	⇧	1.20	0.019	⇧	1.28	7.71E-04
Immune Response & Inflammation									
NM_001145009	2899372	BTN3A1	butyrophilin, subfamily 3, member A1	⇩	1.20	0.001	⇩	1.25	3.48E-05
NM_001197247	2899298	BTN3A2	butyrophilin, subfamily 3, member A2	⇩	1.41	0.001	⇩	1.36	0.007
NM_006994	2899413	BTN3A3	butyrophilin, subfamily 3, member A3	⇩	1.32	6.35E-06	⇩	1.28	1.37E-05
NM_000064	3848039	C3	complement component 3	⇩	1.31	0.017	⇩	1.30	0.011
NM_001771	3830353	CD22	CD22 molecule	⇩	1.31	0.005	⇩	1.31	0.002
NM_016382	2440385	CD244	CD244 molecule, natural killer cell receptor 2B4	⇩	2.05	8.73E-04	⇩	1.75	0.005
NM_014143	3161082	CD274	CD274 molecule	⇩	1.27	0.014	⇩	1.38	5.69E-04
NM_007261	3734379	CD300A	CD300a molecule	⇩	1.29	2.28E-04	⇩	1.24	5.83E-04
NM_000616	3402786	CD4	CD4 molecule	⇩	1.37	0.008	⇩	1.31	0.016

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_001250	3887302	CD40	CD40 molecule, TNF receptor superfamily member 5	⇩	1.32	0.001	⇩	1.37	6.66E-05
NM_001114752	2377229	CD55	CD55 molecule, decay accelerating factor for complement (Cromer blood group)	⇩	1.23	0.006	⇩	1.38	7.02E-06
NM_203330	3368707	CD59	CD59 molecule, complement regulatory protein	⇩	1.20	0.004	⇩	1.27	8.89E-05
NM_000626	3766533	CD79B	CD79b molecule, immunoglobulin-associated beta	⇩	1.29	0.007	⇩	1.20	0.032
NM_002621	4007164	CFP	complement factor properdin	⇩	1.28	0.043	⇩	1.41	0.003
NM_001276	2451593	CHI3L1	chitinase 3-like 1 (cartilage glycoprotein-39)	⇩	1.79	0.008	⇩	1.89	0.002
NM_005127	3443891	CLEC2B	C-type lectin domain family 2, member B	⇩	1.41	0.015	⇩	1.57	6.47E-04
NM_001935	2584018	DPP4	dipeptidyl-peptidase 4	⇩	1.45	0.012	⇩	1.51	0.003
NM_000605	3201319	IFNA2	interferon, alpha 2	⇩	1.48	0.013	⇩	1.60	0.001
NM_001562	3391255	IL18	interleukin 18 (interferon-gamma-inducing factor)	⇧	1.29	0.017	⇧	1.34	0.003
NM_002286	3402757	LAG3	LTV1 homolog (*S. cerevisiae*)	⇩	1.41	0.002	⇩	1.29	0.014
NM_005356	2328841	LCK	lymphocyte-specific protein tyrosine tyrosine kinase	⇧	1.25	0.008	⇧	1.46	3.48E-06
NM_052925	3841474	LENG8	leukocyte receptor cluster (LRC) member 8	⇩	1.23	0.002	⇩	1.24	4.77E-04
NM_138441	2960872	MB21D1	Mab-21 domain containing 1	⇧	1.26	0.002	⇧	1.20	0.008
NM_001172567	2617563	MYD88	myeloid differentiation primary response gene (88)	⇧	1.22	0.004	⇧	1.25	5.04E-04
NM_00136022	3529908	NFATC4	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 4	⇩	1.27	0.002	⇩	1.24	0.003
NM_022162	3660175	NOD2	nucleotide-binding oligomerization domain containing 2	⇩	1.21	0.001	⇩	1.20	9.69E-04
BC008975	3526425	PCID2	PCI domain containing 2	⇩	1.38	7.87E-04	⇩	1.62	1.25E-07
NM_001184714	2440258	SLAMF6	SLAM family member 6	⇩	1.25	0.002	⇩	1.28	2.22E-04
NM_030956	2766192	TLR10	toll-like receptor 10	⇩	1.37	7.79E-05	⇩	1.34	7.28E-05
NM_012452	3747522	TNFRSF13B	tumor necrosis factor receptor superfamily, member 13B	⇩	1.36	0.002	⇩	1.33	0.002
AK303468	2392584	TNFRSF14	tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator)	⇩	1.23	0.011	⇩	1.36	4.53E-05

Ion Binding

NM_017649	3261971	CNNM2	cyclin M2	⇩	1.20	0.003	⇩	1.22	5.18E-04
NM_152516	2484752	COMMD1	copper metabolism (Murr1) domain containing 1	⇧	1.33	4.78E-05	⇧	1.20	0.003
NM_024843	2515240	CYBRD1	cytochrome b reductase 1	⇩	1.22	0.048	⇩	1.34	0.002
NM_002032	3375648	FTH1	ferritin, heavy polypeptide 1	⇩	1.29	0.026	⇩	1.41	0.002
NM_005929	2713111	MFI2	antigen p97 (melanoma associated) identified by monoclonal antibodies 133.2 and 96.5)	⇩	1.32	7.19E-04	⇩	1.29	9.32E-04
NM_012449	3011838	STEAP1	six transmembrane epithelial antigen of the prostate 1	⇩	1.29	0.013	⇩	1.32	0.004

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_152999	3011861	STEAP2	six transmembrane epithelial antigen of the prostate 2	⇩	1.40	0.025	⇩	1.79	5.72E-05

Membrane Trafficking

NM_007189	3079463	ABCF2	ATP-binding cassette, sub-family F (GCN20), member 2	⇧	1.20	0.014	⇧	1.26	9.48E-04
NM_001677	2366422	ATP1B1	ATPase, Na+/K+ transporting, beta 1 polypeptide	⇩	1.66	7.06E-04	⇩	1.37	0.021
NM_001001396	2375706	ATP2B4	ATPase, Ca++ transporting, plasma membrane 4	⇩	1.39	0.020	⇩	1.47	0.004
NM_000052	3982423	ATP7A	ATPase, Cu++ transporting, alpha polypeptide	⇩	1.28	0.011	⇩	1.41	1.58E-04
NM_001286	2320472	CLCN6	chloride channel 6	⇩	1.32	4.73E-05	⇩	1.23	7.09E-04
NM_016433	3470964	GLTP	glyolipid transfer protein	⇧	1.23	0.004	⇧	1.21	0.004
NM_003740	2952834	KCNK5	potassium channel, subfamily K, member 5	⇩	1.26	0.020	⇩	1.42	2.33E-04
NM_153369	2921456	KIAA1919	KIAA1919	⇩	1.25	5.47E-04	⇩	1.27	1.01E-04
NM_001146069	2758043	MFSD10	major facilitator superfamily domain containing 10	⇩	1.21	3.98E-04	⇩	1.21	1.57E-04
NM_001126340	3016768	ORAI2	ORAI calcium release-activated calcium modulator 2	⇧	1.23	0.013	⇧	1.24	0.006
NM_022068	3798829	PIEZO2	piezo-type mechanosensitive ion channel component 2	⇩	1.77	0.027	⇩	1.64	0.037
NM_001174129	3454576	SLC11A2	solute carrier family 11 (proton-coupled divalent metal ion transporters) member 2	⇩	1.24	0.004	⇩	1.43	1.25E-06
NM_001046	2827525	SLC12A2	solute carrier family 12 (sodium/potassium/chloride transporters) member 2	⇩	1.26	0.008	⇩	1.20	0.023
NM_021082	2638728	SLC15A2	solute carrier family 15 (H+/peptide transporter) member 2SLC12A2	⇩	1.36	0.010	⇩	1.27	0.031
NM_001042422	3738629	SLC16A3	solute carrier family 16, member 3 (monocarboxylic acid transporter 4)	⇩	1.41	2.93E-06	⇩	1.36	5.03E-06
NM_012434	2960955	SLC17A5	solute carrier family 17 (anion/sugar transporter), member 5	⇩	1.21	0.010	⇩	1.28	2.94E-04
NM_001039355	3579501	SLC25A29	solute carrier family 25, member 29	⇩	1.32	0.007	⇩	1.31	0.005
NM_032315	2319340	SLC25A33	solute carrier family 25, member 33SLC17A5	⇧	1.57	3.19E-04	⇧	1.29	0.028
NM_00104647	2645275	SLC25A36	solute carrier family 25, member 36	⇩	1.22	0.012	⇩	1.29	4.68E-04
NM_016612	3090006	SLC25A37	solute carrier family 25, member 37	⇩	1.23	0.033	⇩	1.21	0.036
NM_006516	2409104	SLC2A1	solute carrier family 2 (facilitated glucose transporter), member 1	⇩	1.29	0.04	⇩	1.23	0.014
NM_006931	3442854	SLC2A3	solute carrier family 2 (facilitated glucose transporter), member 3	⇩	1.35	9.02E-04	⇩	1.33	6.90E-04
NM_006416	2916345	SLC35A1	solute carrier family 35 (CMP-sialic acid transporter), member 1	⇩	1.36	1.07E-04	⇩	1.24	0.003
NM_015139	2417095	SLC35D1	solute carrier family 35 (UDP-glucuronic acid/UDP-N-acetylgalactosamine dual transporter), member D1	⇩	1.21	0.036	⇩	1.21	0.024
NM_012319	3804195	SLC39A6	solute carrier family 39 (zinc transporter), member 6	⇩	1.22	0.004	⇩	1.23	0.001
NM_033102	2452615	SLC45A3	solute carrier family 45, member 3	⇩	1.22	0.002	⇩	1.20	0.002
NM_001098484	2730746	SLC4A4	solute carrier family 4, sodium bicarbonate cotransporter, member 4	⇩	1.40	0.018	⇩	1.33	0.032
NM_003615	2666904	SLC4A7	solute carrier family 4, sodium bicarbonate cotransporter, member 7	⇩	1.21	0.004	⇩	1.20	0.003

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_006933	3919033	SLC5A3	solute carrier family 5 (sodium/myo-inositol cotransporter), member 3	⇩	1.28	3.54E-06	⇩	1.30	1.73E-07
NM_016354	3892812	SLCO4A1	solute carrier organic anion transporter family member 4A1	⇩	1.32	0.002	⇩	1.20	0.028
NM_030958	3139580	SLC5A1	solute carrier organic anion transporter family member 5A1	⇩	1.41	2.30E-04	⇩	1.33	0.001
NM_003156	3317915	STIM1	stromal interaction molecule 1	⇩	1.43	1.32E-08	⇩	1.31	2.76E-06
NM_001169118	2722377	STIM2	stromal interaction molecule 2	⇩	1.23	0.008	⇩	1.21	0.007
NM_183240	2502842	TMEM37	transmembrane protein 37	⇩	1.32	0.026	⇩	1.29	0.027
NM_001143819	3432678	TPCN1	two pore segment channel 1	⇩	1.26	1.54E-05	⇩	1.22	4.06E-05
NM_016113	3712062	TRPV2	transient receptor potential cation channel, subfamily V, member 2	⇩	1.28	2.54E-04	⇩	1.25	3.46E-04
Metabolism									
NM_016006	2619761	ABHD5	abhydrolase domain containing 5	⇧	1.34	7.33E-04	⇧	1.26	9.84E-04
NM_032169	2695648	ACAD11	acyl-CoA dehydrogenase family, member 11	⇩	1.22	0.002	⇩	1.26	2.31E-04
NM_032592	3328349	ACCS	aminocyclopropane-1-carobxylate synthase homolog (*Arabidopsis*) (non-functional)	⇩	1.42	2.23E-05	⇩	1.33	1.86E-04
NM_00160094	2898562	ACOT13	acyl-CoA thioesterase 13	⇧	1.30	0.001	⇧	1.20	0.014
NM_018269	2538600	ADI1	acireductone dioxygenase 1	⇧	1.32	0.006	⇧	1.34	0.002
NM_020133	2983030	AGPAT4	1-acylglycerol-3-phosphate O-acyltransferase 4 (lysophosphatidic acid acyltransferase, delta)	⇩	1.23	5.62E-04	⇩	1.22	3.93E-04
NM_001628	3073981	AKR1B1	aldo-keto reductase family 1, member B1 (aldose reductase)	⇧	1.27	0.020	⇧	1.25	0.019
NM_000692	3169331	ALDH1B1	aldehyde dehydrogenase 1 family, member B1	⇧	1.25	0.016	⇧	1.23	0.015
NM_000712	2999544	BLVRA	biliverdin reductase A	⇧	1.24	0.009	⇧	1.24	0.005
NM_078476	2899437	BTN2A1	butyrophilin, subfamily 2, member A1	⇩	1.29	3.78E-05	⇩	1.20	0.001
NM_001757	3919785	CBR1	carbonyl reductase 1	⇧	1.21	0.028	⇧	1.31	0.001
NM_022766	3964154	CERK	ceramide kinase	⇧	1.25	0.001	⇧	1.25	4.91E-04
NM_203463	2514122	CERS6	ceramide synthase 6	⇩	1.23	0.011	⇩	1.21	0.012
NM_004820	3138204	CYP7B1	cytochrome P450, family 7, subfamily B, polypeptide 1	⇩	1.39	0.026	⇩	1.34	0.036
NM_001360	3380697	DHCR7	dehydrocholesterol reductase	⇩	1.28	0.002	⇩	1.20	0.012
NM_006209	3150579	ENPP2	ectonucleotide pyrophosphatase/phosphodiesterase 2	⇩	1.59	0.005	⇩	1.44	0.018
NM_032020	2977510	FUCA2	fucosidase, alpha-L-2, plasma	⇩	1.22	0.030	⇩	1.20	0.030
NM_000153	3575103	GALC	galactosylceramidease	⇩	1.21	0.005	⇩	1.29	9.93E-05
NM_001498	2957700	GCLC	glutamate-cysteine ligase, catalytic subunit	⇧	1.23	0.001	⇧	1.22	9.11E-04
NM_024051	3044129	GGCT	gamma-glutamylcyclotransferase	⇧	1.21	0.023	⇧	1.25	0.003
NM_000404	2668205	GLB1	galactosidase, beta 1	⇩	1.22	0.020	⇩	1.27	0.003

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_000181	3053691	GUSB	glucuronidase, beta	⇩	1.24	0.001	⇩	1.25	4.99E-04
NM_004130	2647154	GYG1	Glycogenin 1	⇧	1.36	0.002	⇧	1.38	4.99E-04
NM_152740	3043165	HIBADH	3-hydroxyisobutyrate dehydrogenase	⇧	1.29	0.001	⇧	1.21	0.009
NM_001127205	3646199	HMOX2	heme oxygenase (decycling) 2	⇧	1.23	0.003	⇧	1.27	2.41E-04
NM_031207	2409368	HYI	hydroxypyruvate isomerase (putative)	⇧	1.21	0.043	⇧	1.24	0.012
NM_016133	2502424	INSIG2	insulin induced gene 2	⇩	1.34	0.004	⇩	1.44	1.44E-04
NM_006033	3787855	LIPG	lipase, endothelial	⇩	1.72	2.11E-04	⇩	1.56	9.85E-04
NM_014873	2454485	LPGAT1	lysophosphatidylglycerol acyltransferase 1	⇩	1.30	0.025	⇩	1.30	0.016
NM_004897	3256560	MINPP1	multiple inositol-polyphosphate phosphatase 1	⇩	1.32	6.65E-04	⇩	1.25	0.003
NM_006441	3635125	MTHFS	5,10-methenyltetrahydrofolate synthetase (5-formyltetrahydrofolate cyclo-ligase)	⇧	1.28	0.009	⇧	1.32	0.002
NM_002539	2540157	ODC1	ornithine decarboxylase 1	⇧	1.25	9.26E-04	⇧	1.38	3.83E-07
NM_015900	2638077	PLA1A	phospholipase A1 member A	⇩	1.39	0.013	⇩	1.45	0.002
NM_001031689	3202171	PLAA	phospholipase A2-activating protein	⇧	1.21	0.003	⇧	1.28	4.89E-05
NM_002662	2705445	PLD1	phospholipase D1, phosphatidylcholine-specific	⇩	1.60	0.009	⇩	1.45	0.024
NM_016026	3569401	RDH11	retinol dehydrogenase 11 (all-trans/9-cis/11-cis)	⇩	1.20	0.007	⇩	1.20	0.004
NM_144563	2492938	RPIA	ribose 5-phosphate isomerase A	⇧	1.24	0.002	⇧	1.20	0.004
NM_006745	2750594	SC4MOL	sterol-C4-methyl oxidase-like	⇩	1.20	0.016	⇩	1.21	0.005
NM_006918	3352904	SC5DL	sterol-C5-desaturase (ERG3 delta-5-desaturase homolog, *S. cerevisiae*)	⇩	1.21	0.008	⇩	1.20	0.008
NM_004169	3748323	SHMT1	serine hydroxymethyltransferase 1 (soluble)	⇧	1.28	0.011	⇧	1.36	7.94E-04
NM_003132	2396461	SRM	spermidine synthase	⇧	1.37	7.38E-06	⇧	1.21	0.002
NM_000367	2944025	TPMT	thiopurine S-methyltransferase	⇧	1.64	8.09E-05	⇧	1.50	4.74E-04
NR_033437	2639874	UMPS	uridine monophosphate synthetase	⇧	1.23	0.005	⇧	1.26	9.06E-04
NR_036510	2334279	UROD	uroporphyrinogen decarboxylase	⇧	1.31	2.28E-05	⇧	1.21	0.001

Mitochondrion & the Respiratory Electron Transport Chain

NM_003488	3728097	AKAP1	A kinase (PRKA) anchor protein 1	⇩	1.21	0.008	⇩	1.24	9.43E-04
NM_001001937	3806253	ATP5A1	ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1, cardiac muscle	⇧	1.31	5.92E-04	⇧	1.28	6.44E-04
NM_005175	3725456	ATP5G1	ATP synthase, H+ transporting, mitochondrial Fo complex, subunit C1 (subunit 9)	⇧	1.21	5.14E-04	⇧	1.23	8.17E-05
NM_025147	2521446	COQ10B	coenzyme Q10 homolog B (*S. cerevisiae*)	⇧	1.26	3.21E-04	⇧	1.23	3.99E-04
NM_017421	2966232	COQ3	coenzyme Q3 homolog, methyltransferase (*S. cerevisiae*)	⇧	1.20	5.42E-04	⇧	1.27	2.06E-06

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_004374	3146433	COX6C	cytochrome c oxidase subunit Vic	⇧	1.26	0.033	⇧	1.29	0.012
NM_012062	3410695	DNM1L	dynamin 1-like	⇧	1.36	0.004	⇧	1.44	2.88E-04
AY568085	2950798	MNF1	mitochondrial nucleoid factor 1	⇧	1.22	0.018	⇧	1.33	3.09E-04
NM_001099286	2975655	MTFR2	mitochondrial fission regulator 2	⇧	1.27	0.007	⇧	1.26	0.005
NR_027405	2489172	MTHFD2	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase	⇧	1.23	0.004	⇧	1.26	6.50E-04
NM_014222	3224197	NDUFA8	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 8, 19kDa	⇧	1.34	7.20E-04	⇧	1.29	0.001
NM_016013	3619991	NDUFAF1	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, assembly factor 1	⇧	1.22	0.032	⇧	1.38	2.55E-04
NM_004548	3644220	NDUFB10	NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 10, 22kDa	⇧	1.25	0.006	⇧	1.22	0.008
NM_002493	3203162	NDUFB6	NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 6, 17kDa	⇧	1.28	0.013	⇧	1.32	0.003
NM_004552	2331178	NDUFS5	NADH dehydrogenase (ubiquinone) Fe-S protein 5, 15kDa (NADH-coenzyme Q reductase)	⇧	1.31	0.003	⇧	1.23	0.015
Neurotransmission									
NM_032810	3299255	ATAD1	ATPase family, AAA domain containing 1	⇩	1.30	1.61E-05	⇩	1.30	3.21E-06
NM_033133	3721548	CNP	2',3'-cyclic nucleotide 3' phosphodiesterase	⇧	1.24	0.005	⇧	1.22	0.005
NM_031412	3404636	GABARAPL1	GABA(A) receptor-associated protein like 1	⇧	1.43	0.005	⇧	1.41	0.003
NM_005467	3344142	NAALAD2	N-acetylated alpha-linked acidic dipeptidase 2	⇩	1.36	0.023	⇩	1.40	0.008
NM_006228	3091699	PNOC	prepronociceptin	⇧	1.27	0.009	⇧	1.20	0.028
NM_014849	2434139	SV2A	synaptic vesicle glycoprotein 2A	⇩	1.49	7.63E-04	⇩	1.39	0.003
Nucleosome									
NM_018154	3852565	ASF1B	ASF1 anti-silencing function 1 homolog B (*S. cerevisiae*)	⇧	1.31	0.002	⇧	1.38	6.13E-05
NM_005441	3920003	CHAF1B	chromatin assembly factor 1, subunit B (p60)	⇧	1.24	0.004	⇧	1.43	5.36E-07
NM_017444	3118451	CHRAC1	chromatin accessibility complex 1	⇧	1.26	0.005	⇧	1.25	0.003
NM_005325	2946194	HIST1H1A	histone cluster 1, H1a	⇧	1.37	0.026	⇧	1.65	1.95E-04
NM_080596	2899772	HIST1H2AH	histone cluster 1, H2ah	⇧	1.37	0.008	⇧	1.29	0.020
NM_021018	2946364	HIST1H3F	histone cluster 1, H3f	⇧	1.34	0.021	⇧	1.33	0.017
NM_003538	2899095	HIST1H4A	histone cluster 1, H4a	⇧	1.51	0.007	⇧	1.32	0.048
NM_003544	2946208	HIST1H4B	histone cluster 1, H4b	⇧	1.35	0.019	⇧	1.38	0.007
NM_175055	2384268	HIST3H2BB	histone cluster 3, H2bb	⇧	1.30	0.038	⇧	1.27	0.043
Protein Processing									
NM_018089	2528347	ANKZF1	ankyrin repeat and zinc finger domain containing 1	⇩	1.26	5.00E-04	⇩	1.34	2.45E-06

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_001663	3535000	ARF6	ADP-ribosylation factor 6	⇧	1.31	5.27E-05	⇧	1.21	0.002
NM_198150	2820865	ARSK	arylsulfatase family, member K	⇩	1.59	2.39E-05	⇩	1.54	2.52E-05
NM_004317	3821847	ASNA1	arsA arsenite transporter, ATP-binding, homolog 1 (bacterial)	⇧	1.22	6.46E-04	⇧	1.26	2.24E-05
NM_004775	3803120	B4GALT6	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 6	⇩	1.29	7.99E-04	⇩	1.23	0.003
NM_004282	2911372	BAG2	BCL2-associated athanogene 2	⇧	1.49	9.47E-04	⇧	1.56	1.02E-04
NM_005868	3061651	BET1	blocked early in transport 1 homolog (*S. cerevisiae*)	⇧	1.20	0.026	⇧	1.23	0.006
NM_001487	3416909	BLOC1S1	biogenesis of lysosomal organelles complex-1, subunit 1	⇧	1.39	2.24E-04	⇧	1.24	0.008
NM_025238	3636470	BTBD1	BTB (POZ) domain containing 1	⇧	1.20	1.17E-04	⇧	1.21	3.32E-05
NM_001219	3023060	CALU	calmodulin 1 (phosphorylase kinase, delta)	⇩	1.21	0.033	⇩	1.26	0.007
NM_001762	3003193	CCT6A	chaperonin containing TCP1, subunit 6A (zeta 1)	⇧	1.24	0.020	⇧	1.21	0.023
NM_014169	3557947	CHMP4A	charged multivesicular body protein 4A	⇧	1.42	2.94E-05	⇧	1.36	8.71E-05
NM_018590	3243908	CSGALNACT2	chondroitin sulfate N-acetylgalactosaminyltransferase 2	⇩	1.26	0.002	⇩	1.27	5.81E-04
NM_015397	3203855	DCAF12	DDB1 and CUL4 associated factor 12	⇧	1.24	2.14E-04	⇧	1.24	4.74E-05
NM_003677	3435490	DENR	density-regulated protein	⇧	1.30	0.002	⇧	1.31	5.76E-04
NM_001539	3166718	DNAJA1	DnaJ (Hsp40) homolog, subfamily A, member 1	⇧	1.30	0.019	⇧	1.36	0.004
NM_017629	2330002	EIF2C4	eukaryotic translation initiation factor 2C, 4	⇧	1.22	0.002	⇧	1.20	0.002
NM_003758	3591963	EIF3J	eukaryotic translation initiation factor, subunit J	⇧	1.23	0.012	⇧	1.24	0.006
NM_022170	3008144	EIF4H	eukaryotic translation initiation factor 4H	⇧	1.31	0.005	⇧	1.38	4.23E-04
NM_006459	3303255	ERLIN1	ER lipid raft associated 1	⇩	1.28	0.003	⇩	1.22	0.009
NM_004730	2877465	ETF1	eukaryotic translation termination factor 1	⇧	1.27	6.75E-05	⇧	1.21	7.48E-04
NM_001439	2425400	EXTL2	exostoses (multiple)-like 2	⇩	1.53	3.40E-05	⇩	1.37	8.07E-04
NM_024619	3739108	FN3KRP	fructosamine 3 kinase related protein	⇧	1.24	7.73E-04	⇧	1.33	4.58E-06
NMN_004481	2384788	GALNT2	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyl transferase 2 (GalNAc-T2)	⇩	1.23	5.30E-05	⇩	1.21	6.58E-05
NM_198066	3564872	GNPNAT1	glucosamine-phosphate N-acetyltransferase 1	⇧	1.29	0.004	⇧	1.33	5.93E-04
NM_016548	3212848	GOLM1	golgi membrane protein 1	⇩	1.51	0.008	⇩	1.45	0.010
NM_016072	3407824	GOLT1B	golgi transport 1B	⇩	1.21	0.021	⇩	1.40	1.56E-05
NM_004466	3496409	GPC5	glypican 5	⇩	1.46	0.004	⇩	1.34	0.014
NM_001545	3734575	ICT1	immature colon carcinoma transcript 1	⇧	1.22	0.005	⇧	1.32	4.28E-05
NM_006547	2992863	IGF2BP3	insulin-like growth factor 2 mRNA binding protein 3	⇧	1.35	1.85E-05	⇧	1.26	3.77E-04
NM_018439	3782166	IMPACT	impact homolog (mouse)	⇧	1.27	0.022	⇧	1.32	0.005
NM_030980	2438482	ISG20L2	interferon stimulated exonuclease gene 20kDa-like 2	⇧	1.28	6.09E-05	⇧	1.34	6.43E-07
NM_002268	2703217	KPNA4	karyopherin alpha 4 (importin alpha 3)	⇧	1.27	1.79E-05	⇧	1.20	3.75E-04

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted $p<0.05$, FC $\geq \pm1.20$]

NM_001142292	2565484	LMAN2L	lectin, mannose-binding 2-like	⇩	1.23	0.011	⇩	1.21	0.012
NM_144703	3892452	LSM14B	LSM14B, SCD6 homolog B (*S. cerevisiae*)	⇧	1.35	0.010	⇧	1.28	0.025
NM_006122	3608466	MAN2A2	mannosidase, alpha, class 2A, member 2	⇩	1.26	6.07E-05	⇩	1.26	1.76E-05
NM_005908	2779897	MANBA	mannosidase, beta A, lysosomal	⇩	1.31	3.15E-04	⇩	1.37	6.74E-06
NM_014730	3434525	MLEC	malectin	⇩	1.20	2.99E-04	⇩	1.23	1.07E-05
NM_006302	2560122	MOGS	mannosyl-oligosaccharide glucosidase	⇩	1.21	0.004	⇩	1.25	2.97E-04
NM_014161	2934167	MRPL18	mitochondrial ribosomal protein L18	⇧	1.22	0.005	⇧	1.28	1.85E-04
NM_014180	2836886	MRPL22	mitochondrial ribosomal protein L22	⇧	1.22	0.014	⇧	1.31	4.23E-04
NM_032477	3195344	MRPL41	mitochondrial ribosomal protein L41	⇧	1.43	5.85E-04	⇧	1.27	0.014
NM_020409	2706985	MRPL47	mitochondrial ribosomal protein L47	⇧	1.34	0.003	⇧	1.26	0.011
NM_016497	3441955	MRPL51	mitochondrial ribosomal protein L51	⇧	1.22	1.80E-05	⇧	1.23	1.97E-06
NM_016183	2323559	MRTO4	mRNA turnover 4 homolog (*S. cerevisiae*)	⇧	1.36	9.11E-04	⇧	1.22	0.022
NM_033049	2692883	MUC13	mucin 13, cell surface associated	⇩	1.49	0.025	⇩	1.59	0.002
NM_025146	2689208	NAA50	N(alpha)-acetyltransferase 50, NatE catalytic subunit	⇧	1.23	0.002	⇧	1.28	1.12E-04
NM_016101	3666686	NIP7	nuclear import 7 homolog (*S. cerevisiae*)	⇧	1.34	6.11E-05	⇧	1.32	4.53E-05
NM_006178	3724197	NSF	ethylmaleimide-sensitive factor	⇧	1.20	0.046	⇧	1.36	3.83E-04
NM_002484	3647956	NUBP1	nucleotide binding protein 1 (MinD homolog, *E. coli*)	⇧	1.21	0.003	⇧	1.28	4.28E-05
NM_000917	3294159	P4HA1	prolyl 4-hydroxylase, alpha polypeptide I	⇩	1.25	0.002	⇩	1.31	4.99E-05
NM_004199	2875193	P4HA2	prolyl 4-hydroxylase, alpha polypeptide II	⇩	1.26	0.033	⇩	1.38	0.002
NM_000919	2822215	PAM	peptidylglycine alpha-amidating monooxygenase	⇩	1.27	2.69E-05	⇩	1.26	1.73E-05
NM_001146106	2692060	PARP9	poly (ADP-ribose) polymerase family, member 9	⇧	1.32	0.005	⇧	1.24	0.023
NM_024989	2593407	PGAP1	post-GPI attachment to proteins 1	⇩	1.24	0.011	⇩	1.41	2.14E-05
NM_173074	2551690	PIGF	phosphatidylinositol glycan anchor biosynthesis, class F	⇩	1.23	0.034	⇩	1.45	7.08E-05
NM_080476	3903481	PIGU	phosphatidylinositol glycan anchor biosynthesis, class U	⇩	1.29	0.011	⇩	1.22	0.035
NM_138717	2903075	PPT2	palmitoyl-protein thioesterase 2	⇩	1.22	4.74E-04	⇩	1.30	1.37E-06
NM_018137	2349848	PRMT6	protein arginine methyltransferase 6	⇧	1.29	4.87E-04	⇧	1.26	5.39E-04
NM_002790	2427074	PSMA5	proteasome (prosome, macropain) subunit, alpha type, 5	⇧	1.28	0.001	⇧	1.30	3.36E-04
NM_002798	3707199	PSMB6	proteasome (prosome, macropain) subunit, beta type, 6	⇧	1.48	7.64E-05	⇧	1.26	0.010
NM_002804	3372209	PSMC3	proteasome (prosome, macropain) 26S subunit, ATPase, 3	⇧	1.26	0.002	⇧	1.42	1.94E-06
NM_002805	3730941	PSMC5	proteasome (prosome, macropain) 26S subunit, ATPase, 5	⇧	1.24	0.038	⇧	1.41	5.11E-04
NM_176863	3722152	PSME3	proteasome (prosome, macropain) activator subunit 3 (PA28 gamma; Ki)	⇧	1.21	0.004	⇧	1.25	3.77E-04
NM_017659	3836432	QPCTL	glutaminyl-peptide cyclotransferase-like	⇩	1.26	2.27E-04	⇩	1.20	0.001

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_020673	3890870	RAB22A	RAB22A, member RAS oncogene family	⇧	1.21	0.002	⇧	1.22	6.36E-04
NM_004580	3625271	RAB27A	RAB27A, member RAS oncogene family	⇧	1.31	0.002	⇧	1.26	0.005
NM_173647	2567583	RNF149	ringer finger protein 149	⇩	1.22	0.012	⇩	1.36	5.16E-05
NM_015169	3101622	RRS1	RRS1 ribosome biogenesis regulator homolog (*S. cerevisiae*)	⇧	1.40	1.40E-04	⇧	1.26	0.004
NR_027280	3837132	SAE1	SUMO1 activating enzyme subunit 1	⇧	1.20	0.004	⇧	1.35	6.92E-07
NM_015490	3303478	SEC31B	SEC31 homolog B (*S. cerevisiae*)	⇩	1.25	5.76E-04	⇩	1.26	1.52E-04
NM_013257	3101802	SGK3	serum/glucocorticoid regulated kinase family, member 3	⇧	1.20	0.003	⇧	1.20	0.002
NM_007241	3761632	SNF8	SNF8, ESCRT-II complex subunit, homolog (*S. cerevisiae*)	⇧	1.33	9.36E-04	⇧	1.34	2.84E-04
NM_014035	2826343	SNX24	sorting nexin 24	⇧	1.24	0.028	⇧	1.23	0.023
NM_006100	2633256	ST3GAL6	ST3 beta-galactoside alpha-2,3-sialyltransferase 6	⇩	1.40	0.025	⇩	1.67	2.97E-04
NM_003764	2929127	STX11	syntaxin 11	⇧	1.51	0.001	⇧	1.31	0.018
NM_016360	3730784	TACO1	translational activator of mitochondrially encoded cytochrome c oxidase 1	⇧	1.20	0.004	⇧	1.34	1.12E-06
NM_019022	3812206	TMX3	thioredoxin-related transmembrane protein 3	⇩	1.23	1.12E-04	⇩	1.20	3.51E-04
NM_020243	3945376	TOMM22	translocase of outer mitochondrial membrane 22 homolog (yeast)	⇧	1.26	4.26E-04	⇧	1.23	6.15E-04
NM_0022347	2446240	TOR1AIP2	torsin A interacting protein 2	⇧	1.43	0.007	⇧	1.42	0.004
NM_003596	3005444	TPST1	tyrosylprotein sulfotransferase 1	⇩	1.31	0.018	⇩	1.38	0.003
NM_015049	2594812	TRAK2	trafficking protein, kinesin binding 2	⇧	1.26	0.002	⇧	1.29	2.47E-04
NM_015939	3896524	TRMT6	tRNA methyltransferase 6 homolog (*S. cerevisiae*)	⇧	1.27	1.11E-05	⇧	1.26	5.41E-06
NM_003314	2838042	TTC1	tetratricopeptide repeat domain 1	⇧	1.33	6.88E-04	⇧	1.33	2.48E-04
NM_005783	2566740	TXNDC9	thioredoxin domain containing 9	⇧	1.21	0.001	⇧	1.29	8.42E-06
NM_080678	2534564	UBE2F	ubiquitin-conjugating enzyme E2F (putative)	⇧	1.26	0.004	⇧	1.26	0.002
NM_016021	2964200	UBE2J1	ubiquitin-conjugating enzyme E2, J1 (UBC6 homolog, yeast)	⇧	1.20	0.008	⇧	1.22	0.003
NM_005339	2724472	UBE2K	ubiquitin-conjugating enzyme E2K (UBC1 homolog, yeast)	⇧	1.23	6.65E-05	⇧	1.22	3.92E-05
NM_145049	2837810	UBLCP1	ubiquitin-like domain containing CTD phosphatase 1	⇧	1.27	0.015	⇧	1.37	6.60E-04
NM_152277	2887128	UBTD2	ubiquitin domain containing 2	⇧	1.45	6.18E-05	⇧	1.42	5.35E-05
NM_001048201	3817698	UHRF1	ubiquitin-like with PHD and ring finger domains 1	⇧	1.31	0.041	⇧	1.80	5.01E-06
NM_003368	2339414	USP1	ubiquitin specific peptidase 1	⇧	1.33	8.09E-04	⇧	1.32	4.48E-04
NM_025076	2568968	UXS1	UDP-glucuronate decarboxylase 1	⇩	1.21	0.039	⇩	1.32	0.001
NM_016079	2562821	VPS24	vacuolar protein sorting 24 homolog (*S. cerevisiae*)	⇧	1.26	0.002	⇧	1.34	2.75E-05
NM_022916	3475545	VPS33A	vacuolar protein sorting 33 homolog A (*S. cerevisiae*)	⇧	1.20	0.006	⇧	1.21	0.002
NM_018639	3473727	WSB2	WD repeat and SOCS box-containing 2	⇧	1.25	0.001	⇧	1.27	2.90E-04
NM_022494	3307120	ZDHHC6	zinc finger, DHHC-type containing 6	⇩	1.30	6.49E-06	⇩	1.23	1.05E-04
NM_016032	4021341	ZDHHC9	zinc finger, DHHC-type containing 9	⇩	1.23	0.004	⇩	1.27	5.35E-04

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_024646	2336497	ZYG11B	zyg-11 homolog B (*C. elegans*)	⇧	1.31	1.05E-04	⇧	1.20	0.004

RNA Processing

NM_018702	3273667	ADARB2	adenosine deaminase, RNA-specific, B2	⇩	1.36	0.012	⇩	1.34	0.010
NM_006110	3687698	CD2BP2	CD2 (cytoplasmic tail) binding protein 2	⇧	1.21	0.015	⇧	1.29	4.86E-04
NM_014026	3355114	DCPS	decapping enzyme, scavenger	⇧	1.22	0.003	⇧	1.20	0.003
NM_004728	3250055	DDX21	DEAD (Asp-Glu-Ala-Asp) box polypeptide 21	⇧	1.21	0.004	⇧	1.22	0.001
NM_001159936	2409220	EBNA1BP2	EBNA1 binding protein 2	⇧	1.29	0.003	⇧	1.48	1.04E-06
NM_013393	3035682	FTSJ2	FtsJ homolog 2 (*E. coli*)	⇧	1.30	1.86E-04	⇧	1.20	0.005
NM_004960	3656904	FUS	fused in sarcoma	⇧	1.23	7.50E-04	⇧	1.33	6.02E-07
NM_002109	2878474	HARS	histidyl-tRNA synthetase	⇧	1.20	0.005	⇧	1.20	0.002
NM_006805	2877141	HNRNPA0	heterogeneous nuclear ribonucleoprotein A0	⇧	1.23	2.35E-07	⇧	1.23	4.48E-08
NM_031266	2843619	HNRNPAB	heterogeneous nuclear ribonucleoprotein A/B	⇧	1.26	6.49E-05	⇧	1.29	2.25E-06
NM_019597	3984779	HNRNPH2	heterogeneous nuclear ribonucleoprotein H2 (H')	⇧	1.28	0.024	⇧	1.32	0.006
NM_005968	3819543	HNRNPM	heterogeneous nuclear ribonucleoprotein M	⇧	1.21	0.008	⇧	1.35	2.01E-05
NM_001130089	3699757	KARS	lysyl-tRNA synthetase	⇧	1.20	2.32E-04	⇧	1.23	1.03E-05
NM_012321	3854892	LSM4	LSM4 homolog, U6 small nuclear RNA associated (*S. cerevisiae*)	⇧	1.24	0.008	⇧	1.21	0.012
NM_018648	3617403	NOP10	NOP10 ribonucleoprotein homolog (yeast)	⇧	1.32	0.013	⇧	1.25	0.031
NM_032177	2827156	PHAX	phosphorylated adaptor for RNA export	⇧	1.27	1.79E-04	⇧	1.22	7.09E-04
NM_005837	3015769	POP7	processing of precursor 7, ribonuclease P/MRP subunit (*S. cerevisiae*)	⇧	1.23	0.009	⇧	1.28	0.001
NM_021129	3293280	PPA1	pyrophosphatase (inorganic) 1	⇧	1.34	0.005	⇧	1.20	0.028
NM_017922	3434201	PRPF39	PRP39 pre-mRNA processing factor 39 homolog (*S. cerevisiae*)	⇩	1.24	4.00E-05	⇩	1.21	1.05E-04
NM_004697	3185558	PRPF4	PRP4 pre-mRNA processing factor 4 homolog (yeast)	⇧	1.24	7.62E-05	⇧	1.24	2.10E-05
NM_006328	3336402	RBM14	RNA binding motif protein 14	⇩	1.30	0.002	⇩	1.22	0.012
NM_016836	2583602	RBMS1	RNA binding motif, single stranded interacting protein 1	⇧	1.43	0.034	⇧	1.71	7.17E-04
NM_033112	2907596	RRP36	ribosomal RNA processing 36 homolog (*S. cerevisiae*)	⇧	1.31	0.004	⇧	1.34	0.001
NM_015703	3962448	RRP7A	ribosomal RNA processing 7 homolog A (*S. cerevisiae*)	⇧	1.27	0.002	⇧	1.26	0.001
NM_018130	2682568	SHQ1	SHQ1 homolog (*S. cerevisiae*)	⇧	1.20	0.011	⇧	1.24	0.002
NM_004818	2404377	SNRNP40	small nuclear ribonucleoprotein 40kDa (U5)	⇧	1.30	0.027	⇧	1.50	2.21E-04
NM_003090	3642162	SNRPA1	small nuclear ribonucleoprotein polypeptide A'	⇩	1.27	0.011	⇩	1.40	1.67E-04
NM_003092	3877776	SNRPB2	small nuclear ribonucleoprotein polypeptide B	⇧	1.24	0.040	⇧	1.38	0.001
NM_0203095	3427014	SNRPF	small nuclear ribonucleoprotein polypeptide F	⇧	1.27	0.007	⇧	1.27	0.004
NR_036610	2905118	SRSF3	serine/arginine-rich splicing factor 3	⇧	1.20	0.015	⇧	1.33	9.47E-05

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_015679	3226493	TRUB2	TruB pseudouridine (psi) synthase homolog 2 (*E. coli*)	⇧	1.21	0.002	⇧	1.32	1.86E-06
NR_023349	2371474	TSEN15	tRNA splicing endonuclease 15 homolog (*S. cerevisiae*)	⇧	1.28	0.006	⇧	1.26	0.006
NM_032175	2815455	UTP15	UTP15, U3 small nucleolar ribonucleoprotein, homolog (*S. cerevisiae*)	⇧	1.28	5.25E-04	⇧	1.20	0.005
NM_032334	3112543	UTP23	UTP23, small subunit (SSU) processome component, homolog (yeast)	⇧	1.25	0.001	⇧	1.28	2.38E-04

Sensory Perception

NM_176889	3444476	TAS2R20	taste receptor, type 2, member 20	⇩	1.34	0.030	⇩	1.69	4.07E-05

Signal Transduction

NM_015270	3453252	ADCY6	adenylate cyclase 6	⇩	1.35	1.98E-04	⇩	1.20	0.015
NM_004309	3774283	ARHGDIA	Rho GDP dissociation inhibitor (GDI) alpha	⇧	1.39	0.009	⇧	1.48	8.17E-04
NM_014786	3339812	ARHGEF17	Rho guanine nucleotide exchange factor (GEF) 17	⇩	1.33	0.004	⇩	1.25	0.015
NM_005737	2604390	ARL4C	ADP-ribosylation factor-like 4C	⇧	1.47	2.88E-04	⇧	1.41	5.04E-04
NM_006888	3548346	CALM1	calmodulin 1 (phosphorylase kinase, delta)	⇧	1.24	0.003	⇧	1.35	1.74E-05
NM_001278	3303300	CHUK	conserved helix-loop-helix ubiquitous kinase	⇧	1.33	1.45E-04	⇧	1.37	9.87E-06
NM_020248	2395965	CTNNBIP1	catenin, beta interacting protein 1	⇧	1.27	0.018	⇧	1.26	0.012
NM_001008540	2578028	CXCR4	chemokine (C-X-C motif) receptor 4	⇩	1.70	6.76E-06	⇩	1.57	3.41E-05
NM_020311	2533999	CXCR7	chemokine (C-X-C motif) receptor 7	⇩	1.61	0.009	⇩	1.51	0.015
NM_144973	3449760	DENND5B	DENN/MADD domain containing 5B	⇧	1.27	0.042	⇧	1.31	0.012
NM_005306	3830484	FFAR2	free fatty acid receptor 2	⇩	1.64	0.005	⇩	1.49	0.013
NM_001042747	2403215	FGR	Gardner-Rasheed feline sarcoma viral (v-fgr) oncogene homolog	⇩	1.23	0.009	⇩	1.24	0.003
NM_002019	3507282	FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)	⇩	1.61	0.006	⇩	1.47	0.017
NM_002569	3608398	FURIN	furin (paired basic amino acid cleaving enzyme)	⇩	1.21	0.026	⇩	1.33	2.97E-04
NM_007353	3035892	GNA12	guanine nucleotide binding protein (G protein) alpha 12	⇧	1.24	0.029	⇧	1.28	0.006
NM_031498	3761714	GNGT2	guanine nucleotide binding protein (G protein), gamma transducing activity polypeptide 2	⇧	1.26	0.008	⇧	1.26	0.006
NM_001039966	2987038	GPER	G protein-coupled estrogen receptor 1	⇩	1.26	0.033	⇩	1.29	0.012
NM_016472	3550328	GSKIP	GSK3B interacting protein	⇧	1.47	7.01E-04	⇧	1.43	7.93E-04
NM_000876	2934308	IGF2R	insulin-like growth factor 2 receptor	⇩	1.22	1.49E-04	⇩	1.22	4.83E-05
NM_000208	3848243	INSR	insulin receptor	⇩	1.48	2.59E-04	⇩	1.64	1.01E-06
NM_018697	3002873	LANCL2	LanC lantibiotic synthetase component C-like 2 (bacterial)	⇧	1.49	1.85E-04	⇧	1.55	1.43E-05
NM_002758	3733065	MAP2K6	mitogen-activated protein kinase kinase 6	⇧	1.37	0.009	⇧	1.57	9.65E-05
NM_139068	2890605	MAPK9	mitogen-activated protein kinase 9	⇧	1.20	0.009	⇧	1.28	2.30E-04

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_004759	2376922	MAPKAPK2	mitogen-activated protein kinase-activated protein kinase 2	⇧	1.20	0.011	⇧	1.27	4.46E-04
NM_019094	3426169	NUDT4	nudix (nucleoside diphosphate linked moiety X)-type motif 4	⇩	1.20	0.027	⇩	1.25	0.003
NM_014142	3277751	NUDT5	nudic (nucleoside diphosphate linked moiety X)-type motif 5	⇧	1.39	0.003	⇧	1.31	0.009
NM_001165899	2858134	PDE4D	phosphodiesterase 4D, cAMP-specific	⇩	1.28	0.044	⇩	1.37	0.006
NM_001008709	3378790	PPP1CA	protein phosphatase 1, catalytic subunit, alpha isozyme	⇧	1.24	0.001	⇧	1.32	1.49E-05
NM_212461	3453556	PRKAG1	protein kinase, AMP-activated, gamma 1 non-catalytic subunit	⇧	1.24	1.30E-04	⇧	1.24	4.66E-05
NM_016203	3079803	PRKAG2	protein kinase, AMP-activated, gamma 2 non-catalytic subunit	⇧	1.29	3.28E-04	⇧	1.21	0.003
NM_000960	3866094	PTGIR	prostaglandin I2 (prostacyclin) receptor (IP)	⇩	1.26	0.006	⇩	1.27	0.002
NM_002834	3432333	PTPN11	protein tyrosine phosphatase, non-receptor type 11	⇧	1.24	0.007	⇧	1.34	8.68E-05
NM_006504	3270270	PTPRE	protein tyrosine phosphatase, receptor type, E	⇧	1.20	0.025	⇧	1.28	0.001
NM_002881	2503200	RALB	v-ral simian leukemia viral oncogene homolog B (ras related; GTP binding protein)	⇧	1.23	0.013	⇧	1.21	0.016
NM_178169	3419898	RASSF3	Ras association (RalGDS/AF-6) domain family member 3	⇧	1.36	1.33E-04	⇧	1.25	0.002
NM_012425	3279575	RSU1	Ras suppressor protein 1	⇧	1.28	0.001	⇧	1.30	2.17E-04
NM_178006	3508898	STARD13	StAR-related lipid transfer (START) domain containing 13	⇩	1.27	0.036	⇩	1.27	0.023
NM_012338	3069955	TSPAN12	tetraspanin 12	⇩	1.38	0.021	⇩	1.67	1.05E-04
NM_001025237	3316375	TSPAN4	tetraspanin 4	⇩	1.32	0.008	⇩	1.33	0.002
NM_003383	3160175	VLDLR	very low density lipoprotein receptor	⇩	1.58	0.001	⇩	1.33	0.003
NM_003405	3943207	YWHAH	tyrosine 3-monooxygenase/tryptophoan 5-monooxygenase activation protein, eta polypeptide	⇧	1.27	0.002	⇩	1.66	1.26E-04
NM_016653	2515933	ZAK	sterile alpha motif and leucine zipper containing kinase AZK	⇧	1.27	0.004	⇧	1.32	3.74E-04

Transcription

NM_013375	2899519	ABT1	activator of basal transcription 1	⇧	1.22	0.001	⇧	1.22	4.45E-04
NM_178042	2654023	ACTL6A	actin-like 6A	⇧	1.22	0.016	⇧	1.34	2.03E-04
NM_005171	3414695	ATF1	activating transcription factor 1	⇧	1.43	4.14E-04	⇧	1.31	0.004
NM_003972	3257938	BTAF1	BTAF1 RNA polymerase II, B-TFIID transcription factor-associated, 170kDa (Mot 1 homolog, *S. cerevisiae*)	⇩	1.22	0.002	⇩	1.27	8.75E-05
NM_001755	3665116	CBFB	core-binding factor, beta subunit	⇧	1.23	4.95E-04	⇧	1.23	1.82E-04
NM_001806	3829313	CEBPG	CCAAT/enhancer binding protein (C/EBP), gamma	⇧	1.24	0.008	⇧	1.23	0.007
NM_005225	3903146	E2F1	E2F transcription factor 1	⇧	1.25	2.01E-04	⇧	1.20	0.001
NM_203394	3463112	E2F7	E2F transcription factor 7	⇧	1.21	0.019	⇧	1.41	7.39E-06
NM_024680	3365776	E2F8	E2F transcription factor 8	⇧	1.24	0.012	⇧	1.44	6.61E-06

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_005230	3427098	ELK3	ELK3, ETS-domain protein (SRF accessory protein 2)	⇧	1.27	0.038	⇧	1.25	0.041
NM_012081	2867873	ELL2	elongation factor, RNA polymerase II, 2	⇧	1.25	0.037	⇧	1.47	1.51E-04
NM_002097	3482888	GTF3A	general transcription factor IIIA	⇧	1.35	0.001	⇧	1.31	0.001
NM_138408	2921346	GTF3C6	general transcription factor IIIC, polypeptide 6, alpha 35kDa	⇧	1.30	0.019	⇧	1.33	0.006
NM_004133	3103818	HNF4G	hepatocyte nuclear factor 4, gamma	⇩	1.33	0.008	⇩	1.27	0.018
NM_006060	3001479	IKZF1	IKAROS family zinc finger 1 (ikaros)	⇧	1.32	0.005	⇧	1.35	0.001
NM_021078	3757630	KAT2A	K (lysine) acetyltransferase 2A	⇩	1.26	4.50E-05	⇩	1.24	5.50E-05
NM_006769	2345286	LMO4	LIM domain only 4	⇧	1.20	0.035	⇧	1.32	5.07E-04
NM_145113	3568667	MAX	MYC associated factor X	⇩	1.23	0.005	⇩	1.33	4.46E-05
NM_001001683	3707127	MED11	mediator complex subunit 11	⇧	1.31	0.004	⇧	1.35	7.07E-04
NM_001127392	3333169	MYRF	myelin regulatory factor	⇩	1.22	0.021	⇩	1.26	0.003
NM_004688	2580955	NMI	myc (and STAT) interactor	⇧	1.29	0.046	⇧	1.40	0.004
NM_001080951	2977621	PLAGL1	pleiomorphic adenoma gene-like 1	⇩	1.26	0.018	⇩	1.27	0.009
NM_007212	2371694	RNF2	ring finger protein 2	⇧	1.26	0.008	⇧	1.25	0.006
NM_015138	3590422	RTF1	Rtf1, Paf1/RNA polymerase II complex component, homolog (*S. cerevisiae*)	⇧	1.25	5.80E-04	⇧	1.24	2.72E-04
NM_001001890	3930360	RUNX1	runt-related transcription factor 1	⇧	1.25	0.005	⇧	1.25	0.003
NM_003707	2694123	RUVBL1	RuvB-like 1 (*E. coli*)	⇧	1.29	0.006	⇧	1.31	0.002
NM_006049	3630156	SNAPC5	small nuclear RNA activating complex polypeptide 5, 19kDa	⇧	1.27	0.015	⇧	1.44	8.83E-05
NM_017635	3379390	SUV420H1	suppressor of variegation 4-20 homolog 1 (*Drosophila*)	⇧	1.23	0.004	⇧	1.23	0.002
NM_001135218	2403585	TAF12	TAF12 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 20kDa	⇧	1.30	1.98E-04	⇧	1.27	0.004
NM_005645	4054117	TAF13	TAF13 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 18kDa	⇧	1.38	3.44E-04	⇧	1.27	0.004
NM_015975	4013434	TAF9B	TAF9B RNA polymerase II, TATA box binding protein (TBP)-associated factor, 31kDa	⇧	1.34	0.014	⇧	1.42	0.002
NM_001139466	3967122	TBL1X	transducing (beta)-like 1X-linked	⇧	1.28	0.011	⇧	1.33	0.001
NM_007109	2902178	TCF19	transcription factor 19	⇧	1.31	0.003	⇧	1.29	0.002
NM_021045	3285552	ZNF248	zinc finger protein 248	⇩	1.31	0.002	⇩	1.35	2.23E-04
NM_080764	3954525	ZNF280B	zinc finger protein 280B	⇧	1.35	6.65E-05	⇧	1.20	0.008
NM_199441	3907934	ZNF334	zinc finger protein 334	⇩	1.25	0.024	⇩	1.33	0.002
NM_152493	2329266	ZNF362	zinc finger protein 362	⇧	1.25	0.048	⇧	1.51	1.47E-04
NM_153695	3216319	ZNF367	zinc finger protein 367	⇧	1.25	2.45E-05	⇧	1.25	5.71E-06
NM_024106	3849752	ZNF426	zinc finger protein 426	⇧	1.28	0.001	⇧	1.20	0.008

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_152478	3842724	ZNF583	zinc finger protein 583	⇧	1.20	0.026	⇧	1.29	8.17E-04
NM_015871	2326311	ZNF593	zinc finger protein 593	⇧	1.42	2.94E-04	⇧	1.23	0.020
NM_017865	2466039	ZNF692	zinc finger protein 692	⇩	1.21	2.48E-04	⇩	1.20	2.61E-04
Miscellaneous									
NM_004318	3137530	ASPH	aspartate beta-hydroxylase	⇩	1.38	3.70E-05	⇩	1.21	0.007
NM_001707	3056108	BCL7B	B-cell CLL/lymphoma 7B	⇧	1.21	0.001	⇧	1.28	1.29E-05
NM_001874	3461341	CPM	carboxypeptidase M	⇩	1.45	0.047	⇩	1.47	0.028
NM_001165958	3755903	GSDMB	gasdermin B	⇩	1.28	0.027	⇩	1.62	8.97E-06
NM_015987	3445123	HEBP1	heme binding protein 1	⇧	1.30	0.002	⇧	1.20	0.020
NM_000271	3801411	NPC1	Niemann-Pick disease, type C1	⇩	1.33	2.35E-05	⇩	1.34	3.64E-06
NM_012383	3175119	OSTF1	osteoclast stimulating factor 1	⇧	1.29	0.013	⇧	1.40	3.93E-04
NM_178422	2402431	PAQR7	progestin and adipoQ receptor family member VII	⇩	1.21	0.025	⇩	1.41	2.05E-05
NM_015393	2731636	PARM1	prostate androgen-regulated mucin-like protein 1	⇩	1.67	0.002	⇩	1.41	0.024
NM_002658	3252036	PLAU	plasminogen activator, urokinase	⇩	1.26	0.031	⇩	1.41	6.59E-04
NM_018465	3197528	PLGRKT	plasminogen receptor, C-terminal lysine transmembrane protein	⇧	1.22	0.003	⇧	1.20	0.003
NM_018663	3439178	PXMP2	peroxisomal membrane protein 2, 22kDA	⇧	1.49	7.55E-04	⇧	1.29	0.020
NM_018339	3210457	RFK	riboflavin kinase	⇧	1.28	1.16E-04	⇧	1.21	0.001
NM_003116	3883441	SPAG4	sperm associated antigen 4	⇩	1.27	0.003	⇩	1.43	3.57E-06
NM_001013694	3941010	SRRD	SRR1 domain containing	⇧	1.31	0.002	⇧	1.22	0.013
NM_003714	2887490	STC2	stanniocalcin 2	⇩	1.39	0.006	⇩	1.50	3.60E-04
NM_001171137	3224591	STRBP	spermatid perinuclear RNA binding protein	⇧	1.22	0.001	⇧	1.25	1.57E-04
NM_004237	2798915	TRIP13	thyroid hormone receptor interactor 13	⇧	1.31	0.003	⇧	1.52	1.36E-06
NM_007275	2675192	TUSC2	tumor suppressor candidate 2	⇧	1.24	0.004	⇧	1.22	0.003
Unknown Function									
NM_025092	3315607	ATHL1	ATH1, acid trehalase-like 1 (yeast)	⇩	1.24	0.002	⇩	1.23	0.001
NM_020453	2726072	ATP10D	ATPase, class V, type 10D	⇩	1.36	2.73E-04	⇩	1.21	0.012
NM_001031746	3288518	C10orf72	chromosome 10 open reading frame 72	⇩	1.22	0.022	⇩	1.25	0.005
NM_020374	3441215	C12orf4	chromosome 12 open reading frame 4	⇧	1.21	3.51E-04	⇧	1.28	2.33E-06
BC014661	3474815	C12orf43	chromosome 12 open reading frame 43	⇧	1.20	0.021	⇧	1.36	4.12E-05
AK298857	3473331	C12orf49	chromosome 12 open reading frame 49	⇧	1.23	0.003	⇧	1.20	0.004
BC027935	3862564	C19orf47	chromosome 19 open reading frame 47	⇧	1.21	2.80E-05	⇧	1.20	1.27E-05
NM_023077	2412988	C1orf163	chromosome 1 open reading frame 163	⇧	1.24	9.43E-04	⇧	1.20	0.003

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_032324	2385696	C1orf57	chromosome 1 open reading frame 57	⇧	1.30	0.012	⇧	1.25	0.022
NM_016407	3890218	C20orf43	chromosome 20 open reading frame 43	⇧	1.26	0.003	⇧	1.37	2.80E-05
NM_00110042	3926138	C21orf91	chromosome 21 open reading frame 91	⇧	1.38	1.77E-04	⇧	1.27	0.002
NM_014807	3351895	C2CD2L	C2CD2-like	⇩	1.24	0.005	⇩	1.24	0.002
NM_032359	2633460	C3orf26	chromosome 3 open reading frame 26	⇧	1.24	0.004	⇧	1.24	0.002
NM_173552	2646327	C3orf58	chromosome 3 open reading frame 58	⇩	1.34	1.19E-04	⇩	1.20	0.007
NM_020199	2875929	C5orf15	chromosome 5 open reading frame 15	⇩	1.30	2.68E-04	⇩	1.34	1.25E-05
NM_022090	2884647	C5orf54	chromosome 5 open reading frame 54	⇩	1.29	0.003	⇩	1.29	0.001
AK298490	2931683	C6orf211	chromosome 6 open reading frame 211	⇧	1.29	0.003	⇧	1.37	1.51E-04
NM_032307	3212277	C9orf64	chromosome 9 open reading frame 64	⇧	1.24	0.003	⇧	1.28	3.14E-04
NM_016520	3227121	C9orf78	chromosome 9 open reading frame 78	⇧	1.37	8.53E-05	⇧	1.27	0.001
NM_144609	3759305	CCDC43	coiled-coil domain containing 43	⇧	1.20	8.32E-04	⇧	1.26	1.05E-05
NM_015621	2881860	CCDC69	coiled-coil domain containing 69	⇧	1.27	0.003	⇧	1.29	6.09E-04
NM_025140	3476330	CCDC92	coiled-coil domain containing 92	⇧	1.28	0.030	⇧	1.26	0.027
NM_001008708	2482211	CHAC2	ChaC, cation transport regulator homolog 2 (*E. coli*)	⇧	1.20	0.023	⇧	1.30	6.53E-04
NM_016094	2700500	COMMD2	COMM domain containing 2	⇧	1.32	2.35E-04	⇧	1.20	0.010
NM_017845	2768145	COMMD8	COMM domain containing 8	⇧	1.27	0.009	⇧	1.36	3.26E-04
NM_014186	3369762	COMMD9	COMM domain containing 9	⇧	1.34	3.90E-04	⇧	1.33	2.23E-04
NM_145858	3929821	CRYZL1	crystalline, zeta (quinone reductase)-like 1	⇩	1.26	4.61E-04	⇩	1.21	0.001
NM_032299	3388914	DCUN1D5	DCN1, defective in cullin neddylation 1, domain containing 5 (*S. cerevisiae*)	⇧	1.29	0.004	⇧	1.30	0.001
NM_015291	2321849	DNAJC16	DnaJ (Hsp 40) homolog, subfamily C, member 16	⇩	1.21	0.003	⇩	1.25	2.79E-04
NM_015190	3294280	DNAJC9	DnaJ (Hsp 40) homolog, subfamily C, member 9	⇧	1.22	0.012	⇧	1.27	0.001
NM_173666	2872471	DTWD2	DTW domain containing 2	⇧	1.20	0.018	⇧	1.20	0.012
NM_133455	3941848	EMID1	EMI domain containing 1	⇩	1.32	0.017	⇩	1.33	0.008
NM_014936	2909020	ENPP4	ectonucleotide pyrophosphatase/phosphodiesterase 4 (putative)	⇩	1.43	0.006	⇩	1.44	0.003
NR_034165	3541937	EXD2	exonuclease 3’-5’ domain containing 2	⇩	1.29	0.008	⇩	1.22	0.026
BC064407	3278813	FAM107B	family with sequence similarity 107, member B	⇧	1.55	1.05E-05	⇧	1.36	7.18E-04
NM_024556	3355021	FAM118B	family with sequence similarity 118, member B	⇧	1.39	0.001	⇧	1.54	8.81E-06
NM_001134456	2634058	FAM55C	family with sequence similarity 55, member C	⇧	1.22	0.043	⇧	1.30	0.005
NM_018172	3339167	FAM86C	family with sequence similarity 86, member C	⇧	1.26	0.016	⇧	1.22	0.028
NM_015475	2547716	FAM98A	family with sequence similarity 98, member A	⇧	1.22	0.004	⇧	1.22	0.003
NM_031904	3335131	FRMD8	FERM domain containing 8	⇧	1.26	0.001	⇧	1.24	0.001
NM_001142623	3757745	GHDC	GH3 domain containing	⇩	1.26	1.27E-04	⇩	1.26	3.97E-05

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NR_027264	3698919	GLG1	golgi glycoprotein 1	⇩	1.26	9.38E-06	⇩	1.24	6.70E-06
NM_001164372	3471224	GPN3	GPN-loop GTPase 3	⇧	1.20	0.045	⇧	1.33	8.96E-04
NM_198827	3438061	GPR133	G protein-coupled receptor 133	⇩	1.38	0.027	⇩	1.66	2.31E-04
NM_022036	3734355	GPRC5C	G protein-coupled receptor, family C, group 5, member C	⇩	1.44	0.001	⇩	1.40	0.001
NM_006613	3748659	GRAP	GRB2-related adaptor protein	⇧	1.25	0.005	⇧	1.21	0.010
NM_016185	3770606	HN1	haematological and neurological expressed 1	⇧	1.27	6.16E-04	⇧	1.29	8.84E-05
NR_003086	3243262	HSD17B7P2	hydroxysteroid (17-beta) dehydrogenase 7 pseudogene 2	⇩	1.45	0.003	⇩	1.38	0.006
NR_028045	3444180	KLRAP1	killer cell lectin-like receptor subfamily A pseudogene 1	⇩	1.30	0.001	⇩	1.20	0.014
NM_018113	3453774	LMBR1L	limb region 1 homolog (mouse)-like	⇩	1.24	4.69E-04	⇩	1.36	1.51E-07
AY358681	3396179	LOC100130428	LOC100130428	⇩	1.25	0.015	⇩	1.25	0.009
AY358688	2802681	LOC100133299	LOC100133299	⇩	1.40	0.009	⇩	1.52	5.71E-04
NM_032860	2929036	LTV1	LTV1 homolog (*S. cerevisiae*)	⇧	1.30	0.001	⇧	1.27	0.002
NM_017816	2758686	LYAR	Ly1 antibody reactive homolog (mouse)	⇧	1.28	1.43E-04	⇧	1.28	4.81E-05
NM_203462	2759303	MRFAP1L1	Morf4 family associated protein 1-like 1	⇧	1.27	0.003	⇧	1.45	1.31E-06
NM_001020818	3841076	MYADM	myeloid-associated differentiation marker	⇩	1.25	0.026	⇩	1.23	0.030
NR_024321	2390976	NCRNA00115	non-protein coding RNA 115	⇩	1.20	0.030	⇩	1.34	2.03E-04
NM_016391	2888284	NOP16	NOP16 nucleolar protein homolog (yeast)	⇧	1.27	0.008	⇧	1.22	0.018
NM_024028	2835021	PCYOX1L	prenylcysteine oxidase 1 like	⇩	1.24	0.002	⇩	1.21	0.003
NM_024854	3407793	PYROXD1	pyridine nucleotide-disulphide oxidoreductase domain 1	⇧	1.34	0.003	⇧	1.25	0.015
NM_178865	2328273	SERINC2	serine incorporator 2	⇩	1.48	0.007	⇩	1.83	1.18E-05
NM_001040455	3350775	SIDT2	SID1 transmembrane family, member 1	⇩	1.28	2.17E-05	⇩	1.29	4.48E-06
NM_016045	3911814	SLMO2	slowmo homolog 2 (*Drosophila*)	⇧	1.36	5.88E-05	⇧	1.20	0.008
NM_018373	3570475	SYNJ2BP	synaptojanin 2 binding protein	⇧	1.36	0.002	⇧	1.29	0.004
NM_022484	3068476	TMEM168	transmembrane protein 168	⇩	1.20	0.003	⇩	1.26	6.53E-05
NM_018247	2961317	TMEM30A	transmembrane protein 30A	⇩	1.21	0.004	⇩	1.27	1.16E-04
NM_018266	2690850	TMEM39A	transmembrane protein 39A	⇩	1.26	0.003	⇩	1.33	1.19E-04
NM_024334	2611779	TMEM43	transmembrane protein 43	⇩	1.23	0.001	⇩	1.27	5.39E-05
NM_001136216	2321645	TMEM51	transmembrane protein 51	⇩	1.32	0.005	⇩	1.51	8.59E-06
NM_152588	3424442	TMTC2	transmembrane and tetratricopeptide repeat containing 2	⇩	1.30	0.001	⇩	1.34	1.64E-04
NM_030927	3254521	TSPAN14	tetraspanin 14	⇩	1.26	0.019	⇩	1.33	0.002
NM_024331	3886512	TTPAL	tocopherol (alpha) transfer protein-like	⇧	1.29	0.004	⇧	1.27	0.003
NM_005452	2950561	WDR46	WD repeat domain 46	⇧	1.25	0.001	⇧	1.24	9.39E-04
NM_024908	3591704	WDR76	WD repeat domain 76	⇧	1.23	0.002	⇧	1.40	2.94E-07

Table B9: *C9ORF72* and Non*C9ORF72*-Related_SALS Common Gene List (n=595) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_016258	2327630	YTHDF2	YTH domain family, member 2	⇧	1.24	0.022	⇧	1.25	0.009
NM_018684	4010768	ZC4H2	zinc finger, C4H2 domain containing	⇧	1.21	0.029	⇧	1.26	0.004

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

RefSeq #	Transcript	Symbol	Gene Name	Fold	p-value
Apoptosis					
NM_020371	3617170	AVEN	apoptosis, caspase activation inhibitor	⇧ 1.20	0.004
NM_004323	3203482	BAG1	BCL2-associated athanogene 1	⇧ 1.22	1.18E-04
NM_001015049	3580791	BAG5	BCL2-associated athanogene 5	⇧ 1.51	0.001
NM_003921	2420808	BCL10	B-cell CLL/lymphoma 10	⇧ 1.25	0.001
NM_138578	3902489	BCL2L1	BCL2-like 1	⇧ 1.24	0.003
NM_004050	3529064	BCL2L2	BCL2-like 2	⇩ 1.21	4.61E-05
NM_033338	3264948	CASP7	caspase 7, apoptosis-related cysteine peptidase	⇧ 1.22	0.010
NM_033657	2361036	DAP3	death associated protein 3	⇧ 1.22	8.44E-04
NM_00114196	2950668	DAXX	death-domain associated protein	⇧ 1.20	2.22E-05
NM_004944	2678298	DNASE1L3	deoxyribonuclease I-like 3	⇩ 1.70	0.007
NM_001375	3851826	DNASE2	deoxyribonuclease II, lysosomal	⇩ 1.29	1.36E-05
NM_00103303	2644702	FAIM	Fas apoptotic inhibitory molecule	⇧ 1.37	3.30E-04
NM_001564	2753952	ING2	inhibitor of growth family, member 2	⇧ 1.33	4.20E-06
NM_020360	3743701	PLSCR3	phospholipid scramblase 3	⇧ 1.21	8.41E-05
NM_015316	3580876	PPP1R13B	protein phosphatase 1, regulatory (inhibitor) subunit 13B	⇧ 1.24	2.14E-04
NM_013258	3688311	PYCARD	PYD and CARD domain containing	⇧ 1.31	7.39E-04
NM_194271	3434823	RNF34	ring finger protein 34	⇧ 1.29	6.18E-05
NM_004760	2999485	STK17A	serine/threonine kinase 17a	⇧ 1.23	7.77E-04
NM_003844	3127775	TNFRSF10A	tumor necrosis factor receptor superfamily, member 10a	⇩ 1.27	0.002
NM_003840	3127745	TNFRSF10D	tumor necrosis factor receptor superfamily, member 10d, decoy with truncated death domain	⇩ 1.32	0.005
NM_001066	2320727	TNFRSF1B	tumor necrosis factor receptor superfamily, member 1B	⇩ 1.21	0.019
NM_005802	3203135	TOPORS	topoisomerase I binding, arginine/serine-rich, E3 ubiquitin protein ligase	⇧ 1.20	0.004
NM_000546	3743906	TP53	tumor protein p53	⇧ 1.35	1.34E-05
Autophagy					
NM_020773	2717165	TBC1D14	TBC1 domain family, member 14	⇧ 1.20	7.75E-04
NM_006405	3557898	TM9SF1	transmembrane 9 superfamily member 1	⇩ 1.21	0.013
NM_004872	2413578	TMEM59	transmembrane protein 59	⇩ 1.25	0.001
Cell Adhesion/Extracellular Matrix					
NM_000610	3326635	CD44	CD44 molecule (Indian blood group)	⇧ 1.22	0.036

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_001777	2687739	CD47	CD47 molecule	⇩	1.24	6.37E-04
NM_022478	3557069	CDH24	cadherin 24, type 2	⇩	1.35	2.09E-06
NM_016946	2440476	F11R	F11 receptor	⇩	1.32	8.68E-06
NM_000201	3820443	ICAM1	intercellular adhesion molecule 1	⇩	1.26	1.90E-04
NM_004517	3318890	ILK	integrin-linked kinase	⇧	1.22	9.94E-06
NM_181501	2809128	ITGA1	integrin, alpha 1	⇩	1.35	0.020
NM_000425	4026798	L1CAM	L1 cell adhesion molecule	⇩	1.20	0.005
NM_005567	3772719	LGALS3BP	lectin, galactoside-binding, soluble, 3 binding protein	⇩	1.42	0.014
NM_001143995	3374402	LPXN	leupaxin	⇧	1.21	3.05E-05
NM_005926	3621692	MFAP1	microfibrillar-associated protein 1	⇧	1.28	4.53E-06
NM_004385	2818517	VCAN	versican	⇩	1.43	0.025
NM_003461	3029129	ZYX	zyxin	⇧	1.28	4.99E-05

Cellular Response to Stress

NM_012111	3545466	AHSA1	AHA1, activator of heat shock 90kDa protein ATPase homolog 1 (yeast)	⇧	1.37	1.26E-05
NM_152392	2484552	AHSA2	AHA1, activator of heat shock 90kDa protein ATPase homolog 2 (yeast)	⇩	1.22	0.003
NM_000067	3105600	CA2	carbonic anhydrase II	⇧	1.37	0.004
NM_001752	3326400	CAT	catalase	⇧	1.23	0.001
NM_016230	2915490	CYB5R4	cytochrome b5 reductase 4	⇧	1.20	0.004
NM_004417	2887309	DUSP1	dual specificity phosphatase 1	⇩	1.41	0.002
NM_007207	2457261	DUSP10	dual specificity phosphatase 10	⇧	1.31	1.13E-04
NM_014584	3564790	ERO1L	ERO1-like (*S. cerevisiae*)	⇩	1.21	0.013
NM_019891	2462329	ERO1LB	ERO1-like beta (*S. cerevisiae*)	⇩	1.33	1.55E-04
NM_000402	4027416	G6PD	glucose-6-phosphate dehydrogenase	⇧	1.20	3.57E-04
NM_032569	3678395	GLYR1	glyoxylate reductase 1 homolog (*Arabidopsis*)	⇧	1.22	0.010
NM_201397	2674229	GPX1	glutathione peroxidase 1	⇩	1.22	0.001
NM_000178	3903670	GSS	glutathione synthetase	⇧	1.21	4.77E-04
NM_001031720	2738314	GSTCD	glutathione S-transferase, C-terminal domain containing	⇧	1.21	8.13E-04
NM_013332	3022814	HILPDA	hypoxia inducible lipid droplet-associated	⇩	1.50	0.003
NM_005348	3580179	HSP90AA1	heat shock protein 90kDa alpha (cytosolic), class A member 1	⇧	1.31	1.42E-05
NM_002154	2828856	HSPA4	heat shock 70kDa protein 4	⇧	1.22	0.002
NM_006644	3508330	HSPH1	heat shock 105kDa/110kDa protein 1	⇧	1.27	0.003
NM_203500	3850363	KEAP1	kelch-like ECH-associated protein 1	⇧	1.25	0.001

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_000903	3696666	NQO1	NAD(P)H dehydrogenase, quinone 1	⇧	1.47	1.41E-05
NM_016332	3676262	SEPX1	selenoprotein X, 1	⇧	1.34	0.009
NM_000454	3917851	SOD1	superoxide dismutase 1	⇧	1.34	3.36E-04
NM_006819	3334224	STIP1	stress-induced-phosphoprotein 1	⇧	1.23	0.001

Cytoskeleton

NM_001005386	2485784	ACTR2	ARP2 actin-related protein 2 homolog (yeast)	⇧	1.35	0.001
NM_016824	3263555	ADD3	adducing 3 (gamma)	⇧	1.21	0.006
NM_016293	3454841	BIN2	bridging integrator 2	⇧	1.32	0.013
NM_006136	3020444	CAPZA2	capping protein (actin filament) muscle Z-line, alpha 2	⇧	1.40	6.34E-04
NM_005507	3377886	CFL1	cofilin 1 (non-muscle)	⇧	1.27	1.45E-07
NM_018204	3490655	CKAP2	cytoskeleton associated protein 2	⇧	1.21	5.92E-04
NM_014063	2999710	DBNL	drebrin-like	⇧	1.22	2.75E-04
NM_00104251	3515965	DIAPH3	diaphanous homolog 3 (*Drosophila*)	⇧	1.36	6.90E-05
NM_144666	3318731	DNHD1	dynein heavy chain domain 1	⇩	1.28	0.003
NM_007044	2978957	KATNA1	katanin p60 (ATPase-containing) subunit A1	⇧	1.23	9.33E-05
NM_001014380	3507962	KATNAL1	katanin p60 subunit A-like 1	⇧	1.20	0.012
NM_014846	3152220	KIAA0196	KIAA0196	⇧	1.20	0.001
NM_015634	3250093	KIAA1279	KIAA1279	⇧	1.20	0.007
NM_004523	3258168	KIF11	kinesin family member 11	⇧	1.30	4.47E-04
NM_020242	2620256	KIF15	kinesin family member 15	⇧	1.41	7.49E-05
NM_024704	3898796	KIF16B	kinesin family member 16B	⇧	1.25	5.63E-04
NM_138555	3599811	KIF23	kinesin family member 23	⇧	1.25	2.93E-04
NM_007054	2875419	KIF3A	kinesin family member 3A	⇩	1.32	0.006
NM_004798	3881824	KIF3B	kinesin family member 3B	⇧	1.29	1.53E-04
NM_012310	3980560	KIF4A	kinesin family member 4A	⇧	1.20	1.53E-04
NM_006148	3719980	LASP1	LIM and SH3 protein 1	⇧	1.22	6.46E-05
NM_001113546	3454331	LIMA1	LIM domain and actin binding 1	⇧	1.21	0.020
NM_002314	3008108	LIMK1	LIM domain kinase 1	⇧	1.23	1.04E-04
NM_005573	2827185	LMNB1	lamin B1	⇧	1.32	2.00E-04
AK023285	2331505	MACF1	microtubule-actin crosslinking factor 1	⇩	1.27	0.040
NM_012325	3882069	MAPRE1	microtubule-associated protein, RP/EB family, member 1	⇧	1.23	2.97E-05
NM_001172303	3240012	MASTL	microtubule-associated serine/threonine kinase-like	⇧	1.21	2.16E-05
NM_013262	2896784	MYLIP	myosin regulatory light chain interacting protein	⇩	1.22	0.009

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_006901	3631794	MYO9A	myosin IXA	⇧	1.20	4.58E-04
NM_144573	2343231	NEXN	nexilin (F actin binding protein)	⇧	1.43	0.002
NM_016418	3942062	NF2	neurofibromin 2	⇧	1.34	3.14E-07
NM_020992	3301218	PDLIM1	PDZ and LIM domain 1	⇧	1.25	2.37E-05
NM_005022	3742400	PFN1	profilin 1	⇧	1.24	0.015
NM_016274	2358044	PLEKHO1	pleckstrin homology domain containing, family O member 1	⇧	1.27	5.01E-06
NM_001080855	3474372	PXN	paxillin	⇧	1.35	1.84E-06
NM_021021	3150844	SNTB1	syntrophin, beta 1 (dystrophin-associated protein A1, 59kDa, basic component 1)	⇧	1.42	5.75E-04
NM_006750	3666601	SNTB2	syntrophin, beta 2 (dystrophin-associated protein A1, 59kDa, basic component 2)	⇧	1.27	2.22E-05
NM_001024858	3568485	SPTB	spectrin, beta, erythrocytic	⇩	1.22	0.010
NM_003128	2482505	SPTBN1	spectrin, beta, non-erythrocytic 1	⇩	1.22	9.67E-06
NM_001130965	2986825	SUN1	Sad1 and UNC84 domain containing 1	⇩	1.34	9.33E-07
NM_001079515	2386418	TBCE	tubulin folding cofactor E	⇧	1.34	2.66E-06
NM_015602	2446244	TOR1AIP1	torsin A interacting protein 1	⇩	1.30	1.11E-04
NM_012112	3881443	TPX2	TPX2, microtubule-associated, homolog (*Xenopus laevis*)	⇧	1.21	7.03E-04
NR_027779	3962734	TTLL1	tubulin tyrosine ligase-like family, member 1	⇧	1.22	2.60E-04
NR_003659	3612166	WASH3P	WAS protein family homolog 3 pseudogene	⇩	1.23	0.024
NM_017491	2760371	WDR1	WD repeat domain 1	⇧	1.22	8.86E-05

Development

NM_152698	2505793	AMER3	APC membrane recruitment protein 3	⇩	1.21	8.55E-04
NM_001002858	3627248	ANXA2	annexin A2	⇧	1.23	0.002
NM_031301	3597521	APH1B	anterior pharynx defective 1 homolog B (*C. elegans*)	⇩	1.21	0.003
NM_147147	2967249	BVES	blood vessel epicardial substance	⇩	1.33	0.001
BC022092	3432641	C12orf52	chromosome 12 open reading frame 52	⇧	1.20	4.15E-04
NM_006324	3699508	CFDP1	craniofacial development protein 1	⇧	1.20	0.003
NM_145234	4018080	CHRDL1	chordin-like 1	⇩	1.31	1.05E-04
NM_025212	2780388	CXXC4	CXXC finger protein 4	⇧	1.44	4.33E-04
NM_016651	3538087	DACT1	dapper, antagonist of beta-catenin, homolog 1 (*Xenopus laevis*)	⇧	1.23	0.041
NM_005227	2360633	EFNA4	ephrin-A4	⇩	1.21	0.038
NM_000399	3291601	EGR2	early growth response 2	⇧	1.23	0.018
NM_003633	2862696	ENC1	ectodermal-neural cortex 1 (with BTB-like domain)	⇧	1.40	0.004
NM_018063	3258910	HELLS	helicase, lymphoid-specific	⇧	1.33	3.40E-04

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_022475	2745899	HHIP	hedgehog interacting protein	⇩	1.20	0.031
NM_000597	2527253	IGFBP2	isulin-like growth factor binding protein 2, 36kDa	⇩	1.28	4.47E-04
NM_016269	2781138	LEF1	lymphoid enhancer-binding factor 1	⇩	1.46	0.026
NM_022458	3081613	LMBR1	limb region 1 homolog (mouse)	⇩	1.44	2.31E-05
NM_014839	2348514	LPPR4	lipid phosphate phosphatase-related protein type 4	⇩	1.28	0.001
NM_015884	3971329	MBTPS2	membrane-bound transcription factor peptidase, site 2	⇩	1.22	0.011
NM_001012334	3329343	MDK	midkine (neurite growth-promoting factor 2)	⇩	1.20	0.042
NM_014791	3168508	MELK	maternal embryonic leucine zipper kinase	⇧	1.38	3.11E-04
NM_006154	3625539	NEDD4	neural precursor cell expressed, developmentally up-regulated 4, E3 ubiquitin protein ligase	⇧	1.21	0.011
NM_015514	3529156	NGDN	neuroguidin, EIF4E binding protein	⇧	1.25	0.002
NM_153026	3451375	PRICKLE1	prickle homolog 1 (*Drosophila*)	⇧	1.28	0.005
NM_006717	3178416	SPIN1	spindlin 1	⇧	1.21	0.003
NM_153365	2761941	TAPT1	transmembrane anterior posterior transformation 1	⇩	1.31	8.09E-07
NM_005149	2366184	TBX19	T-box 19	⇩	1.25	4.09E-04
NM_001135243	2835440	TCOF1	Treacher Collins-Franceschetti syndrome 1	⇧	1.22	7.97E-06
NM_015631	3301556	TCTN3	tectonic family member 3	⇩	1.23	0.002
NM_020457	3665846	THAP11	THAP domain containing 11	⇧	1.27	1.47E-04
NM_181783	3425134	TMTC3	transmembrane and tetratricopeptide repeat containing 3	⇩	1.21	8.40E-04
NM_020648	3778372	TWSG1	twisted gastrulation homolog 1 (*Drosophila*)	⇩	1.31	0.002
NM_138959	2353283	VANGL1	vang-like 1 (van gogh, *Drosophila*)	⇧	1.37	0.016
NM_004626	3382523	WNT11	wingless-type MMTV integration site family, member 11	⇩	1.24	0.025

DNA Damage & Repair

NM_139178	3328214	ALKBH3	alkB, alkylation repair homolog 3 (*E. coli*)	⇧	1.28	4.14E-05
NM_138775	3389878	ALKBH8	alkB, alkylation repair homolog 8 (*E. coli*)	⇧	1.21	7.09E-05
NM_014481	3978620	APEX2	APEX nuclease (apurinic/apyrimidinic endonuclease) 2	⇧	1.21	1.90E-04
NM_024857	3716893	ATAD5	ATPase family, AAA domain containing 5	⇧	1.24	0.001
NM_001033549	3824153	BABAM1	BRISC and BRCA1 A complex member 1	⇧	1.20	2.26E-04
NM_032408	3056044	BAZ1B	bromodomain adjacent to zinc finger domain, 1B	⇧	1.20	7.07E-05
NM_000057	3608298	BLM	Bloom syndrome, RecQ helicase-like	⇧	1.43	7.44E-06
NM_007300	3758317	BRCA1	breast cancer 1, early onset	⇧	1.44	4.57E-06
NM_000059	3484641	BRCA2	breast cancer 2, early onset	⇧	1.26	9.43E-04
NM_024332	3996755	BRCC3	BRCA1/BRCA2-containing complex, subunit 3	⇧	1.26	0.002

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted $p<0.05$, FC $\geq \pm 1.20$]

NM_032043	3765580	BRIP1	BRCA1 interacting protein C-terminal helicase 1	⇧	1.32	1.05E-05
NM_001114122	3354799	CHEK1	CHK1 checkpoint homolog (*S. pombe*)	⇧	1.29	1.49E-05
NM_022111	2406420	CLSPN	claspin	⇧	1.39	1.14E-04
NM_00103385	3278977	DCLRE1C	DNA cross-link repair 1C	⇧	1.21	0.005
NM_016448	2378937	DTL	denticleless homolog (*Drosophila*)	⇧	1.25	6.88E-04
NM_139076	2776088	FAM175A	family with sequence similarity 175, member A	⇧	1.22	0.004
NM_00101811	4000370	FANCB	Fanconi anemia, complementation group B	⇧	1.25	2.29E-04
NM_000136	3215701	FANCC	Fanconi anemia, complementation group C	⇧	1.35	1.24E-05
NM_021922	2904663	FANCE	Fanconi anemia, complementation group E	⇧	1.20	4.56E-05
NM_00111337	3607537	FANCI	Fanconi anemia, complementation group I	⇧	1.38	1.19E-05
NM_202002	3440598	FOXM1	forkhead box M1	⇧	1.39	4.55E-06
NM_015675	3816509	GADD45B	growth arrest and DNA-damage-inducible, beta	⇩	1.27	0.017
NM_007266	2474681	GPN1	GPN-loop GTPase 1	⇧	1.21	0.002
NM_016426	3949055	GTSE1	G-2 and S-phase expressed 1	⇧	1.27	2.48E-05
NM_001130688	2793951	HMGB2	high-mobility group box 2	⇧	1.31	0.003
NM_014736	3629103	KIAA0101	KIAA0101	⇧	1.47	1.12E-04
NM_000251	2480992	MSH2	mutS homolog 2, colon cancer, nonpolyposis type 1 (*E. coli*)	⇧	1.35	6.98E-05
NM_000179	2481142	MSH6	mutS homolog 6 (*E. coli*)	⇧	1.25	1.05E-04
NM_173685	3114878	NSMCE2	non-SMC element 2, MMS21 homolog (*S. cerevisiae*)	⇧	1.29	2.18E-04
NM_024675	3685329	PALB2	partner and localizer of BRCA2	⇧	1.26	6.30E-06
NM_002690	3096171	POLB	polymerase (DNA directed), beta	⇧	1.22	9.80E-05
NM_199420	2691575	POLQ	polymerase (DNA directed), theta	⇧	1.26	0.005
NM_005053	3822074	RAD23A	RAD23 homolog A (*S. cerevisiae*)	⇧	1.20	2.71E-04
NM_058216	3728776	RAD51C	RAD51 homolog C (*S. cerevisiae*)	⇧	1.44	4.01E-06
NM_134424	3439836	RAD52	RAD52 homolog (*S. cerevisiae*)	⇩	1.22	4.37E-05
NM_003579	2334646	RAD54L	RAD54-like (*S. cerevisiae*)	⇧	1.20	0.002
NM_002945	3706000	RPA1	replication protein A1, 70kDa	⇧	1.21	3.50E-05
NM_006666	3838118	RUVBL2	RuvB-like 2 (*E. coli*)	⇧	1.22	3.32E-04
NM_001042550	3182781	SMC2	structural maintenance of chromosomes 2	⇧	1.32	6.79E-05
NM_005496	2650199	SMC4	structural maintenance of chromosomes 4	⇧	1.21	0.002
NM_003350	3097208	UBE2V2	ubiquitin-conjugating enzyme E2 variant 2	⇧	1.22	0.017
NM_003362	3430926	UNG	uracil-DNA glycosylase	⇧	1.30	5.61E-05
NM_005431	3080283	XRCC2	X-ray repair complementing defective repair in Chinese hamster cells 2	⇧	1.50	2.89E-04

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_022550	2818454	XRCC4	X-ray repair complementing defective repair in Chinese hamster cells 4	⇧	1.22	0.003
NM_032143	2577700	ZRANB3	zinc finger, RAN-binding domain containing 3	⇧	1.25	0.002

DNA Replication & the Cell Cycle

NM_015120	2488785	ALMS1	Alstrom syndrome 1	⇧	1.26	0.009
NM_198433	3910785	AURKA	aurora kinase A	⇧	1.27	0.002
NM_058243	3853193	BRD4	bromodomain containing 4	⇧	1.26	0.001
NM_001211	3589697	BUB1B	BUB1 mitotic checkpoint serine/threonine kinase B	⇧	1.26	2.83E-04
NM_001100619	3781531	CABLES	Cdk5 and Abl enzyme substrate 1	⇧	1.22	2.71E-04
NM_001743	2551924	CALM2	calmodulin 2 (phosphorylase kinase, delta)	⇧	1.25	0.022
NM_005184	3836841	CALM3	calmodulin 3 (phosphorylase kinase, delta)	⇧	1.25	8.06E-07
NM_001237	2784113	CCNA2	cyclin A2	⇧	1.32	9.36E-05
NM_031966	2813414	CCNB1	cyclin B1	⇧	1.25	0.002
NM_004701	3595979	CCNB2	cyclin B2	⇧	1.26	6.56E-04
NM_057749	3145107	CCNE2	cyclin E2	⇧	1.52	3.82E-04
NM_004748	3625326	CCPG1	cell cycle progression 1	⇩	1.25	0.004
NM_006023	3235461	CDC123	cell division cycle 123 homolog (*S. cerevisiae*)	⇧	1.32	3.04E-06
NM_001255	2333136	CDC20	cell division cycle 20 homolog (*S. cerevisiae*)	⇧	1.30	0.032
NM_021873	3874439	CDC25B	cell division cycle 25 homolog B (*S. pombe*)	⇧	1.22	1.06E-05
NM_001178010	3936913	CDC45	cell division cycle 45 homolog (*S. cerevisiae*)	⇧	1.37	1.33E-04
NM_001254	3720896	CDC6	cell division cycle 6 homolog (*S. cerevisiae*)	⇧	1.62	8.87E-05
NM_152562	3090697	CDCA2	cell division cycle associated 2	⇧	1.26	0.002
NM_031942	2516023	CDCA7	cell division cycle associated 7	⇧	1.27	0.002
NM_001127370	3040897	CDCA7L	cell division cycle associated 7-like	⇧	1.24	0.027
NM_018101	2330773	CDCA8	cell division cycle associated 8	⇧	1.44	1.80E-04
NM_000075	3458783	CDK4	cyclin-dependent kinase 4	⇧	1.20	0.003
NM_001260	3482498	CDK8	cyclin-dependent kinase 8	⇧	1.21	0.003
NM_004064	3405440	CDKN1B	cyclin-dependent kinase inhibitor 1B (p27, Kip1)	⇩	1.20	0.018
NM_005192	3536336	CDKN3	cyclin-dependent kinase inhibitor 3	⇧	1.31	6.29E-06
NM_006733	3984655	CENPI	centromere protein I	⇧	1.30	6.71E-04
NM_022145	2859667	CENPK	centromere protein K	⇧	1.25	0.004
NM_024322	2473284	CENPO	centromere protein O	⇧	1.33	4.69E-04
NM_001012267	3179359	CENPP	centromere protein P	⇧	1.42	6.13E-05

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_018132	2909723	CENPQ	centromere protein Q	⇧	1.24	0.003
NM_018131	3258444	CEP55	centrosomal protein 55kDa	⇧	1.36	1.21E-04
NM_024899	3799542	CEP76	centrosomal protein 76kDa	⇧	1.20	1.17E-04
NM_004344	4026263	CETN2	centrin, EF-hand protein, 2	⇧	1.36	1.63E-05
NM_005483	3817501	CHAF1A	chromatin assembly factor 1, subunit A (p150)	⇧	1.32	3.84E-08
NM_001039690	369454	CHTF8	CTF8, chromosome transmission fidelity factor 8 homolog (*S. cerevisiae*)	⇧	1.24	8.92E-05
NM_001827	3178583	CKS2	CDC28 protein kinase regulatory subunit 2	⇧	1.27	0.014
NM_014711	3651018	CP110	centriolar coiled coil protein 110kDa	⇧	1.23	0.003
NM_015986	3752002	CRLF3	cytokine receptor-like factor 3	⇧	1.22	7.69E-04
NM_00114601	3565663	DLGAP5	discs, large (*Drosophila*) homolog-associated protein 5	⇧	1.22	0.013
NM_014689	2601648	DOCK10	dedicator of cytokinesis 10	⇧	1.25	0.001
NM_024094	3150715	DSCC1	defective in sister chromatid cohesion 1 homolog (*S. cerevisiae*)	⇧	1.31	3.26E-05
NM_001943	3783529	DSG2	desmoglein 2	⇩	1.60	0.007
NM_207042	2434490	ENSA	endosulfine alpha	⇩	1.32	2.09E-04
NM_017669	4012142	ERCC6L	excision repair cross-complementing rodent repair deficiency, complementation group 6-like	⇧	1.21	2.73E-04
NM_030919	3884892	FAM83D	family with sequence similarity 83, member D	⇧	1.25	0.003
NM_012177	2980241	FBXO5	F-box protein 5	⇧	1.35	3.22E-05
NM_033417	3854218	HAUS8	HAUS augmin-like complex, subunit 8	⇧	1.21	3.80E-05
NM_033402	3105430	LRRCC1	leucine rich repeat and coiled-coil domain containing 1	⇧	1.48	7.34E-07
NM_182751	3235789	MCM10	minichromosome maintenance complex component 10	⇧	1.52	5.02E-06
NM_004526	2640855	MCM2	minichromosome maintenance complex component 2	⇧	1.29	3.41E-05
NM_002388	2957126	MCM3	minichromosome maintenance complex component 3	⇧	1.30	8.17E-05
NM_005915	2577896	MCM6	minichromosome maintenance complex component 6	⇧	1.23	8.93E-04
NM_018944	3929038	MIS18A	MIS18 kinetochore protein homolog A (*S. pombe*)	⇧	1.24	2.25E-06
NM_022045	3113456	MTBP	Mdm2, transformed 3T3 cell double minute 2, p53 binding protein (mouse) binding protein, 104kDa	⇧	1.30	6.93E-05
NM_002466	3886223	MYBL2	v-myb myeloblastosis viral oncogene homolog (avian)-like 2	⇧	1.41	3.70E-04
NM_015261	3399545	NCAPD3	non-SMC condensin II complex, subunit D3	⇧	1.22	4.65E-04
NM_022346	2720251	NCAPG	non-SMC condensin I complex, subunit G	⇧	1.24	0.003
NM_017760	3082181	NCAPG2	non-SMC condensin II complex, subunit G2	⇧	1.30	2.46E-04
NM_015341	2494484	NCAPH	non-SMC condensin I complex, subunit H	⇧	1.30	3.57E-04
NM_006101	3776139	NDC80	NDC80 homolog, kinetochore complex component (*S. cerevisiae*)	⇧	1.46	4.89E-06
NM_004542	3841198	NDUFA3	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 3, 9kDa	⇧	1.39	0.004
NM_002497	2454444	NEK2	NIMA (never in mitosis gene a)-related kinase 2	⇧	1.28	0005

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_003157	2676352	NEK4	NIMA (never in mitosis gene a)-related kinase 4	⇧	1.21	0.001
NM_004741	3261492	NOLC1	nucleolar and coiled-body phosphoprotein 1	⇧	1.26	5.22E-04
NM_001033714	3442024	NOP2	NOP2 nucleolar protein homolog (yeast)	⇧	1.22	5.71E-04
NM_001042549	2454838	NSL1	NSL1, MIND kinetochore complex component, homolog (*S. cerevisiae*)	⇧	1.22	2.73E-05
NM_016359	3590388	NUSAP1	nucleolar and spindle associated protein 1	⇧	1.20	7.16E-04
NM_007280	3619945	OIP5	Opa interacting protein 5	⇧	1.38	7.77E-06
NM_004153	2412799	ORC1	origin recognition complex, subunit 1	⇧	1.27	0.001
NM_006191	3417309	PA2G4	proliferation-associated 2G4, 38kDa	⇧	1.21	3.75E-05
NM_017884	3124180	PINX1	PIN2/TERF1 interacting, telomerase inhibitor 1	⇧	1.24	1.74E-04
NM_014264	2742985	PLK4	polo-like kinase 4	⇧	1.31	3.01E-04
NM_016937	3972093	POLA1	polymerase (DNA directed), alpha 1, catalytic subunit	⇧	1.31	8.12E-04
NM_006591	3340269	POLD3	polymerase (DNA-directed), delta 3, accessory subunit	⇧	1.37	2.86E-06
NR_027261	3221646	POLE3	polymerase (DNA directed), epsilon 3 (p17 subunit)	⇧	1.20	4.54E-04
NM_005973	2361731	PRCC	papillary renal cell carcinoma (translocation-associated)	⇧	1.21	8.56E-05
NM_000946	3458133	PRIM1	primase, DNA, polypeptide 1 (49kDa)	⇧	1.26	2.43E-04
NM_000321	3489020	RB1	retinoblastoma 1	⇧	1.23	0.004
NR_030725	2327482	RCC1	regulator of chromosome condensation 1	⇧	1.20	3.80E-04
NM_002916	2709486	RFC4	replication factor C (activator 1) 4, 37kDa	⇧	1.23	0.012
NM_181578	3433747	RFC5	replication factor C (activator 1) 5, 36.5kDa	⇧	1.26	2.31E-04
NM_024945	3176999	RMI1	RMI1, RecQ mediated genome instability 1, homolog (*S. cerevisiae*)	⇧	1.24	0.001
NM_006397	3821908	RNASEH2A	ribonuclease H2, subunit A	⇧	1.22	3.03E-04
NM_001033	3318009	RRM1	ribonucleotide reductase M1	⇧	1.31	1.00E-04
NM_144710	2569908	SEPT10	septin 10	⇧	1.91	0.008
NM_001012410	2665572	SGOL1	shugoshin-like 1 (*S. pombe*)	⇧	1.24	0.005
NM_152524	2522212	SGOL2	shugoshin-like 2 (*S. pombe*)	⇧	1.22	0.004
NM_182620	3764738	SKA2	spindle and kinetochore associated complex subunit 2	⇧	1.43	0.005
NM_145061	3504617	SKA3	spindle and kinetochore associated complex subunit 3	⇧	1.36	1.01E-04
NM_005983	2806517	SKP2	S-phase kinase-associated protein 2 (p45)	⇧	1.25	4.01E-05
NM_006306	4009238	SMC1A	structural maintenance of chromosomes 1A	⇧	1.27	7.12E-04
NM_020675	2585933	SPC25	SPC25, NDC80 kinetochore complex component, homolog (*S. cerevisiae*)	⇧	1.52	3.88E-05
NM_017785	2840002	SPDL1	spindle apparatus coiled-coil protein 1	⇧	1.29	0.002
NM_001048166	2411228	STIL	SCL/TAL1 interrupting locus	⇧	1.23	0.008
NM_003173	3976797	SUV39H1	suppressor of variegation 3-9 homolog 1 (*Drosophila*)	⇧	1.45	1.18E-05

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_001193424	3236448	SUV39H2	suppressor of variegation 3-9 homolog 2 (*Drosophila*)	⇧	1.22	5.95E-04
NM_006342	2714955	TACC3	transforming, acidic coiled-coil containing protein 3	⇧	1.34	9.79E-05
NM_001071	3775842	TYMS	thymidylate synthetase	⇧	1.20	2.24E-04
NM_015045	3298738	WAPAL	wings apart-like homolog (*Drosophila*)	⇧	1.21	3.64E-05
NM_007086	3565571	WDHD1	WD repeat and HMG-box DNA binding protein 1	⇧	1.37	2.21E-06
NM_004724	3391769	ZW10	ZW10, kinetochore associated, homolog (*Drosophila*)	⇧	1.25	3.27E-05
NR_003105	3598721	ZWILCH	Zwilch, kinetochore associated, homolog (*Drosophila*)	⇧	1.41	1.56E-05
NM_032997	3290210	ZWINT	ZW10 interactor	⇧	1.57	5.09E-05

Hormone Function

NM_001124	3320123	ADM	adrenomedullin	⇩	1.62	0.002
NM_022640	3766480	CSH1	chorionic somatomammotropin hormone 1 (placental lactogen)	⇩	1.42	0.008
NM_000805	3721421	GAST	gastrin	⇩	1.21	0.029
NM_000515	3766512	GH1	growth hormone 1	⇩	1.22	0.019
NM_000233	2552368	LHCGR	luteinizing hormone/choriogonadot ropin receptor	⇩	1.24	0.002
NM_005575	2821413	LNPEP	leucyl/cystinyl aminopeptidase	⇩	1.65	1.37E-05

Immune Response & Inflammation

NM_181780	2688717	BTLA	B and T lymphocyte associated	⇩	1.25	0.001
NM_007047	2899333	BTN3A2	butyrophilin, subfamily 3, member A2	⇩	1.24	0.046
NM_148672	2855542	CCL28	chemokine (C-C motif) ligand 28	⇩	1.22	0.038
NM_002984	3718930	CCL4	chemokine (C-C motif) ligand 4	⇩	1.21	0.049
NM_002985	3753860	CCL5	chemokine (C-C motif) ligand 5	⇩	1.24	0.037
NM_001838	3756319	CCR7	chemokine (C-C motif) receptor 7	⇩	1.21	2.28E-04
NM_001004196	2636125	CD200	CD200 molecule	⇩	1.53	2.50E-04
NM_006139	2523801	CD28	CD28 molecule	⇩	2.18	3.68E-04
NM_002389	2377427	CD46	CD46 molecule, complement regulatory protein	⇩	1.29	7.80E-08
NM_005191	2690900	CD80	CD80 molecule	⇩	1.35	7.24E-06
NM_001184879	2440295	CD84	CD84 molecule	⇩	1.43	0.001
NM_198390	3670772	CMIP	c-Maf-inducing protein	⇧	1.21	4.49E-04
NM_001142343	3470193	CMKLR1	chemokine-like receptor 1	⇩	1.29	0.013
NM_000757	2351063	CSF1	colony stimulating factor 1 (macrophage)	⇩	1.24	0.018
NM_014395	2737318	DAPP1	dual adaptor of phosphotyrosine and 3-phosphoinositides	⇧	1.32	1.83E-04
NM_005755	3817380	EBI3	Epstein-Barr virus induced 3	⇩	1.32	1.67E-05

Table B10: Non*C9ORF72*-Related_*SALS* Specific Gene List (n=1,201) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_001040458	2868131	ERAP1	endoplasmic reticulum aminopeptidase 1	⇩	1.23	0.002
NM_001007253	3053380	ERV3	endogenous retroviral sequence 3	⇧	1.33	0.024
NM_002001	2362537	FCER1A	Fc fragment of IgE, high affinity I, receptor for; alpha polypeptide	⇩	1.22	0.023
NM_031282	2438938	FCRL4	Fc receptor-like 4	⇧	1.46	0.008
NM_002053	2421883	GBP1	guanylate binding protein 1, interferon-inducible, 67kDa	⇧	1.38	0.003
NM_004951	3522662	GPR183	G protein-coupled receptor 183	⇩	1.22	0.005
NM_012206	2883317	HAVCR1	hepatitis A virus cellular receptor 1	⇩	1.24	2.08E-04
NM_032782	2883349	HAVCR2	hepatitis A virus cellular receptor 2	⇩	1.44	0.017
NM_005335	2691668	HCLS1	hematopoietic cell-specific Lyn substrate 1	⇧	1.21	0.001
NM_002119	2950307	HLA-DOA	major histocompatibility complex, class II, DO alpha	⇩	1.27	0.002
NM_005516	2901620	HLA-E	major histocompatibility complex, class I, E	⇩	1.20	3.51E-04
NM_001098479	2900974	HLA-F	major histocompatibility complex, class I, F	⇩	1.37	6.11E-07
NR_027822	2901463	HLA-L	major histocompatibility complex, class I, L	⇩	1.22	0.048
NM_005533	3722338	IFI35	interferon-induced protein 35	⇧	1.22	0.027
NM_002038	2403261	IFI6	interferon, alpha-inducible protein 6	⇩	1.22	0.009
NM_001548	3257246	IFIT1	interferon-induced protein with tetratricopeptide repeats 1	⇧	1.38	0.021
NM_021068	3201188	IFNA4	interferon, alpha 4	⇩	1.33	0.033
NM_000416	2976113	IFNGR1	interferon gamma receptor 1	⇩	1.33	0.005
NM_016584	3417557	IL23A	interleukin 23, alpha subunit p19	⇩	1.21	0.015
NM_002184	2857416	IL6ST	interleukin 6 signal transducer (gp130, oncostatin M receptor)	⇩	1.21	0.006
NM_002339	3317071	LSP1	lymphocyte-specific protein 1	⇧	1.31	2.61E-05
NM_002349	2583254	LY75	lymphocyte antigen 75	⇩	1.33	2.81E-05
NM_002348	2363248	LY9	lymphocyte antigen 9	⇩	1.26	0.033
NM_002432	2362333	MNDA	myeloid cell nuclear differentiation antigen	⇧	1.36	0.035
NM_012340	3909553	NFATC2	nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 2	⇧	1.41	0.008
NM_020393	2435961	PGLYRP4	peptidoglycan recognition protein 4	⇩	1.20	0.005
BC035736	3442249	PIANP	PILR alpha associated neural protein	⇩	1.22	0.003
NM_017831	3783723	RNF125	ring finger protein 125	⇧	1.49	0.005
NM_015474	3904691	SAMHD1	SAM domain and HD domain 1	⇧	1.41	8.63E-04
NM_021966	3578152	TCL1A	T-cell leukemia/lymphoma 1A	⇧	1.23	0.004
NM_006068	2766262	TLR6	toll-like receptor 6	⇩	1.39	8.88E-04
NM_001561	2395146	TNFRSF9	tumor necrosis factor receptor superfamily, member 9	⇩	1.28	0.036
NM_003701	3487299	TNFSF11	tumor necrosis factor (ligand) superfamily, member 11	⇧	1.38	0.004

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_003141	3360142	TRIM21	tripartite motif-containing 21	⇧	1.21	0.021
NM_015294	3764680	TRIM37	tripartite motif-containing 37	⇧	1.21	3.47E-05
NM_198057	4017381	TSC22D3	TSC22 domain family, member 3	⇩	1.30	0.029

Ion Binding

NM_002197	3166477	ACO1	aconitase 1, soluble	⇧	1.25	0.001
NM_000146	3838094	FTL	ferritin, light polypeptide	⇩	1.53	0.001
NM_003234	2712632	TFRC	transferrin receptor (p90, CD71)	⇩	1.23	4.19E-05

Membrane Trafficking

NM_001089	3676763	ABCA3	ATP-binding cassette, sub-family A (ABC1), member 3	⇩	1.23	7.28E-04
NM_018672	3768969	ABCA5	ATP-binding cassette, sub-family A (ABC1), member 5	⇩	1.30	0.001
NM_005689	2599993	ABCB6	ATP-binding cassette, sub-family B (MDR/TAP), member 6	⇩	1.28	9.71E-07
NM_00102509	2901687	ABCF1	ATP-binding cassette, sub-family F (GCN20), member 1	⇧	1.20	3.21E-05
NM_173872	2751385	CLCN3	chloride channel 3	⇩	1.22	5.66E-05
NM_004004	3504193	GJB2	gap junction protein, beta 2, 26kDa	⇧	1.38	0.033
NM_005497	3759335	GJC1	gap junction protein, gamma 1, 45kDa	⇩	1.58	0.018
NM_020401	3421177	N⇧107	nucleoporin 107kDa	⇧	1.24	2.36E-04
NM_024057	3468261	N⇧37	nucleoporin 37kDa	⇧	1.20	0.001
NM_018698	3986933	NXT2	nuclear transport factor 2-like export factor 2	⇧	1.21	0.009
NM_002560	3434760	P2RX4	purinergic receptor P2X, ligand-gated ion channel, 4	⇩	1.26	0.001
NM_002561	3741547	P2RX5	purinergic receptor P2X, ligand-gated ion channel, 5	⇩	1.45	0.025
NM_001042496	3617312	SLC12A6	solute carrier family 12 (potassium/chloride transporters), member 6	⇩	1.20	0.002
NM_016582	3375091	SLC15A3	solute carrier family 15, member 3	⇩	1.22	0.025
NM_145648	3477917	SLC15A4	solute carrier family 15, member 4	⇩	1.23	4.94E-05
NM_018593	2921402	SLC16A10	solute carrier family 16, member 10 (aromatic amino acid transporter)	⇩	1.43	0.004
NM_005116	3896078	SLC23A2	solute carrier family 23 (nucleobase transporters), member 2	⇩	1.50	0.010
NM_024103	3847873	SLC25A23	solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 23	⇧	1.31	4.07E-04
AF495725	3090053	SLC25A37	solute carrier family 25, member 37	⇩	1.20	0.028
NM_133496	2349043	SLC30A7	solute carrier family 30 (zinc transporter), member 7	⇩	1.20	7.71E-04
NM_004733	2701927	SLC33A1	solute carrier family 33 (acetyl-CoA transporter), member 1	⇩	1.27	0.003
NM_012243	2348702	SLC35A3	solute carrier family 35 (UDP-N-acetylglucosamine (UDP-GlcNAc) transporter), member A3	⇩	1.23	0.003
NM_017945	2636185	SLC35A5	solute carrier family 35, member A5	⇩	1.21	0.002
NM_178148	2955061	SLC35B2	solute carrier family 35, member B2	⇩	1.31	0.002

Table B10: Non*C9ORF72*-Related_*SALS* Specific Gene List (n=1,201) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_024881	3854000	SLC35E1	solute carrier family 35, member E1	⇩	1.20	3.61E-05
NM_025181	2571979	SLC35F5	solute carrier family 35, member F5	⇩	1.21	1.34E-04
NM_014437	2436378	SLC39A1	solute carrier family 39 (zinc transporter), member 1	⇩	1.22	2.59E-05
NM_001128431	3089360	SLC39A14	solute carrier family 39 (zinc transporter), member 14	⇩	1.23	0.032
NM_006979	2903470	SLC39A7	solute carrier family 39 (zinc transporter), member 7	⇩	1.28	0.002
NM_001012661	3333711	SLC3A2	solute carrier family 3 (activators of dibasic and neutral amino acid transport), member 2	⇩	1.27	8.12E-04
NM_018112	3183364	TMEM38B	transmembrane protein 38B	⇩	1.39	8.37E-04
NM_003304	2645951	TRPC1	transient receptor potential cation channel, subfamily C, member 1	⇩	1.46	2.82E-04
NM_032646	3734236	TTYH2	tweety homolog 2 (*Drosophila*)	⇩	1.38	0.004

Metabolism

NM_017436	3962578	A4GALT	alpha 1,4-galactosyltransferase	⇧	1.22	0.026
NM_005763	3070183	AASS	aminoadipate-semialdehyde synthase	⇩	1.33	0.002
NR_033426	2641341	ACAD9	acyl-CoA dehydrogenase family, member 9	⇧	1.21	0.012
NM_005891	2934131	ACAT2	acetyl-CoA acetyltransferase 2	⇧	1.22	0.006
NM_152331	3543714	ACOT4	acyl-CoA thioesterase 4	⇧	1.27	0.002
NM_001099	2642720	ACPP	acid phosphatase, prostate	⇩	1.28	0.048
NM_001995	2796553	ACSL1	acyl-CoA synthetase long-chain family member 1	⇩	1.21	0.001
NM_001159280	3591365	ADAL	adenosine deaminase-like	⇧	1.21	0.002
NM_006721	3252170	ADK	adenosine kinase	⇧	1.20	0.002
NM_000026	3946351	ADSL	adenylosuccinate lyase	⇧	1.24	1.04E-04
NM_018361	3083936	AGPAT5	1-acylglycerol-3-phosphate O-acyltransferase 5 (lysophosphatidic acid acyltransferase, epsilon)	⇩	1.24	1.44E-05
NM_003659	2517408	AGPS	alkylgylcerone phosphate synthase	⇧	1.27	1.04E-05
NM_000696	2442103	ALDH9A1	aldehyde dehydrogenase 9 family, member A1	⇧	1.27	2.66E-04
NM_015957	3369249	APIP	APAF1 interacting protein	⇧	1.44	0.040
NM_177924	3126087	ASAH1	N-acylsphingosine amidohydrolase (acid ceramidase) 1	⇩	1.27	4.39E-04
NM_006085	2456805	BPNT1	3’(2’), 5’-bisphosphate nucleotidase 2	⇧	1.23	2.61E-04
NM_000078	3662417	CETP	cholesteryl ester transfer protein, plasma	⇩	1.20	0.029
NM_138809	2848265	CMBL	carboxymethylenebute nolidase homolog (*Pseudomonas*)	⇧	1.39	0.002
NM_001905	2332144	CTPS	CTP synthase	⇧	1.30	0.001
NM_000774	3833967	CYP2F1	cytochrome P450, family 2, subfamily F, polypeptide 1	⇩	1.28	0.038
NM_015954	3406493	DERA	deoxyribose-phosphate aldolase (putative)	⇧	1.31	7.62E-04
NM_016029	3567187	DHRS7	dehydrogenase/reductase (SDR family) member 7	⇩	1.26	2.67E-05

Table B10: Non*C9ORF72*-Related_*SALS* Specific Gene List (n=1,201) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_005700	3336238	DPP3	dipeptidyl-peptidase 3	⇧	1.23	0.014
NM_138924	3845175	GAMT	guanidinoacetate N-methyltransferase	⇧	1.21	0.014
NM_000161	3565524	GCH1	GTP cyclohydrolase 1	⇧	1.23	0.008
NM_000169	4015763	GLA	galactosidase, alpha	⇩	1.27	0.017
NM_000405	2835792	GM2A	GM2 ganglioside activator	⇩	1.23	0.003
NM_002079	3302990	GOT1	glutamic-oxaloacetic transaminase 1, soluble (aspartate aminotransferase 1)	⇧	1.21	0.003
NM_000521	2815791	HEXB	hexosaminidase B	⇩	1.21	8.27E-04
NM_002035	3811459	KDSR	ketodihydrosphingosine reductase	⇩	1.21	9.42E-05
NM_000221	2474240	KHK	ketohexokinase (fructokinase)	⇧	1.46	0.007
NM_001145437	3935243	LSS	lanosterol synthase (2,3-oxidosqualene-lanosterol cyclase)	⇩	1.26	0.003
NM_002395	2962820	ME1	malic enzyme 1, NADP(+)-dependent, cytosolic	⇧	1.52	0.003
NM_018396	3022841	METTL2B	methyltransferase like 2B	⇩	1.25	4.25E-04
NM_004685	3506153	MTMR6	myotubularin related protein 6	⇧	1.30	6.90E-04
NM_000434	2949471	NEU1	sialidase 1 (lysosomal sialidase)	⇩	1.28	1.10E-04
NM_198175	3726934	NME1	non-metastatic cells 1, protein (NM23A) expressed in	⇧	1.37	2.41E-04
NM_002513	3676113	NME3	non-metastatic cells 3, protein expressed in	⇩	1.29	6.63E-05
NM_024829	3445544	PLBD1	phospholipase B domain containing 1	⇧	1.29	0.002
NM_018129	3724969	PNPO	pyridoxamine 5’-phosphate oxidase	⇧	1.22	0.009
NM_002778	3293762	PSAP	prosaposin	⇩	1.20	0.003
NM_144660	3252534	SAMD8	sterile alpha motif domain containing 8	⇩	1.20	0.004
NR_027783	3971806	SAT1	spermidine/spermine N1-acetyltransferase 1	⇩	1.21	0.014
NM_030791	3568108	SGPP1	sphingosine-1-phosphate phosphatase 1	⇩	1.21	0.004
NM_000199	3773340	SGSH	N-sulfoglucosamine sulfohydrolase	⇩	1.29	4.52E-06
NM_021947	3706219	SRR	serine racemase	⇧	1.34	0.009
NM_003896	2562529	ST3GAL5	ST3 beta-galactoside alpha-2,3-sialyltransferase 5	⇩	1.31	0.002
NM_006755	3316208	TALDO1	transaldolase 1	⇧	1.29	8.50E-05
NR_027483	3402935	TPI1	triosephosphate isomerase 1	⇩	1.23	0.003
NM_022445	3077766	TPK1	thiamin pyrophosphokinase 1	⇧	1.26	6.13E-05
NM_000375	3311715	UROS	uroporphyrinogen III synthase	⇧	1.26	2.67E-04

Mitochondrion & the Respiratory Electron Transport Chain

NM_000690	3432090	ALDH2	aldehyde dehydrogenase 2 family (mitochondrial)	⇧	1.36	0.006
NM_017812	3073597	CHCHD3	coiled-coil-helix-coiled-coil-helix domain containing 3	⇧	1.35	3.94E-05

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_015697	2775965	COQ2	coenzyme Q2 homolog, prenyltransferase (yeast)	⇧	1.32	0.011
NM_016035	3190339	COQ4	coenzyme Q4 homolog (*S. cerevisiae*)	⇧	1.23	5.94E-06
NM_004077	3457614	CS	citrate synthase	⇧	1.27	6.36E-04
NM_030579	3666732	CYB5B	cytochrome b5 type B (outer mitochondrial membrane)	⇧	1.22	5.14E-06
NM_001359	3106310	DECR1	2,4-dienoyl CoA reductase 1, mitochondrial	⇧	1.22	0.002
NM_001931	3348852	DLAT	dihydrolipoamide S-acetyltransferase	⇧	1.23	7.26E-05
NM_024417	3770457	FDXR	ferredoxin reductase	⇧	1.21	4.27E-04
NM_001012515	3809621	FECH	ferrochelatase	⇧	1.28	8.80E-05
NM_017547	3355056	FOXRED1	FAD-dependent Oxidoreductase domain containing 1	⇧	1.30	0.001
NM_000144	3173831	FXN	frataxin	⇧	1.22	0.002
NM_025196	2759404	GRPEL1	GrpE-like 1, mitochondrial (*E. coli*)	⇧	1.30	2.18E-06
NM_005333	3968664	HCCS	holocytochrome c synthase	⇧	1.23	0.018
NM_004493	4009288	HSD17B10	hydroxysteroid (17-beta) dehydrogenase 10	⇧	1.20	0.007
NM_016098	2984616	MPC1	mitochondrial pyruvate carrier 1	⇧	1.29	3.26E-04
NM_018116	2360989	MSTO1	misato homolog 1 (*Drosophila*)	⇩	1.23	0.003
NM_014342	3372368	MTCH2	mitochondrial carrier homolog 2 (*C. elegans*)	⇧	1.21	6.69E-06
ENST0000361681	4037708	ND6	NADH dehydrogenase, subunit 9 (complex I)	⇩	1.34	0.020
NM_17883	2780099	NHEDC2	Na+/H+ exchanger domain containing 2	⇩	1.24	0.011
NM_001161778	3107342	PDP1	pyruvate dehydrogenase phosphatase catalytic subunit 1	⇧	1.23	7.41E-04
NM_018292	2919873	QRSL1	glutaminyl-tRNA synthase (glutamine-hydrolyzing)-like 1	⇧	1.31	3.51E-04
NM_003850	3513293	SUCLA2	succinate-CoA ligase, ADP-forming, beta subunit	⇧	1.33	1.05E-05
AK295839	2663083	TAMM41	TAM41, mitochondrial translocation assembly and maintenance protein homolog (*S. cerevisiae*)	⇩	1.29	0.005
NM_003201	3247784	TFAM	transcription factor A, mitochondrial	⇧	1.20	0.002
NM_012456	3373946	TIMM10	translocase of inner mitochondrial membrane 10 homolog (yeast)	⇧	1.44	0.001
NM_006335	2374956	TIMM17A	translocase of inner mitochondrial membrane 17 homolog A (yeast)	⇧	1.25	0.020

Neurotransmission

NM_004857	3540068	AKAP5	A kinase (PRKA) anchor protein 5	⇧	1.24	0.002
NM_000721	2370433	CACNA1E	calcium channel, voltage-dependent, R type, alpha 1E subunit	⇩	1.36	0.047
NM_005183	4007919	CACNA1F	calcium channel, voltage-dependent, L type, alpha 1F subunit	⇩	1.20	0.003
NM_001039771	3558270	CBLN3	cerebellin 3 precursor	⇩	1.22	0.013
NM_014848	3608638	SV2B	synaptic vesicle glycoprotein 2B	⇩	1.38	9.29E-04
NM_152280	2361154	SYT11	synaptotagmin XI	⇩	1.31	1.32E-04

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_199245	3441941	VAMP1	vesicle-associated membrane protein 1 (synaptobrevin 1)	⇩	1.32	0.001

Nucleosome

NM_014034	2923359	ASF1A	ASF1 anti-silencing function 1 homolog A (*S. cerevisiae*)	⇧	1.23	0.006
NM_012412	3639479	H2AFV	H2A histone family, member V	⇧	1.22	9.15E-04
NM_002105	3394183	H2AFX	H2A histone family, member X	⇧	1.24	9.11E-05
NM_004893	2876479	H2AFY	H2A histone family, member Y	⇧	1.24	0.001
NM_005324	3770944	H3F3B	H3 histone, family 3B (H3.3B)	⇧	1.26	0.024
NM_003642	2515369	HAT1	histone acetlytransferase 1	⇧	1.35	1.62E-04
NM_005322	2947073	HIST1H1B	histone cluster 1, H1b	⇧	1.39	0.003
NM_021058	2946681	HIST1H2BJ	histone cluster 1, H2bj	⇧	1.29	0.014
NM_080593	2946714	HIST1H2BK	histone cluster 1, H2bk	⇧	1.37	0.009
NM_003529	2899090	HIST1H3A	histone cluster 1, H3a	⇧	1.22	0.041
NM_003531	2899102	HIST1H3C	histone cluster 1, H3c	⇧	1.22	0.006
NM_003535	2947095	HIST1H3J	histone cluster 1, H3j	⇧	1.47	0.002
NM_003545	2899216	HIST1H4E	histone cluster 1, H4e	⇧	1.21	0.024
NM_003543	2946383	HIST1H4H	histone cluster 1, H4h	⇧	1.25	0.011
NM_004537	3462843	NAP1L1	nucleosome assembly protein 1-like 1	⇧	1.29	0.005

Protein Processing

NM_018672	3768969	AAGAB	alpha- and gamma-adaptin binding protein	⇧	1.33	1.16E-06
NM_001144	3692856	AMFR	autocrine motility factor receptor	⇩	1.21	0.001
NM_003916	4000704	AP1S2	adaptor-related protein complex 1, sigma 2 subunit	⇧	1.20	4.13E-04
NM_007347	3593770	AP4E1	adaptor-related protein complex 4, epsilon 1 subunit	⇧	1.20	4.13E-04
NM_006577	2484841	B3GNT2	UDP-GlcNAc:betaGalbeta-1,3-N-acetylglucosaminyltransferase 2	⇩	1.28	8.53E-05
NM_033637	3261165	BTRC	beta-transducin repeat containing E3 ubiquitin protein ligase	⇧	1.24	7.21E-08
NM_012073	2801526	CCT5	chaperonin containing TCP1, subunit 5 (epsilon)	⇧	1.32	2.80E-04
NM_001083314	3704896	CHMP1A	charged multivesicular body protein 1A	⇧	1.20	1.46E-05
NM_152284	3105033	CHMP4C	charged multivesicular body protein 4C	⇧	1.21	0.006
NM_006493	3494502	CLN5	ceroid-lipofuscinosis, neuronal 5	⇩	1.40	4.52E-07
NM_153607	2841491	CREBRF	CREB3 regulatory factor	⇩	1.36	0.002
NM_004388	2420467	CTBS	chitobiase, di-N-acetyl-	⇩	1.22	0.022
NM_147780	3124537	CTSB	cathepsin B	⇩	1.42	3.96E-05
NM_001909	3358950	CTSD	cathepsin D	⇩	1.25	0.002

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NM_004079	2434575	CTSS	cathepsin S	⇩	1.21	2.48E-04
NM_006145	3852783	DNAJB1	DnaJ (Hsp40) homolog, subfamily B, member 1	⇧	1.28	0.001
NM_058246	3034027	DNAJB6	DnaJ (Hsp40) homolog, subfamily B, member 6	⇧	1.27	0.004
NM_012328	3018866	DNAJB9	DnaJ (Hsp40) homolog, subfamily B, member 9	⇩	1.28	0.044
NM_018198	2394841	DNAJC11	DnaJ (Hsp40) homolog, subfamily C, member 11	⇧	1.25	2.59E-04
NR_037148	3184940	DNAJC25	DnaJ (Hsp40) homolog, subfamily C, member 25	⇩	1.21	6.79E-04
NM_003315	3757487	DNAJC7	DnaJ (Hsp40) homolog, subfamily C, member 7	⇧	1.23	3.66E-06
NM_001402	2960903	EEF1A1	eukaryotic translation elongation factor 1 alpha 1	⇩	1.29	5.02E-05
NR_027062	3484436	EEF1DP3	eukaryotic translation elongation factor 1 delta pseudogene 3	⇩	1.30	7.07E-04
NM_004280	2940920	EEF1E1	eukaryotic translation elongation factor 1 epsilon 1	⇧	1.27	0.008
NM_032325	3378024	EIF1AD	eukaryotic translation initiation factor 1A domain containing	⇧	1.20	2.52E-05
NM_004681	4031136	EIF1AY	eukaryotic translation initiation factor 1A, Y-linked	⇧	1.67	0.016
NM_004836	2563654	EIF2AK3	eukaryotic translation initiation factor 2-alpha kinase 3	⇩	1.24	0.003
NM_020365	2409904	EIF2B3	eukaryotic translation initiation factor 2B, subunit 3 gamma, 58kDa	⇧	1.44	1.29E-04
NM_004096	3250699	EIF4EBP2	eukaryotic translation initiation factor 4E binding protein 2	⇧	1.32	6.27E-05
NM_001418	3362719	EIF4G2	eukaryotic translation initiation factor 4 gamma, 2	⇧	1.22	3.89E-06
NM_015904	2495881	EIF5B	eukaryotic translation initiation factor 5B	⇧	1.21	3.32E-04
NM_019053	3258260	EXOC6	exocyst complex component 6	⇧	1.26	0.011
NM_052966	2447877	FAM129A	family with sequence similarity 129, member A	⇧	1.33	0.015
NM_012166	3205506	FBXO10	F-box protein 10	⇧	1.23	7.68E-04
NM_012176	2807886	FBXO4	F-box protein 4	⇧	1.20	0.003
NM_017946	3043936	FKBP14	FK506 binding protein 14, 22kDa	⇩	1.43	1.31E-04
NM_002013	3562721	FKBP3	FK506 binding protein 3, 25kDa	⇧	1.24	0.003
NM_198335	3375951	GANAB	glucosidase, alpha; neutral AB	⇩	1.22	3.26E-04
NM_001097634	3175494	GCNT1	glucosaminyl (N-acetyl) transferase 1, core 2	⇧	1.56	0.013
NM_004751	3596147	GCNT3	glucosaminyl (N-acetyl) transferase 3, mucin type	⇩	1.25	0.041
NM_005836	3145980	HRSP12	heat-responsive protein 12	⇧	1.26	0.004
NM_018085	2374872	IPO9	importin 9	⇧	1.20	5.82E-04
NM_002267	3513883	KPNA3	karyopherin alpha 3 (importin alpha 4)	⇧	1.21	4.29E-05
NM_022126	3269065	LHPP	phospholysine phosphohistidine inorganic pyrophosphate phosphatase	⇧	1.21	2.99E-04
NM_005570	3810472	LMAN1	lectin, mannose-binding, 1	⇩	1.32	6.32E-07
NM_005907	2971801	MAN1A1	mannosidase, alpha, class 1A, member 1	⇩	1.28	0.003
NM_024641	2917767	MANEA	mannosidase, endo-alpha	⇩	1.27	0.032

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NM_005885	2801608	MARCH6	membrane-associated ring finger (C3HC4) 6	⇩	1.24	1.66E-06
NM_006838	3426917	METAP2	methionyl aminopeptidase 2	⇧	1.21	8.83E-04
NM_020236	2732611	MRPL1	mitochondrial ribosomal protein L1	⇧	1.28	0.001
NM_014078	3150797	MRPL13	mitochondrial ribosomal protein L13	⇧	1.21	0.004
NM_022915	2529782	MRPL44	mitochondrial ribosomal protein L44	⇧	1.21	0.040
NM_022163	3638048	MRPL46	mitochondrial ribosomal protein L46	⇧	1.29	0.001
NM_019051	3218067	MRPL50	mitochondrial ribosomal protein L50	⇧	1.20	0.045
NM_015969	3003143	MRPS17	mitochondrial ribosomal protein S17	⇧	1.46	0.014
NM_018997	2358153	MRPS21	mitochondrial ribosomal protein S21	⇩	1.27	2.34E-05
NM_016070	3764002	MRPS23	mitochondrial ribosomal protein S23	⇧	1.24	0.013
NM_005830	3510925	MRPS31	mitochondrial ribosomal protein S31	⇧	1.24	0.002
NM_023936	3676127	MRPS34	mitochondrial ribosomal protein S34	⇧	1.34	4.23E-07
NM_021821	3409330	MRPS35	mitochondrial ribosomal protein S35	⇧	1.23	0.001
NM_033281	2813465	MRPS36	mitochondrial ribosomal protein S36	⇧	1.21	5.15E-04
NM_031902	2564599	MRPS5	mitochondrial ribosomal protein S5	⇧	1.20	0.003
NM_003491	4026902	NAA10	N(alpha)-acetyltransferase 10, NatA catalytic subunit	⇧	1.20	0.001
NM_022080	3901191	NAPB	N-ethylmaleimide-sensitive factor attachment protein, beta	⇩	1.40	4.37E-06
NM_005381	2603460	NCL	nucleolin	⇧	1.23	3.41E-05
NM_173474	3681674	NTAN1	N-terminal asparagine amidase	⇧	1.21	0.002
NM_016118	3032017	NUB1	negative regulator of ubiquitin-like proteins	⇧	1.21	0.004
NM_016297	2487696	PCYOX1	prenylcysteine oxidase 1	⇩	1.28	0.018
NM_001185181	2903588	PFDN6	prefoldin subunit 6	⇧	1.21	3.48E-04
NM_005482	2418929	PIGK	phosphatidylinositol glycan anchor biosynthesis, class K	⇩	1.23	0.045
NM_004278	3711986	PIGL	phosphatidylinositol glycan anchor biosynthesis, class L	⇩	1.33	1.75E-05
NM_033198	3750740	PIGS	phosphatidylinositol glycan anchor biosynthesis, class S	⇩	1.20	0.002
NM_178517	3719150	PIGW	phosphatidylinositol glycan anchor biosynthesis, class W	⇧	1.20	0.011
NM_032906	2777412	PIGY	phosphatidylinositol glycan anchor biosynthesis, class Y	⇧	1.20	0.021
NM_015227	3934867	POFUT2	protein O-fucosyltransferase 2	⇩	1.28	2.61E-06
NM_014337	3938244	PPIL2	peptidylprolyl isomerase (cyclophilin)-like 2	⇧	1.21	3.70E-04
NM_002795	3719962	PSMB3	proteasome (prosome, macropain) subunit, beta type, 3	⇧	1.33	0.002
NM_002803	3017206	PSMC2	proteasome (prosome, macropain) 26S subunit, ATPase, 2	⇧	1.33	0.009
NM_002807	2531712	PSMD1	proteasome (prosome, macropain) 26S subunit, non-ATPase, 1	⇧	1.30	2.24E-04
NM_002815	3717737	PSMD11	proteasome (prosome, macropain) 26S subunit, non-ATPase, 11	⇧	1.24	2.07E-05

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NM_014814	2679864	PSMD6	proteasome (prosome, macropain) 26S subunit, non-ATPase, 6	⇧	1.30	4.44E-06
NM_002818	3557811	PSME2	proteasome (prosome, macropain) activator subunit 2 (PA28 beta)	⇧	1.27	0.041
NM_004578	2384562	RAB4A	RAB4A. member RAS oncogene family	⇧	1.24	0.005
NM_201434	3757664	RAB5C	RAB5C, member RAS oncogene family	⇧	1.20	0.003
NM_002869	3381607	RAB6A	RAB6A, member RAS oncogene family	⇧	1.35	0.009
NM_005370	3823554	RAB8A	RAB8A, member RAS oncogene family	⇧	1.26	2.03E-04
NM_002871	245149	RABIF	RAB interacting factor	⇧	1.21	0.030
NM_006013	3996306	RPL10	ribosomal protein L10	⇩	1.36	5.40E-04
NM_033251	3674146	RPL13	ribosomal protein L13	⇩	1.29	0.016
NM_000985	3807487	RPL17	ribosomal protein L17	⇩	1.28	0.004
NR_002229	2482683	RPL23AP32	ribosomal protein L23a pseudogene 32	⇩	1.23	0.007
NR_026982	3951136	RPL23AP82	ribosomal protein L23a pseudogene 82	⇩	1.21	0.002
NM_000969	2346863	RPL5	ribosomal protein L5	⇩	1.28	8.73E-05
NR_002775	3333086	RPLP0P2	ribosomal protein, large, P0 pseudogene 2	⇩	1.22	0.003
NM_002950	2694397	RPN1	ribophorin I	⇩	1.21	0.002
NM_001008	4028512	RPS4Y1	ribosomal protein S4, Y-linked 1	⇧	1.61	0.041
NM_018144	3235414	SEC61A2	Sec61 alpha 2 subunit (*S. cerevisiae*)	⇩	1.27	2.89E-05
NM_005065	3574207	SEL1L	sel-1 suppressor of lin-12-like 1 (*C. elegans*)	⇩	1.24	3.60E-05
NM_015670	3708798	SENP3	SUMO1/sentrin/SMT3 specific peptidase 3	⇧	1.21	8.04E-05
NM_001037633	2877639	SIL1	SIL1 homolog, endoplasmic reticulum chaperone (*S. cerevisiae*)	⇩	1.35	0.001
NM_153816	2963313	SNX14	sorting nexin 14	⇩	1.23	1.94E-04
NM_002959	2427007	SORT1	sortilin 1	⇧	1.56	0.013
NM_001002255	2930698	SUMO4	SMT3 suppressor of mif two 3 homolog 4 (*S. cerevisiae*)	⇩	1.34	0.001
NM_201631	3621080	TGM5	transglutaminase 5	⇩	1.40	0.010
NM_007364	3603687	TMED3	transmembrane emp24 protein transport domain containing 3	⇩	1.24	1.81E-05
NM_182547	3048778	TMED4	transmembrane emp24 protein transport domain containing 4	⇩	1.30	5.78E-06
NM_015476	3804358	TPGS2	tubulin polyglutamylase complex subunit 2	⇧	1.29	5.57E-05
NM_000391	3361041	TPP1	tripeptidyl peptidase I	⇩	1.21	0.002
NM_018955	3712041	UBB	ubiquitin B	⇧	1.25	0.003
NM_003336	3988874	UBE2A	ubiquitin-conjugating enzyme E2A (RAD6 homolog)	⇧	1.20	0.006
NM_003337	2829275	UBE2B	ubiquitin-conjugating enzyme E2B (RAD6 homolog)	⇩	1.20	0.020
NM_020131	2437893	UBQLN4	ubiquilin 4	⇧	1.22	0.025
NM_175748	3549220	UBR7	ubiquitin protein ligase E3 component n-recognin 7 (putative)	⇧	1.38	7.44E-04

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NM_004181	2725013	UCHL1	ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase)	⇧	1.53	0.024
NM_015984	2448971	UCHL5	ubiquitin carboxyl-terminal hydrolase L5	⇧	1.20	6.48E-04
NM_001040697	3365487	UEVLD	UEV and lactate/malate dehydrogenase domains	⇧	1.24	0.001
NM_003940	2654091	USP13	ubiquitin specific peptidase 13 (isopeptidase T-3)	⇧	1.20	0.004
NM_020718	3685051	USP31	ubiquitin specific peptidase 31	⇧	1.21	2.48E-05
NM_022832	2769063	USP46	ubiquitin specific peptidase 46	⇧	1.22	0.001
NM_004505	3748400	USP6	ubiquitin specific peptidase 6 (Tre-2 oncogene)	⇩	1.46	1.73E-04
NM_004654	4030063	USP9Y	ubiquitin specific peptidase 9, Y-linked	⇧	1.43	0.015
NM_024667	3475838	VPS37B	vacuolar protein sorting 37 homolog B (*S. cerevisiae*)	⇧	1.21	0.022
NM_006370	3569374	VTI1B	vesicle transport through interaction with t-SNAREs homolog 1B (yeast)	⇧	1.30	0.012
NM_007014	3666897	WWP2	WW domain containing E3 ubiquitin protein ligase 2	⇧	1.25	2.19E-05
NM_001102420	3209623	ZFAND5	zinc finger, AN1-type domain 5	⇩	1.30	4.01E-04
NM_144588	3260018	ZFYVE27	zinc finger, FYVE domain containing 27	⇩	1.29	4.40E-07

RNA Processing

NR_036460	3699707	ADAT1	adenosine deaminase, tRNA-specific 1	⇧	1.28	7.55E-04
NM_006303	2988882	AIMP2	aminoacyl tRNA synthetase complex-interacting multifunctional protein 2	⇧	1.25	0.004
NM_001042476	3679533	CARHSP1	calcium regulated heat stable protein 1, 24kDa	⇧	1.21	6.62E-04
NM_030937	2391532	CCNL2	cyclin L2	⇩	1.21	0.005
NR_027856	2594497	CLK1	CDC-like kinase 1	⇩	1.36	8.73E-04
NM_020666	2889698	CLK4	CDC-like kinase 4	⇩	1.32	5.00E-05
NM_017437	3548788	CPSF2	cleavage and polyadenylation specific factor 2, 100kDa	⇧	1.21	3.91E-04
NM_016207	2468920	CPSF3	cleavage and polyadenylation specific factor 3, 73kDa	⇧	1.26	1.40E-05
NM_016652	3899954	CRNKL1	crooked neck pre-mRNA splicing factor-like 1 (*Drosophila*)	⇧	1.21	9.28E-05
NM_030877	3884324	CTNNBL1	catenin, beta like 1	⇧	1.23	2.00E-05
NM_005869	2812120	CWC27	CWC27 spliceosome-associated protein homolog (*S. cerevisiae*)	⇧	1.22	0.003
NM_004939	2470654	DDX1	DEAD (Asp-Glu-Ala-Asp) box polypeptide 1	⇧	1.26	1.53E-04
NM_00112266	4030162	DDX3Y	DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, Y-linked	⇧	1.64	0.028
NM_014314	3203086	DDX58	DEAD (Asp-Glu-Ala-Asp) box polypeptide 58	⇧	1.29	0.016
NM_022720	3937183	DGCR8	DiGeorge syndrome critical region gene 8	⇧	1.25	3.30E-05
NM_198963	2549007	DHX57	DEAH (Asp-Glu-Ala-Asp/His) box polypeptide 57	⇧	1.24	0.001
NR_033302	2370991	DHX9	DEAH (Asp-Glu-Ala-Asp/His) box polypeptide 9	⇧	1.21	0.015
NM_133375	3598613	DIS3L	DIS3 mitotic control homolog (*S. cerevisiae*)-like	⇧	1.20	0.006

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_001363	3996667	DKC1	dyskeratosis congenita 1, dyskerin	⇧	1.26	3.63E-05
NM_013235	2851965	DROSHA	drosha, ribonuclease type III	⇧	1.20	3.80E-04
NM_014285	3191695	EXOSC2	exosome component 2	⇧	1.27	3.17E-06
NM_015962	3544216	FCF1	FCF1 small subunit (SSU) prcessome component homolog (*S. cerevisiae*)	⇧	1.22	0.001
NM_017647	3766373	FTSJ3	FtsJ homolog 3 (*E. coli*)	⇧	1.21	0.002
NM_015721	3739812	GEMIN4	gem (nuclear organelle) associated protein 4	⇧	1.24	2.11E-04
NM_031370	2775463	HNRNPD	heterogeneous nuclear ribonucleoprotein D (AU-rich element RNA binding protein 1, 37kDa)	⇧	1.21	1.03E-05
NM_033416	2505501	IMP4	IMP4, U3 small nucleolar ribonucleoprotein, homolog (yeast)	⇧	1.22	2.50E-04
NM_017813	3136413	IMPAD1	inositol monophosphatase domain containing 1	⇩	1.26	0.011
NM_020701	2694617	ISY1	ISY1 splicing factor homolog (*S. cerevisiae*)	⇧	1.31	3.26E-05
NM_007080	2746269	LSM6	LSM6 homolog, U6 small nuclear RNA associated (*S. cerevisiae*)	⇧	1.23	1.29E-04
NM_016424	3726772	LUC7L3	LUC7-like 3 (*S. cerevisiae*)	⇩	1.20	0.004
NM_018388	4022106	MBNL3	muscleblind-like splicing regulator 3	⇧	1.25	0.006
NM_002486	3181302	NCBP1	nuclear cap binding protein subunit 1, 80kDa	⇧	1.21	0.002
NM_001145408	3980887	NONO	non-POU domain containing, octamer-binding	⇧	1.29	1.45E-04
NM_003703	2758076	NOP14	NOP14 nucleolar protein homolog (yeast)	⇧	1.23	4.09E-05
NM_032141	2343170	NSRP1	nuclear speckle splicing regulatory protein 1	⇩	1.21	2.12E-04
NM_005016	3416036	PCBP2	poly(rC) binding protein 2	⇧	1.23	0.011
NM_031307	3396736	PUS3	pseudouridylate synthase 3	⇧	1.26	6.95E-04
NM_016732	3882720	RALY	RNA binding protein, autoantigenic (hnRNP-associated with lethal yellow (mouse))	⇧	1.22	6.04E-06
NM_017793	3633236	RPP25	ribonuclease P/MRP 25kDa subunit	⇧	1.30	7.51E-05
NM_015056	3923218	RRP1B	ribosomal RNA processing 1 homolog B (*S. cerevisiae*)	⇧	1.22	0.001
NM_016625	2649532	RSRC1	arginine/serine-rich coiled-coil 1	⇧	1.39	4.09E-05
NM_006802	2407439	SF3A3	splicing factor 3a, subunit 3, 60kDa	⇧	1.20	1.18E-06
NM_005066	2406064	SFPQ	splicing factor proline/glutamine-rich	⇧	1.24	2.23E-04
NM_006527	2757319	SLBP	stem-loop binding protein	⇧	1.28	0.003
NM_024571	3642572	SNRNP25	small nuclear ribonucleoprotein 25kDa (U11/U12)	⇧	1.32	3.29E-05
NM_003093	2904248	SNRPC	small nuclear ribonucleoprotein polypeptide C	⇧	1.24	7.91E-04
NM_006938	3781082	SNRPD1	small nuclear ribonucleoprotein polypeptide 16kDa	⇧	1.43	7.62E-05
NM_005701	3633522	SNUPN	snurportin 1	⇧	1.22	0.002
NM_003142	2514566	SSB	Sjogren syndrome antigen B (autoantigen La)	⇧	1.21	7.59E-06
NM_014393	3140640	STAU2	staufen, RNA binding protein, homolog 2 (*Drosophila*)	⇧	1.22	7.68E-04
NM_001159677	2963407	SYNCRIP	synaptotagmin binding, cytoplasmic RNA interacting protein	⇧	1.23	0.002

Table B10: Non*C9ORF72*-Related_*SALS* Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_152295	2805786	TARS	threonyl-tRNA synthetase	⇧	1.24	0.005
NM_014290	3181193	TDRD7	tudor domain containing 7	⇧	1.22	4.97E-04
NM_024831	3098935	TGS1	trimethylguanosine synthase 1	⇧	1.26	6.41E-05
NM_017872	2837479	THG1L	tRNA-histidine guanylyltransferase 1-like (*S. cerevisiae*)	⇧	1.20	7.90E-04
AB052759	3041550	TRA2A	transformer 2 alpha homolog (*Drosophila*)	⇩	1.31	0.013
NM_004593	2709062	TRA2B	transformer 2 beta homolog (*Drosophila*)	⇧	1.23	1.82E-05
NM_006701	3814734	TXNL4A	thioredoxin-like 4A	⇧	1.24	2.86E-04
NM_016037	2330899	UTP11L	UTP11-like, U3 small nucleolar ribonucleoprotein, (yeast)	⇧	1.27	0.001
NM_006649	3990566	UTP14A	UTP14, U3 small nucleolar ribonucleoprotein, homolog A (yeast)	⇧	1.40	3.24E-06
NM_014503	3428447	UTP20	UTP20, small subunit (SSU) processome component, homolog (yeast)	⇧	1.20	0.007
NM_018428	3752437	UTP6	UTP6, small subunit (SSU) processome component, homolog (yeast)	⇧	1.24	1.04E-04
NM_018256	2595443	WDR12	WD repeat domain 12	⇧	1.23	0.001
NM_024102	2427930	WDR77	WD repeat domain 77	⇧	1.41	6.98E-06
NM_032345	3457315	WIBG	within bgcn homolog (*Drosophila*)	⇧	1.24	5.82E-06

Sensory Perception

NM_001004473	2362270	OR10K1	olfactory receptor, family 10, subfamily K, member 1	⇩	1.21	0.008
NM_001004474	3395811	OR10S1	olfactory receptor, family 10, subfamily S, member 1	⇩	1.42	0.002
NM_001004458	3331692	OR1S	olfactory receptor, family 1, subfamily S, member 1	⇩	1.34	9.14E-05
NM_001001659	3029521	OR2A14	olfactory receptor, family 2, subfamily A, member 14	⇩	1.23	0.002
NM_001005180	3318495	OR56B1	olfactory receptor, family 56, subfamily B, member 1	⇩	1.32	0.045
NM_001004738	3330786	OR5L1	olfactory receptor, family 5, subfamily L, member 1	⇩	1.20	0.031
NM_001005283	3331686	OR9Q2	olfactory receptor, family 9, subfamily Q, member 2	⇩	1.22	2.09E-04
NM_005388	3224341	PDCL	phosducin-like	⇧	1.20	0.011
NM_024065	2496280	PDCL3	phosducin-like 3	⇧	1.21	8.72E-05
NM_016943	3027943	TAS2R3	taste receptor, type 2, member 3	⇩	1.23	0.010
NM_176885	3444503	TAS2R31	taste receptor, type 2, member 31	⇩	1.33	0.036
NM_016944	3027956	TAS2R4	taste receptor, type 2, member 4	⇩	1.37	0.017

Signal Transduction

NM_007313	3191724	ABL1	abl oncogene 1, non-receptor tyrosine kinase	⇧	1.30	1.63E-04
NM_006869	3034987	ADAP1	ArfGAP with dual PH domains 1	⇧	1.28	0.003
NM_182901	3319685	AKIP1	A kinase (PRKA) interacting protein 1	⇧	1.27	0.002
NM_001014432	3581132	AKT1	v-akt murine thymoma viral oncogene homolog 1	⇧	1.24	2.89E-06

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_004308	3371673	ARHGAP1	Rho GTPase activating protein 1	⇧	1.26	5.13E-06
NM_014783	3587457	ARHGAP11A	Rho GTPase activating protein 11A	⇧	1.28	1.43E-04
NM_152432	3346147	ARHGAP42	Rho GTPase activating protein 42	⇧	1.20	0.008
NM_015313	3352503	ARHGEF12	Rho guanine nucleotide exchange factor (GEF) 12	⇧	1.43	7.56E-04
NM_178815	3237548	ARL5B	ADP-ribosylation factor-like 5B	⇩	1.20	0.003
NM_018482	3153428	ASAP1	ArfGAP with SH3 domain, ankyrin repeat and PH domain 1	⇧	1.24	0.003
NM_005186	3334954	CAPN1	calpain 1, (mu/I) large subunit	⇧	1.23	1.13E-04
NM_0017848	2382117	CAPN2	calpain 2, (mu/II) large subunit	⇧	1.43	0.008
NM_004357	3316344	CD151	CD151 molecule (Raph blood group)	⇩	1.36	0.005
NM_001780	3457160	CD63	CD63 molecule	⇩	1.23	3.10E-04
NM_002231	3328520	CD82	CD82 molecule	⇩	1.24	4.21E-05
NM_078481	3822657	CD97	CD97 molecule	⇩	1.23	1.33E-05
NM_007236	3590341	CHP	calcium binding protein P22	⇧	1.25	0.001
NM_000740	2387606	CHRM3	cholinergic receptor, muscarinic 3	⇩	1.23	2.95E-04
NM_001004419	3404436	CLEC2D	C-type lectin domain family 2, member D	⇩	1.29	5.79E-04
NM_003653	3747717	COPS3	COP9 constitutive photomorphogenic homolog subunit 3 (*Arabidopsis*)	⇧	1.23	2.03E-04
NM_016129	2733928	COPS4	COP9 constitutive photomorphogenic homolog subunit 4 (*Arabidopsis*)	⇧	1.33	2.09E-04
NM_177559	3894228	CSNK2A1	casein kinase 2, alpha 1 polypeptide	⇧	1.25	1.72E-05
NM_004227	3037251	CYTH3	cytohesin 3	⇩	1.34	0.016
NM_139179	3037344	DAGLB	diacylglycerols lipase, beta	⇩	1.23	1.83E-05
NM_013993	2901970	DDR1	discoidin domain receptor tyrosine kinase 1	⇩	1.22	0.015
NM_015213	3362263	DENND5A	DENN/MADD domain containing 5A	⇧	1.28	0.002
NM_003647	3727962	DGKE	diacylglycerol kinase, epsilon 64kDa	⇩	1.23	0.006
NM_004717	3074912	DGKI	diacylglycerol kinase, iota	⇩	1.21	0.025
NM_004418	3565119	DUSP2	dual specificity phosphatase 2	⇩	1.21	0.006
NM_005228	3002640	EGFR	epidermal growth factor receptor	⇩	1.29	0.001
NM_001098785	3335338	FAM89B	family with sequence similarity 89, member B	⇧	1.31	0.005
NM_207123	2745547	GAB1	GRB2-associated binding protein 1	⇩	1.32	0.008
NM_057169	3471005	GIT2	G protein-coupled receptor kinase interacting ArfGAP 2	⇧	1.29	3.93E-05
NM_002069	3010439	GNAI1	guanine nucleotide binding protein (G protein), alpha inhibiting activity polypeptide 1	⇧	1.23	0.022
NM_021629	2706938	GNB4	guanine nucleotide binding protein (G protein), beta polypeptide 4	⇧	1.24	2.62E-04
NM_004126	3012978	GNG11	guanine nucleotide binding protein (G protein), gamma 11	⇧	1.32	9.52E-04
NM_001145772	3662808	GPR56	G protein-coupled receptor 56	⇩	1.23	0.009

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NM_003608	3547375	GPR65	G protein-coupled receptor 65	⇩	1.22	0.003
NM_003979	3405587	GPRC5A	G protein-coupled receptor, family C, group 5, member A	⇩	1.35	3.07E-04
NM_212492	3738490	GPS1	G protein pathway suppressor 1	⇧	1.21	1.54E-04
NM_015666	3892509	GTPBP5	GTP binding protein 5 (putative)	⇧	1.25	3.92E-06
NM_000867	2603395	HTR2B	5-hydroxytryptamine (serotonin) receptor 2B	⇩	1.20	0.038
NM_001130699	2980449	IPCEF1	interaction protein for cytohesin exchange factors 1	⇧	1.43	8.27E-04
NM_015541	2680591	LRIG1	leucine-rich repeats and immunoglobulin-like domains 1	⇩	1.35	0.003
NM_004631	2413203	LRP8	low density lipoprotein receptor-related protein associated protein 8, apolipoprotein E receptor	⇩	1.25	1.39E-05
NM_002337	2758298	LRPAP1	low density lipoprotein receptor-related protein associated protein 1	⇩	1.25	0.002
NM_145109	3714729	MAP2K3	mitogen-activated protein kinase kinase 3	⇧	1.20	0.001
NM_005204	3240987	MAP3K8	mitogen-activated protein kinase kinase kinase 8	⇩	1.20	0.006
NM_004579	3377091	MAP4K2	mitogen-activated protein kinase kinase kinase kinase 2	⇧	1.25	1.86E-04
NM_001006617	3225456	MAPKAP1	mitogen-activated protein kinase associated protein 1	⇧	1.21	1.81E-04
NM_002436	4027585	MPP1	membrane protein, palmitoylated 1, 55kDa	⇧	1.24	0.012
NM_000906	2359780	NPR1	natriuretic peptide receptor A/guanylate cyclase A (atrionatriuretic peptide receptor A)	⇩	1.24	0.009
NM_201266	2524301	NRP2	neuropilin 2	⇩	1.37	2.32E-05
NM_017906	2894663	PAK1IP1	PAK1 interacting protein 1	⇧	1.41	2.87E-05
NM_002603	3138464	PDE7A	phosphodiesterase 7A	⇧	1.30	0.001
NM_002609	2881239	PDGFRB	platelet-derived growth factor receptor, beta polypeptide	⇩	1.22	0.008
NM_006207	3087703	PDGFRL	platelet-derived growth factor receptor-like	⇩	1.24	0.002
NM_002567	3433796	PEBP1	phosphatidylethanolamine binding protein 1	⇧	1.35	0.020
NM_002649	3018309	PIK3CG	phosphoinositide-3-kinase, catalytic, gamma polypeptide	⇧	1.44	0.019
NM_052880	3957790	PIK3IP1	phosphoinositide-3-kinase interacting protein 1	⇩	1.33	1.81E-04
NM_003629	2410470	PIK3R3	phosphoinositide-3-kinase, regulatory subunit 3 (gamma)	⇧	1.28	0.006
NM_005028	3281068	PIP4K2A	phosphatidylinositol-5-phosphate 4-kinase, type II, alpha	⇧	1.20	1.80E-05
NM_006224	3740304	PITPNA	phosphatidylinositol transfer protein, alpha	⇧	1.24	0.001
NM_181671	3732230	PITPNC1	phosphatidylinositol transfer protein, cytoplasmic 1	⇩	1.66	0.004
NM_001195608	3268274	PLEKHA1	pleckstrin homology domain containing, family A (phosphoinositide binding specific) member 1	⇩	1.23	0.024
NM_002481	2375212	PPP1R12B	protein phosphatase 1, regulatory (inhibitor) subunit 12B	⇩	1.39	3.92E-05
NM_006241	2712147	PPP1R2	protein phosphatase 1, regulatory (inhibitor) subunit 2	⇩	1.49	1.04E-06
NM_002712	2536183	PPP1R7	protein phosphatase 1, regulatory (inhibitor) subunit 7	⇧	1.21	2.24E-04
NM_000944	2449638	PPP3CA	protein phosphatase 3, catalytic subunit, alpha isozyme	⇧	1.30	0.003
NM_001042388	3798291	PPP4R1	protein phosphatase 4, regulatory subunit 1	⇧	1.27	3.72E-04

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_006247	3836760	PPP5C	protein phosphatase 5, catalytic subunit	⇧	1.22	6.06E-04
NM_014931	3871256	PPP6R1	protein phosphatase 6, regulatory subunit 1	⇧	1.20	1.16E-05
NM_005399	2433209	PRKAB2	protein kinase, AMP-activated, beta 2 non-catalytic subunit	⇩	1.33	2.66E-05
NM_002730	3852529	PRKACA	protein kinase, cAMP-dependent, catalytic, alpha	⇧	1.30	1.54E-06
NM_182948	2344393	PRKACB	protein kinase, cAMP-dependent, catalytic, beta	⇧	1.36	0.013
NM_016457	3866135	PRKD2	protein kinase D2	⇧	1.22	1.01E-04
NM_080391	2404819	PTP4A2	protein tyrosine phosphatase type IVA, member 2	⇧	1.32	4.08E-05
NM_014369	2505529	PTPN18	protein tyrosine phosphatase, non-receptor type 18 (brain-derived)	⇧	1.20	7.76E-05
NM_080549	3403092	PTPN6	protein tyrosine phosphatase, non-receptor type 6	⇧	1.21	3.11E-09
NM_002833	3633460	PTPN9	protein tyrosine phosphatase, non-receptor type 9	⇧	1.23	0.002
NM_002843	3329983	PTPRJ	protein tyrosine phosphatase, receptor type, J	⇩	1.54	0.004
NM_006861	3474228	RAB35	RAB35, member RAS oncogene family	⇧	1.22	5.63E-05
NM_001100426	2736853	RAP1GDS1	RAP1, GTP-GDP dissociation stimulator 1	⇧	1.29	0.007
NM_005739	3618736	RASGRP1	RAS guanyl releasing protein 1 (calcium and DAG-regulated)	⇩	1.36	0.017
NM_002928	2447148	RGS16	regulator of G-protein signalling 16	⇧	1.23	0.034
NM_001039467	3914307	RGS19	regulator of G-protein signalling 19	⇧	1.23	0.001
NM_002923	2372858	RGS2	regulator of G-protein signalling 2, 24kDa	⇧	1.74	0.002
NM_021205	2384401	RHOU	ras homolog gene family, member U	⇧	1.42	0.001
NM_033103	3858852	RHPN2	rhophilin, Rho GTPase binding protein 2	⇧	1.27	0.005
NM_002966	2435383	S100A10	S100 calcium binding protein A10	⇧	1.43	0.003
NM_017789	2565592	SEMA4C	sema domain, immunoglobulin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 4C	⇩	1.32	5.97E-05
NM_003612	3632907	SEMA7A	semaphorin 7A, GPI membrane anchor (John Milton Hagen blood group)	⇩	1.22	8.72E-05
NM_004844	2664209	SH3BP5	SH3-domain binding protein 5 (BTK-associated)	⇧	1.36	0.030
NM_003028	3205659	SHB	Src homology 2 domain containing adaptor protein B	⇩	1.22	0.024
NM_024745	3689880	SHCBP1	SHC SH2-domain binding protein 1	⇧	1.44	2.40E-05
NM_003930	3042610	SKAP2	src kinase associated phosphoprotein 2	⇧	1.22	5.55E-04
NM_005900	2746119	SMAD1	SMAD family member 1	⇧	1.32	0.029
NM_021069	2796995	SORBS2	sorbin and SH3 domain containing 2	⇧	1.25	0.003
NM_181784	2556752	SPRED2	sprout-related, EVH1 domain containing 2	⇧	1.30	0.001
NM_012108	2729667	STAP1	signal transducing adaptor family member 1	⇧	1.27	0.008
NM_018201	3190737	TBC1D13	TBC1 domain family, member 13	⇧	1.21	3.24E-04
NM_004257	2568630	TGFBRAP1	transforming growth factor, beta receptor associated protein 1	⇧	1.32	5.72E-07

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_012339	3250373	TSPAN15	tetraspanin 15	⇩	1.48	0.001
NM_213655	3400384	WNK1	WNK lysine deficient protein kinase 1	⇩	1.35	0.010
NM_003404	3886639	YWHAB	tyrosine 3-monooxygenase/tryptophoan 5-monooxygenase activation protein, beta polypeptide	⇧	1.21	9.37E-04
NR_024058	3740126	YWHAE	tyrosine 3-monooxygenase/tryptophoan 5-monooxygenase activation protein, epsilon polypeptide	⇧	1.24	4.48E-04

Transcription

NM_018011	3524618	ARGLU1	arginine and glutamate rich 1	⇩	1.26	2.52E-05
NM_004674	3094447	ASH2L	ash 2 (absent, small, or homeotic)-like (*Drosophila*)	⇧	1.29	5.94E-07
NM_014670	2522439	BZW1	basic leucine zipper and W2 domains 1	⇧	1.22	0.016
NM_138414	3686587	CCDC101	coiled-coil domain containing 101	⇧	1.28	2.10E-05
NM_015076	2969467	CDK19	cyclin-dependent kinase 19	⇧	1.24	1.79E-04
NM_015442	2616018	CNOT10	CCR4-NOT transcription complex, subunit 10	⇧	1.20	1.21E-04
NM_004779	2836856	CNOT8	CCR4-NOT transcription complex, subunit 8	⇧	1.20	6.46E-04
NM_182898	2994558	CREB5	cAMP responsive element binding protein 5	⇩	1.27	0.023
NM_001039618	3385003	CREBZF	CREB/ATF bZIP transcription factor	⇩	1.26	3.82E-05
NM_183013	3242353	CREM	cAMP responsive element modulator	⇧	1.27	6.12E-05
NM_005730	3458911	CTDSP2	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase 2	⇧	1.22	7.21E-04
NM_014633	3320301	CTR9	Ctr9, Paf1/RNA polymerase II complex component, homolog (*S. cerevisiae*)	⇧	1.22	5.02E-04
NM_003472	2944068	DEK	DEK oncogene	⇧	1.30	7.87E-06
NM_194249	2878461	DND1	dead end homolog 1 (zebrafish)	⇩	1.21	0.034
NM_001130823	3850069	DNMT1	DNA (cytosine-5-)-methyltransferase 1	⇧	1.32	9.61E-06
NM_014597	2423597	DNTTIP2	deoxynucleotidyltransferase, terminal, interacting protein 2	⇧	1.30	7.72E-05
NM_032574	2547386	DPY30	dpy-30 homolog (*C. elegans*)	⇧	1.21	0.002
NM_001950	3665288	E2F4	E2F transcription factor 4, p107/p130-binding	⇧	1.30	2.80E-05
NM_024757	3195400	EHMT1	euchromatic histone-lysine N-methyltransferase 1	⇧	1.23	2.49E-04
NM_001421	4021433	ELF4	E74-like factor 4 (ets domain transcription factor)	⇧	1.27	2.58E-05
NR_036472	3111530	ENY2	enhancer of yellow 2 homolod (*Drosophila*)	⇧	1.24	0.014
NM_015630	2509832	EPC2	enhancer of polycomb homolog 2 (*Drosophila*)	⇧	1.28	7.83E-05
NM_002017	3355733	FLI1	Friend leukemia virus integration 1	⇧	1.22	0.004
NM_004514	3775147	FOXK2	forkhead box K2	⇩	1.26	4.41E-04
NM_003934	3191589	FUBP3	far upstream element (FUSE) binding protein 3	⇧	1.23	6.94E-04
NM_005254	3623683	GABPB1	GA binding protein transcription factor, beta subunit 1	⇧	1.21	1.48E-04
NM_001002295	3234277	GATA3	GATA binding protein 3	⇧	1.22	0.037

Table B10: Non*C9ORF72*-Related_*SALS* Specific Gene List (n=1,201) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_017660	3825713	GATAD2A	GATA zinc finger domain containing 2A	⇧	1.28	1.77E-05
NM_006582	2327603	GMEB1	glucocorticoid modulatory element binding protein 1	⇧	1.23	7.98E-05
NM_001514	2421753	GTF2B	general transcription factor IIB	⇧	1.27	0.001
NM_005513	2638467	GTF2E1	general transcription factor IIE, polypeptide 1, alpha 56kDa	⇧	1.26	0.003
NM_207118	29335522	GTF2H5	general transcription factor IIH, polypeptide 5	⇧	1.39	0.020
NR_033441	2970532	HDAC2	histone deacetylase 2	⇧	1.20	1.64E-05
NM_030763	4013828	HMGN5	high-mobility group nucleosome binding domain 5	⇧	1.48	0.001
NM_001163280	3992521	HTATSF1	HIV-1 Tat specific factor 1	⇧	1.28	3.48E-04
NM_002166	2468622	ID2	inhibitor of DNA binding 2, dominant negative helix-loop-helix protein	⇧	1.30	0.014
NM_003884	2613441	KAT2B	K(lysine) acetyltransferase 2B	⇧	1.23	0.002
NM_003597	2469213	KLF11	Kruppel-like factor 11	⇧	1.23	0.046
NM_031918	3845553	KLF16	Kruppel-like factor 16	⇧	1.26	7.89E-05
NM_001730	3493543	KLF5	Kruppel-like factor 5 (intestinal)	⇧	1.22	0.001
NM_030973	3838947	MED25	mediator complex subunit 25	⇧	1.27	1.56E-08
NM_006337	3453882	MCRS1	microspherule protein 1	⇧	1.20	6.87E-05
NM_005098	3140213	MSC	musculin	⇧	1.28	7.16E-04
NM_006800	3968833	MSL3	male-specific lethal 3 homolog (*Drosophila*)	⇩	1.29	0.001
NM_005966	2520225	NAB1	NGFI-A binding protein 1 (EGR1 binding protein 1)	⇩	1.29	0.006
NM_052876	3822195	NACC1	nucleus accumbens associated 1, BEN and BTB (POZ) domain containing	⇧	1.29	9.63E-07
NM_147223	2473149	NCOA1	nuclear receptor coactivator 1	⇧	1.34	6.71E-07
NM_020967	3907652	NCOA5	nuclear receptor coactivator 5	⇧	1.35	2.94E-05
NM_003204	3725035	NFE2L1	nuclear factor (erythroid-derived 2)-like 1	⇩	1.25	9.84E-05
NM_205843	3816919	NFIC	nuclear factor I/C (CCAAT-binding transcription factor)	⇧	1.20	8.77E-05
NM_021005	3610110	NR2F2	nuclear receptor subfamily 2, group F, member 2	⇧	1.45	0.022
NM_012345	3512449	NUFIP1	nuclear fragile X mental retardation protein interacting protein 1	⇧	1.24	7.46E-04
NM_018165	2676219	PBRM1	polybromo 1	⇧	1.20	0.002
NM_020524	2436938	PBXIP1	pre-B-cell leukemia homeobox interacting protein 1	⇩	1.31	4.48E-06
NM_003662	4000560	PIR	pirin (iron-binding nuclear protein)	⇧	1.22	0.048
NM_002657	3902682	PLAGL2	pleiomorphic adenoma gene-like 2	⇧	1.20	0.007
NM_018082	3430129	POLR3B	polymerase (RNA) III (DNA directed) polypeptide B	⇧	1.26	0.001
NM_032305	2432571	POLR3GL	polymerase (RNA) III (DNA directed) polypeptide G (32kD)-like	⇧	1.32	2.96E-09
NM_007062	3430552	PWP1	PWP1 homolog (S. cerevisiae)	⇧	1.27	2.45E-06
NM_014868	3434413	RNF10	ring finger protein 10	⇧	1.20	4.96E-04

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_024604	3452622	RPAP3	RNA polymerase II associated protein 3	⇧	1.32	5.74E-06
NM_002957	3193339	RXRA	retinoid X receptor, alpha	⇧	1.26	4.73E-04
NM_005870	3480657	SAP18	Sin3A-associated protein, 18kDa	⇧	1.20	0.012
NR_024084	2836665	SAP30L	SAP30-like	⇧	1.21	2.76E-04
NM_012237	3861689	SIRT2	sirtuin 2	⇧	1.21	0.019
NM_024755	3626704	SLTM	SAFB-like, transcription modulator	⇧	1.29	8.81E-04
NM_003079	3756344	SMARCE1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily E, member 1	⇧	1.23	1.87E-05
NM_020197	2379754	SMYD2	SET and MYND domain containing 2	⇧	1.35	3.53E-05
NM_001167740	2464909	SMYD3	SET and MYND domain containing 3	⇧	1.21	3.01E-04
NM_003113	2531377	SP100	SP100 nuclear antigen	⇧	1.20	0.006
NM_003121	3839346	SPIB	Spi-B transcription factor (Spi-1/PU.1 related)	⇧	1.32	0.002
NM_145716	2413685	SSBP3	single stranded DNA binding protein 3	⇧	1.36	0.005
NM_003146	3373724	SSRP1	structure specific recognition protein 1	⇧	1.29	2.72E-04
NM_006713	2805581	SUB1	SUB1 homolog (*S. cerevisiae*)	⇧	1.21	0.013
NM_139215	3718791	TAF15	TAF15 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 68kDa	⇧	1.20	4.58E-05
NM_005680	2469094	TAF1B	TATA box binding protein (TBP)-associated factor, RNA polymerase I, B, 63kDa	⇧	1.23	0.009
NM_138572	2907018	TAF8	TAF8 RNA polymerase II, TATA box binding protein (TBP)-associated factor 43kDa	⇧	1.20	0.003
NM_001006933	3985644	TCEAL3	transcription elongation factor A (SII)-like 3	⇧	1.20	0.005
NM_007111	3502710	TFDP1	transcription factor Dp-1	⇧	1.32	3.18E-08
NM_007005	3176209	TLE4	transducin-like enhancer of split 4 (E(sp1) homolog, *Drosophila*)	⇧	1.38	9.07E-05
NM_033502	2954025	TRERF1	transcriptional regulating factor 1	⇩	1.21	0.038
NM_001076683	3758967	UBTF	⇧stream binding transcription factor, RNA polymerase I	⇧	1.26	5.49E-07
NM_003796	3828162	URI1	URI1, prefoldin-like chaperone	⇧	1.22	1.95E-04
NM_007146	3764066	VEZF1	vascular endothelial zinc finger 1	⇧	1.21	2.66E-04
NM_025234	3634588	WDR61	WD repeat domain 61	⇧	1.20	7.41E-04
NM_006530	3421523	YEATS4	YEATS domain containing 4	⇧	1.22	0.003
NM_006977	3568310	ZBTB25	zinc finger and BTB domain containing 25	⇩	1.35	1.28E-04
NM_014383	3830680	ZBTB32	zinc finger and BTB domain containing 32	⇩	1.26	0.011
NM_015898	3846594	ZBTB7A	zinc finger and BTB domain containing 7A	⇧	1.21	1.22E-06
NM_153688	3668898	ZFP1	zinc finger protein 1 homolog (mouse)	⇧	1.24	3.27E-04
NM_001143823	3797015	ZFP161	zinc finger protein 161 homolog (mouse)	⇧	1.24	8.88E-04
NM_020828	3842794	ZFP28	zinc finger protein 28 homolog (mouse)	⇧	1.30	0.005
NM_133458	3666282	ZFP90	zinc finger protein 90 homolog (mouse)	⇧	1.20	0.007

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_003411	4028568	ZFY	zinc finger protein Y-linked	⇧	1.25	0.008
NM_006624	3231389	ZMYND11	zinc finger, MYND domain containing 11	⇧	1.25	5.99E-04
NM_033204	3825911	ZNF101	zinc finger protein 101	⇧	1.22	0.025
NM_003431	2465551	ZNF124	zinc finger protein 124	⇧	1.25	0.003
NM_003432	2808290	ZNF131	zinc finger protein 131	⇧	1.27	0.003
NM_013256	3864921	ZNF180	zinc finger protein 180	⇧	1.23	0.002
NR_024565	3784509	ZNF271	zinc finger protein 271	⇧	1.21	0.006
NM_001172674	3870135	ZNF347	zinc finger protein 347	⇧	1.31	0.002
NM_001007094	3243164	ZNF37A	zinc finger protein 37A	⇧	1.20	0.002
NM_007130	4007086	ZNF41	zinc finger protein 41	⇧	1.20	2.26E-04
NM_001001668	3842839	ZNF470	zinc finger protein 470	⇧	1.22	9.59E-04
NM_144684	3840142	ZNF480	zinc finger protein 480	⇧	1.41	2.96E-04
NM_020855	3826803	ZNF492	zinc finger protein 492	⇧	1.34	0.005
NR_003699	3840944	ZNF525	zinc finger protein 525	⇧	1.22	0.007
NM_020951	3860552	ZNF529	zinc finger protein 529	⇩	1.21	0.008
NM_018181	3790361	ZNF532	zinc finger protein 532	⇧	1.25	0.017
NR_033418	3842675	ZNF542	zinc finger protein 542	⇧	1.36	1.81E-04
NM_014630	3605832	ZNF592	zinc finger protein 592	⇧	1.24	4.94E-04
NM_025040	3869379	ZNF614	zinc finger protein 614	⇧	1.24	0.004
NM_145295	3821301	ZNF627	zinc finger protein 627	⇧	1.21	0.021
NM_152320	3453120	ZNF641	zinc finger protein 641	⇧	1.20	0.009
NM_023070	3453120	ZNF643	zinc finger protein 643	⇧	1.27	6.36E-04
NM-152373	2331974	ZNF684	zinc finger protein 684	⇧	1.20	2.84E-06
NM_001042510	3147020	ZNF706	zinc finger protein 706	⇩	1.24	0.014
NM_153028	3645816	ZNF75A	zinc finger protein 75A	⇧	1.30	0.004
AK093979	3645836	ZNF75A	zinc finger protein 75A	⇧	1.33	0.005
NM_001008401	3840857	ZNF761	zinc finger protein 761	⇧	1.22	0.032
NR_027788	3078656	ZNF767	zinc finger protein 767	⇩	1.21	0.010
NM_015694	3078597	ZNF777	zinc finger protein 777	⇧	1.21	3.42E-04
NR_027049	3821701	ZNF788	zinc finger protein 788	⇧	1.26	1.91E-05
NM_001145434	3840194	ZNF880	zinc finger protein 880	⇩	1.28	0.024
NM_152626	3005069	ZNF92	zinc finger protein 92	⇧	1.24	6.18E-04

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

Miscellaneous

NM_001143948	2941972	ADTRP	androgen-dependent TFPI-regulatory protein	⇩	1.30	0.019
NM_018046	2816563	AGGF1	angiogenic factor with G patch and FHA domains 1	⇧	1.23	1.66E-04
NM_031917	3850020	ANGPTL6	angiopoietin-like 6	⇩	1.28	3.80E-04
NM_145343	3944404	APOL1	apolipoprotein L, 1	⇩	1.31	0.025
NR_027833	3959350	APOL3	apolipoprotein L, 3	⇧	1.22	0.008
NM_001174150	2632453	ARL13B	ADP-ribosylation factor-like 13B	⇧	1.23	1.18E-04
NM_001183	3996381	ATP6AP1	ATPase, H+ transporting, lysosomal accessory protein 1	⇩	1.27	6.13E-05
NM_004047	2333658	ATP6V0B	ATPase, H+ transporting, lysosomal 21kDa, V0 subunit b	⇩	1.27	0.002
NM_012105	3921933	BACE2	beta-site APP-cleaving enzyme 2	⇩	1.55	0.010
NM_001042440	2821194	CAST	calpastatin	⇧	1.23	1.46E-05
NM_007097	2888304	CLTB	clathrin, light chain B	⇧	1.21	3.75E-05
NM_001304	3716411	CPD	carboxypeptidase D	⇩	1.24	0.014
NM_182485	2719361	CPEB2	cytoplasmic polyadenylation element binding protein 2	⇩	1.20	0.022
NM_001308	3303227	CPN1	carboxypeptidase N, polypeptide 1	⇧	1.20	0.033
NM_006565	3665603	CTCF	CCCTC-binding factor (zinc finger protein)	⇧	1.20	1.36E-04
NM_00112605	3859761	DMKN	dermokine	⇩	1.21	0.032
NM_182314	4021633	ENOX2	ecto-NOX disulphide-thiol exchanger 2	⇧	1.32	2.37E-05
NM_018145	3619595	FAM82A2	family with sequence similarity 82, member A2	⇩	1.23	6.37E-04
NR_024042	3382698	GUCY2E	guanylate cyclase 2E	⇩	1.23	0.005
NM_001142556	2838656	HMMR	hyaluronan-mediated motility receptor (RHAMM)	⇧	1.21	0.048
NM_020153	3393834	IFT46	intraflagellar transport 46 homolog (*Chlamydomonas*)	⇧	1.20	8.72E-04
NM_016004	3886179	IFT52	intraflagellar transport 52 homolog (*Chlamydomonas*)	⇧	1.26	4.00E-05
NM_198690	3923857	KRTAP10-9	keratin associated protein 10-9	⇩	1.23	0.005
NM_181605	3917582	KRTAP6-3	keratin associated protein 6-3	⇩	1.35	0.003
NM_002294	4019849	LAMP2	lysosomal-associated membrane protein 2	⇩	1.23	0.003
NM_178428	2359377	LCE2A	late cornified envelope 2A	⇩	1.30	8.90E-04
NM_000427	2359646	LOR	loricrin	⇧	1.21	0.033
NM_001136493	2331679	MFSD2A	major facilitator superfamily domain containing 2A	⇩	1.20	0.004
NM_152649	3699080	MLKL	mixed lineage kinase domain-like	⇧	1.20	0.031
NM_032117	2748163	MND1	meiotic nuclear divisions 1 homolog (*S. cerevisiae*)	⇧	1.47	6.57E-04
NM_018365	3625761	MNS1	meiosis-specific nuclear structural 1	⇧	1.39	4.19E-05

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_000252	3994795	MTM1	myotubularin 1	⇧	1.41	6.29E-05
NM_006432	3571904	NPC2	Niemann-Pick disease, type C2	⇩	1.21	2.35E-04
NM_002616	3744150	PER1	period homolog 1 (*Drosophila*)	⇩	1.21	0.016
NM_003847	3638566	PEX11A	peroxisomal biogenesis factor 11 alpha	⇩	1.22	0.002
NM_000941	3009229	POR	P450 (cytochrome) oxidoreductase	⇩	1.23	0.001
NM_016488	3412008	PPHLN1	periphilin 1	⇧	1.22	1.23E-05
NM_000311	3874751	PRNP	prion protein	⇩	1.26	0.004
NM_007238	3903169	PXMP4	peroxisomal membrane protein 4, 24kDa	⇩	1.23	2.86E-04
NM_004160	3758775	PYY	peptide YY	⇩	1.26	0.008
NR_024210	3942805	RNF185	ring finger protein 185	⇧	1.22	0.013
NM_001031709	3299408	RNLS	renalase, FAD-dependent amine oxidase	⇧	1.24	0.002
NM_006461	3750785	SPAG5	sperm associated antigen 5	⇧	1.20	0.004
NM_004890	3742415	SPAG7	sperm associated antigen 7	⇧	1.21	0.001
NM_080608	3907507	SPATA25	spermatogenesis associated 25	⇩	1.34	5.99E-06
NM_145207	2742134	SPATA5	spermatogenesis associated 5	⇧	1.26	8.44E-05
NM_001100422	2522094	SPATS2L	spermatogenesis associated, serine-rich 2-like	⇧	1.39	8.44E-05
NM_004099	3223928	STOM	stomatin	⇩	1.20	0.011
NM_032300	3431318	TCHP	trichoplein, keratin filament binding	⇧	1.24	5.78E-05
NM_018073	3360189	TRIM68	tripartite motif-containing 68	⇧	1.27	1.78E-05
NM_004622	2503618	TSN	translin	⇧	1.21	9.99E-04
NM_178562	3023318	TSPAN33	tetraspanin 33	⇩	1.22	0.002
NM_003920	3457824	TIMELESS	timeless homolog (*Drosophila*)	⇧	1.22	0.003
NM_014688	3277468	USP6NL	USP6 N-terminal like	⇧	1.35	8.93E-05
NM_172005	3887004	WFDC13	WAP four-disulfide core domain 13	⇩	1.21	0.007
NM_032312	2476176	YIPF4	Yip1 domain family, member 4	⇩	1.26	9.68E-04

Unknown Function

NM_020676	2626097	ABHD6	adhydrolase domain containing 6	⇩	1.51	1.06E-04
NM_020186	3013952	ACN9	ACN9 homolog (*S. cerevisiae*)	⇧	1.29	1.12E-06
NM_139056	2800026	ADAMTS16	ADAM metallopeptidase with thromospondin type 1 motif, 16	⇩	1.26	3.31E-05
NM_178563	3025678	AGBL3	ATP/GTP binding protein-like 3	⇩	1.20	0.048
NR_026903	3767280	AMZ2P1	archaelysin family metallopeptidase 2 pseudogene 1	⇩	1.22	0.008
NM_017664	3525679	ANKRD10	ankyrin repeat domain 10	⇩	1.28	2.46E-05

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NR_003366	2564520	ANKRD20B	ankyrin repeat domain 20B	⇩	1.22	0.012
NM_032139	3858659	ANKRD27	ankyrin repeat domain 27 (VPS9 domain)	⇧	1.33	8.03E-04
NM_052855	3762416	ANKRD40	ankyrin repeat domain 40	⇧	1.23	1.92E-04
NM_030920	2434319	ANP32E	acidic (leucine-rich) nuclear phosphoprotein 32 family, member E	⇧	1.34	1.91E-04
NM_174890	3286975	ANUBL1	AN1, ubiquitin-like, homolog (*Xenopus laevis*)	⇧	1.25	0.002
NM_006407	2628682	ARL6IP5	ADP-ribosylation-like factor 6 interacting protein 5	⇩	1.25	0.003
NM_182482	3924929	BAGE2	B melanoma antigen family, member 2	⇩	1.30	0.019
NM_004326	2356818	BCL9	B-cell CLL/lymphoma 9	⇧	1.29	3.38E-04
NM_032320	3363645	BTBD10	BTB (POZ) domain containing 10	⇧	1.28	1.81E-04
NM_022153	3293724	C10orf54	chromosome 10 open reading frame 54	⇩	1.34	1.51E-04
NM_025125	3254337	C10orf57	chromosome 10 open reading frame 57	⇩	1.27	0.004
NM_170746	3331603	C11orf31	chromosome 11 open reading frame 31	⇩	1.22	4.86E-04
BC056402	3333999	C11orf84	chromosome 11 open reading frame 84	⇧	1.23	4.88E-06
NM_018169	3410384	C12orf35	chromosome 12 open reading frame 35	⇧	1.21	0.033
NM_138779	3523855	C13orf27	chromosome 13 open reading frame 27	⇧	1.39	8.70E-06
NM_032490	3577256	C14orf142	chromosome 14 open reading frame 142	⇧	1.67	3.03E-04
NM_152446	3573933	C14orf145	chromosome 14 open reading frame 145	⇧	1.41	3.89E-04
NM_152446	3573994	C14orf145	chromosome 14 open reading frame 145	⇧	1.23	0.011
NM_015492	3602116	C15orf39	chromosome 15 open reading frame 39	⇧	1.23	0.001
NM_020314	3651057	C16orf62	chromosome 16 open reading frame 62	⇧	1.21	0.006
NM_024109	3647368	C16orf68	chromosome 16 open reading frame 68	⇩	1.21	3.76E-04
NM_030806	2371547	C1orf21	chromosome 1 open reading frame 21	⇩	1.39	0.029
NM_020317	2402111	C1orf63	chromosome 1 open reading frame 63	⇩	1.21	0.003
NM_012261	3876084	C20orf103	chromosome 20 open reading frame 103	⇧	1.82	0.006
NM_017896	3893072	C20orf11	chromosome 20 open reading frame 11	⇧	1.22	0.001
NM_016470	3906821	C20orf111	chromosome 20 open reading frame 111	⇩	1.20	0.042
NM_022106	3891643	C20orf177	chromosome 20 open reading frame 177	⇧	1.22	2.46E-04
AF391113	3923982	C21orf70	chromosome 21 open reading frame 70	⇧	1.38	8.61E-05
NR_026997	3965102	C22orf34	chromosome 22 open reading frame 34	⇩	1.22	0.036
NM_00100988	3963676	C22orf9	chromosome 22 open reading frame 9	⇧	1.22	0.005
AF236158	2627080	C3orf14	chromosome 3 open reading frame 14	⇧	1.25	0.005
NM_178339	2617148	C3orf35	chromosome 3 open reading frame 35	⇩	1.21	0.005
NM_178496	2711034	C3orf59	chromosome 3 open reading frame 59	⇩	1.77	0.002

Table B10: Non*C9ORF72*-Related_*SALS* Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_017867	2793310	C4orf27	chromosome 4 open reading frame 27	⇧	1.31	0.001
NM_198567	2842429	C5orf25	chromosome 5 open reading frame 25	⇧	1.26	1.94E-05
NM_198566	2855614	C5orf34	chromosome 5 open reading frame 34	⇧	1.22	0.003
NM_021243	2927967	C6orf115	chromosome 6 open reading frame 115	⇧	1.33	0.005
NR_024185	3074101	C7orf49	chromosome 7 open reading frame 49	⇧	1.20	0.018
NM_001001551	3176933	C9orf103	chromosome 9 open reading frame 103	⇧	1.21	0.002
NM_016390	3226709	C9orf114	chromosome 9 open reading frame 114	⇧	1.20	0.003
AY598327	3182199	C9orf30	chromosome 9 open reading frame 30	⇧	1.42	1.05E-05
NR_024274	3164999	C9orf53	chromosome 9 open reading frame 53	⇩	1.38	1.81E-04
NM_153045	3186207	C9orf91	chromosome 9 open reading frame 91	⇩	1.28	8.45E-04
NM_005093	3882533	CBFA2T2	core-binding factor, runt domain, alpha subunit 2; translocated to, 2	⇩	1.22	8.53E-04
NM_201453	3208355	CBWD3	COBW domain containing 3	⇩	1.41	0.008
NM_138442	3824648	CCDC124	coiled-coil domain containing 124	⇧	1.29	1.22E-05
NM_176816	2860614	CCDC125	coiled-coil domain containing 125	⇧	1.22	5.46E-04
NM_024821	3947096	CCDC134	coiled-coil domain containing 134	⇩	1.20	0.026
NR_036647	3748449	CCDC144B	coiled-coil domain containing 144B	⇩	1.43	0.046
NM_025004	3354389	CCDC15	coiled-coil domain containing 15	⇧	1.27	1.66E-05
NM_206886	2347023	CCDC18	coiled-coil domain containing 18	⇧	1.20	0.031
NM_199342	2409069	CCDC23	coiled-coil domain containing 23	⇧	1.41	0.048
NM_018246	3129121	CCDC25	coiled-coil domain containing 25	⇧	1.20	1.70E-04
NM_030771	3367036	CCDC34	coiled-coil domain containing 34	⇧	1.32	5.57E-06
NM_020198	3766334	CCDC47	coiled-coil domain containing 47	⇩	1.21	1.27E-04
NM_024661	2673257	CCDC51	coiled-coil domain containing 51	⇧	1.20	0.003
NM_005436	3290785	CCDC6	coiled-coil domain containing 6	⇧	1.22	1.82E-05
NM_032358	3400190	CCDC77	coiled-coil domain containing 77	⇧	1.20	3.07E-04
NM_024098	3332548	CCDC86	coiled-coil domain containing 86	⇧	1.22	0.002
NM_018074	3817400	CCDC94	coiled-coil domain containing 94	⇧	1.20	9.83E-05
NM_052848	3834149	CCDC97	coiled-coil domain containing 97	⇧	1.22	9.77E-05
NM_176096	3724989	CDK5RAP3	CDK5 regulatory subunit associated protein 3	⇩	1.25	1.37E-04
NM_207390	3822849	CLEC17A	C-type lectin domain family 17, member A	⇩	1.28	1.07E-04
NM_024734	3577940	CLMN	calmin (calponin-like, transmembrane)	⇩	1.49	0.008
NM_001294	3835935	CLPTM1	cleft lip and palate associated transmembrane protein 1	⇩	1.20	7.15E-04
NM_020184	2494709	CNNM4	cyclin M4	⇩	1.31	0.002

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_001031717	2610136	CRELD1	cysteine-rich with EGF-like domains 1	⇩	1.26	5.71E-05
NM_033027	2669930	CSRNP1	cysteine-serine-rich nuclear protein 1	⇩	1.26	0.008
NM_024040	3304355	CUEDC2	CUE domain containing 2	⇧	1.20	5.12E-06
BC001220	3982242	CXorf26	chromosome X open reading frame 26	⇧	1.26	4.60E-04
NM_138496	3158697	CYHR1	cysteine/histidine-rich 1	⇩	1.20	0.002
NM_032576	4031068	CYorf15B	chromosome Y open reading frame 15B	⇧	1.44	0.032
NM_018369	2858592	DEPDC1B	DEP domain containing 1B	⇧	1.34	1.05E-04
NM_024308	3719210	DHRS11	dehydrogenase/reductase (SDR family) member 11	⇧	1.22	0.004
NM_017613	3929775	DONSON	upstream neighbour of SON	⇧	1.23	8.53E-04
NM_152726	3504791	EFHA1	EF-hand domain family, member A1	⇧	1.23	1.37E-04
NM_015036	3345427	ENDOD1	endonuclease domain containing 1	⇩	1.21	0.005
NM_014805	2669157	EPM2AIP1	EPM2A (laforin) interacting protein 1	⇩	1.22	5.93E-05
NM_020728	3082248	ESYT2	extended synaptotagmin-like protein 2	⇩	1.21	2.90E-05
NM_138348	2802739	FAM105B	family with sequence similarity 105, member B	⇧	1.22	0.002
NM_198947	3331903	FAM111B	family with sequence similarity 111, member B	⇧	1.59	1.18E-06
NM_00107952	2889241	FAM153B	family with sequence similarity 153, member B	⇩	1.23	0.008
NM_199133	2848233	FAM173B	family with sequence similarity 173, member B	⇧	1.20	0.039
NM_198507	2821981	FAM174A	family with sequence similarity 174, member A	⇩	1.32	0.003
NM_207446	3639406	FAM174B	family with sequence similarity 174, member B	⇩	1.38	0.010
NM_004816	3173974	FAM189A2	family with sequence similarity 189, member A2	⇩	1.27	0.001
NM_198076	2464484	FAM36A	family with sequence similarity 36, member A	⇩	1.29	0.002
NM_017709	2353988	FAM46C	family with sequence similarity 46, member C	⇧	1.50	0.033
BC017297	3153328	FAM49B	family with sequence similarity 49, member B	⇧	1.29	5.39E-04
NM_152450	3596109	FAM81A	family with sequence similarity 81, member A	⇧	1.20	0.004
AK123321	2536996	FLJ41327	FLJ41327 protein	⇩	1.44	0.002
AK127732	3902372	FLJ45832	FLJ45832 protein	⇩	1.20	0.009
NM_207647	3183238	FSD1L	fibronectin type III and SPRY domain containing 1-like	⇧	1.27	0.013
NM_015660	3031556	GIMAP2	GTPase, IMAP family member 2	⇧	1.32	0.004
NM_024711	3079103	GIMAP6	GTPase, IMAP family member 6	⇧	1.33	0.011
NM_016080	3739827	GLOD4	glyoxalase domain containing 4	⇧	1.26	3.62E-04
NM_144669	3437500	GLT1D1	glycosyltransferase 1 domain containing 1	⇧	1.36	0.036
NM_015698	4007815	GPKOW	G patch domain and KOW motifs	⇧	1.22	2.26E-04
NM_001136557	3191338	GPR107	G protein-coupled receptor 107	⇩	1.28	1.73E-05

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_001136557	3191273	GPR107	G protein-coupled receptor 107	⇩	1.26	9.66E-07
NM_001033045	2587790	GPR155	G protein-coupled receptor 155	⇩	1.21	0.025
NM_014373	2651835	GPR160	G protein-coupled receptor 160	⇧	1.50	0.005
NM_001146321	2827057	GRAMD3	GRAM domain containing 3	⇧	1.30	0.034
NR_003081	3955070	GSTTP1	glutathione S-transferase theta pseudogene 1	⇩	1.29	0.027
NM_014170	2636272	GTPBP8	GTP-binding protein 8 (putative)	⇧	1.20	0.010
NR_003660	2958861	GUSBP4	glucuronidase, beta pseudogene 4	⇩	1.32	0.004
NM_014282	3180957	HABP4	hyaluronan binding protein 4	⇧	1.21	0.008
AY358246	2948169	HCG8	HLA complex group 8	⇩	1.27	0.022
NM_016063	2972759	HDDC2	HD domain containing 2	⇧	1.21	0.003
NM_001001520	3817546	HDGFRP2	hepatoma-derived growth factor-related protein 2	⇧	1.21	1.21E-04
NM_001135565	3998444	HDHD1	haloacid dehalogenase-like hydrolase domain containing 1	⇧	1.32	1.89E-04
NM_024746	2457496	HHIPL2	HHIP-like 2	⇩	1.20	0.008
NM_145014	3354879	HYLS1	hydrolethalus syndrome 1	⇧	1.20	0.006
NM_001542	2429914	IGSF3	immunoglobulin superfamily, member 3	⇩	1.25	8.68E-04
NM_006844	3853063	ILVBL	ilvB (bacterial acetolactate synthase)-like	⇩	1.21	1.40E-05
NM_004867	4013549	ITM2A	integral membrane protein 2A	⇩	1.22	0.016
NM_017969	2574884	IWS1	IWS1 homolog (*S. cerevisiae*)	⇧	1.27	5.65E-05
NM_001039846	3816225	IZUMO4	IZUMO family member 4	⇩	1.37	6.75E-05
NM_032505	2628260	KBTBD8	kelch repeat and BTB (POZ) domain containing 8	⇧	1.23	0.025
NM_152387	2594435	KCTD18	potassium channel tetramerisation domain containing 18	⇧	1.21	0.007
NM_018992	3645204	KCTD5	potassium channel tetramerisation domain containing 5	⇧	1.23	2.24E-04
NM_153033	3005684	KCTD7	potassium channel tetramerisation domain containing 7	⇩	1.24	0.004
NM_014949	2437753	KIAA0907	KIAA0907	⇩	1.20	6.35E-04
NM_001080392	3076753	KIAA1147	KIAA1147	⇩	1.26	0.021
NR_026716	3841525	KIR3DX1	killer cell immunoglobulin-like receptor, three domain, X1	⇧	1.23	0.049
ENST00000392647	2514563	KLHL23	kelch-like 23 (*Drosophila*)	⇧	1.22	0.028
NM_017644	2655113	KLHL24	kelch-like 24 (*Drosophila*)	⇩	1.28	0.007
NM_016027	3139950	LACTB2	lactamase, beta 2	⇧	1.26	0.006
NM_014713	2542737	LAPTM4A	lysosomal protein transmembrane 4 alpha	⇩	1.20	5.77E-04
NM_144652	3094611	LETM2	lymphoid enhancer-binding factor 1	⇩	1.21	0.006
NM_032338	3460584	LLPH	LLP homolog, long-term synaptic facilitation (Aplysia)	⇧	1.34	2.60E-04
AY358109	3440998	LOC100128816	LOC100128816	⇧	1.28	0.001

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NR_034127	2855443	LOC100132356	hypothetical LOC100132356	⇩	1.22	0.002
XM_003119162	2464129	LOC100506975	hypothetical protein LOC100506975	⇩	1.20	0.020
NR_024333	3850501	LOC147727	hypothetical LOC147727	⇩	1.30	0.001
NM_030891	3923764	LRRC3	leucine rich repeat containing 3	⇩	1.21	0.002
NM_001105659	2418339	LRRIQ3	leucine-rich repeats and IQ motif containing 3	⇧	1.27	0.005
NM_001128301	3651588	LYRM1	LYR motif containing 1	⇧	1.23	5.32E-05
NM_153374	3624273	LYSMD2	LysM, putative peptidoglycan-binding, domain containing 2	⇧	1.22	0.013
NR_002776	3924518	MCM3AP-AS	MCM3AP antisense RNA (non-protein coding)	⇩	1.28	4.15E-04
NR_027350	3496366	MIR17HG	MIR17 host gene (non-protein coding)	⇩	1.26	0.005
NM_024761	3202316	MOBKL2B	MOB1, Mps One Binder kinase activator-like 2B (yeast)	⇧	1.45	6.11E-04
AB014771	2775390	MOP-1	MOP-1	⇩	1.24	0.013
NM_015529	2974413	MOXD1	monooxygenase, DBH-like 1	⇧	1.60	0.018
NM_018229	3537557	MUDENG	MU-2/AP1M2 domain containing, death-inducing	⇧	1.24	1.01E-04
NM_052818	3508644	N4BP2L1	NEDD4 binding protein 2-like 1	⇩	1.23	0.015
NM_174928	3504392	N6AMT2	N-6 adenine-specific DNA methyltransferase 2 (putative)	⇧	1.21	0.002
AY168775	3996598	NCRNA00204	non-protein coding RNA 204	⇩	1.48	0.029
NR_024277	2983138	NCRNA00241	non-protein coding RNA 241	⇩	1.21	0.016
NM_018376	3182984	NIPSNAP3B	nipsnap homolog 3B (*C. elegans*)	⇩	1.44	4.48E-04
NM_130464	3684100	NPIPL3	nuclear pore complex interacting protein-like 3	⇩	1.20	0.013
NM_001128211	3148796	NUDCD1	NudC domain containing 1	⇧	1.21	0.005
NM_018233	3662041	OGFOD1	2-oxoglutarate and iron-dependent oxygenase domain containing 1	⇧	1.24	3.38E-04
NM_016018	3116535	PHF20L1	PHD finger protein 20-like 1	⇧	1.22	0.002
NM_024297	3743464	PHF23	PHD finger protein 23	⇧	1.30	1.22E-04
NM_016619	2775909	PLAC8	placenta-specific 8	⇧	1.23	0.033
NM_020143	2486740	PNO1	partner of NOB1 homolog (*S. cerevisiae*)	⇧	1.28	0.001
NR_034180	2360939	POU5F1P4	POU class 5 homeobox 1 pseudogene 4	⇩	1.34	7.77E-06
NM_001102559	3131881	PPAPDC1B	phosphatidic acid phosphatase type 2 domain containing 1B	⇩	1.31	4.35E-05
NM_018304	3728964	PRR11	proline rich 11	⇧	1.22	0.011
NM_004676	4031692	PRY	PTPN13-like, Y-linked	⇩	1.49	0.005
NM_030664	3236786	PTER	phosphotriesterase related	⇧	1.26	2.41E-05
NM_017432	3839006	PTOV1	prostate tumor overexpressed 1	⇧	1.29	4.25E-04
NM_019042	3066436	PUS7	pseudouridylate synthase 7 homolog (*S. cerevisiae*)	⇧	1.20	0.006
NM_015361	2507380	R3HDM1	R3H domain containing 1	⇧	1.21	3.03E-04

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted p<0.05, FC ≥ ±1.20]

NM_024805	3795466	RBFA	ribosome binding factor A (putative)	⇧	1.23	9.61E-05
NM_016024	3990795	RBMX2	RNA binding motif protein, X-linked 2	⇧	1.34	1.54E-05
NM_001268	3513549	RCBTB2	regulator of chromosome condensation (RCC1) and BTB (POZ) domain containing 2	⇧	1.46	3.07E-04
NM_002901	3325503	RCN1	reticulocalbin 1, EF-hand calcium binding domain	⇩	1.41	0.010
NM_002902	3602723	RCN2	reticulocalbin 2, EF-hand calcium binding domain	⇩	1.28	0.003
NM_172239	3143112	REXO1L1	REX1, RNA exonuclease 1 homolog (*S. cerevisiae*)-like 1	⇩	1.62	0.002
NM_031480	2893721	RIOK1	RIO kinase 1 (yeast)	⇧	1.23	0.001
NM_032194	2921374	RPF2	ribosome production factor 2 homolog (*S. cerevisiae*)	⇧	1.29	4.22E-04
BC0171734	3383046	RPS20P27	ribosomal protein S20 pseudogene 27	⇩	1.30	0.005
NM_152260	3589997	RPUSD2	RNA pseudouridylate synthase domain containing 2	⇧	1.21	8.54E-05
NM_198467	3010030	RSBN1L	round spermatid basic protein 1-like	⇧	1.21	0.001
NM_032167	3648412	RUNDC2A	RUN domain containing 2A	⇩	1.21	0.002
NM_016940	3928040	RWDD2B	RWD domain containing 2B	⇧	1.24	0.005
NM_152682	2796066	RWDD4	RWD domain containing 4	⇧	1.26	0.046
NM_017654	3061438	SAMD9	sterile alpha motif domain containing 9	⇧	1.30	0.015
NR_004859	3605780	SCAND2	SCAN domain containing 2, pseudogene	⇩	1.21	2.04E-04
NM_001143998	3735752	SEC14L1	SEC14-like 1 (*S. cerevisiae*)	⇧	1.22	0.003
NM_015187	2764192	SEL1L3	sel-1 suppressor of lin-12-like 3 (*C. elegans*)	⇩	1.32	0.041
NM_020755	2972310	SERINC1	serine incorporator 1	⇩	1.31	7.62E-07
NM_001174072	2864449	SERINC5	serine incorporator 5	⇩	1.25	0.015
NM_002640	3791996	SERPINB8	serpin peptidase inhibitor, clade B (ovalbumin), member 8	⇧	1.41	5.40E-04
NM_006216	2601414	SERPINE2	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 2	⇩	1.22	0.040
NM_032840	3455973	SPRYD3	SPRY domain containing 3	⇧	1.22	9.62E-04
NM_018079	2551327	SRBD1	S1 RNA binding domain 1	⇧	1.36	2.15E-06
NM_022906	3006133	STAG3L4	stromal antigen 3-like 4	⇩	1.28	0.005
NM_020799	3257031	STAMBPL1	STAM binding protein-like 1	⇧	1.23	0.017
NM_012453	3056131	TBL2	transducing (beta)-like 2	⇩	1.26	2.16E-05
NM_198524	3594986	TEX9	testis expressed 9	⇧	1.48	0.008
NM_024838	3239380	THNSL1	threonine synthase-like 1 (*S. cerevisiae*)	⇧	1.36	8.25E-04
NM_017736	3683783	THUMPD1	THUMP domain containing 1	⇧	1.21	2.88E-04
NM_145715	2735598	TIGD2	tigger transposable element derived 2	⇧	1.29	2.35E-04
NM_003258	3772158	TK1	thymidine kinase 1, soluble	⇧	1.46	1.69E-06
NM_078474	3642358	TM2D3	TM2 domain containing 3	⇩	1.45	1.47E-06

Table B10: Non*C9ORF72*-Related_SALS Specific Gene List (n=1,201) [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

NM_020123	3301857	TM9SF3	transmembrane 9 superfamily member 3	⇩	1.20	0.004
NM_014742	3881686	TM9SF4	transmembrane 9 superfamily protein member 4	⇩	1.22	6.56E-06
NM_020698	3466206	TMCC3	transmembrane and coiled-coil domain family 3	⇧	1.25	0.007
NM_018447	2662491	TMEM111	transmembrane protein 111	⇩	1.23	0.002
NM_031925	3057520	TMEM120A	transmembrane protein 120A	⇩	1.26	0.030
NM_018295	3025740	TMEM140	transmembrane protein 140	⇩	1.31	1.80E-04
NM_024943	2766289	TMEM156	transmembrane protein 156	⇧	1.35	0.037
NM_017814	3855506	TMEM161A	transmembrane protein 161A	⇩	1.20	4.54E-04
NM_198536	3850832	TMEM205	transmembrane protein 205	⇩	1.20	0.004
NM_018252	2454661	TMEM206	transmembrane protein 206	⇩	1.27	0.002
NM_014187	3665357	TMEM208	transmembrane protein 208	⇩	1.40	8.90E-06
NM_152417	3136015	TMEM68	transmembrane protein 68	⇩	1.26	0.010
NM_015497	3620515	TMEM87A	transmembrane protein 87A	⇩	1.23	9.16E-05
NM_016456	2450668	TMEM9	transmembrane protein 9	⇩	1.27	1.48E-04
NM_001042595	3834176	TMEM91	transmembrane protein 91	⇩	1.26	0.037
NM_003449	2948259	TRIM26	tripartite motif-containing 26	⇧	1.46	1.39E-06
NM_017583	3326842	TRIM44	tripartite motif-containing 44	⇧	1.21	2.55E-04
NM_032765	2845078	TRIM52	tripartite motif-containing 52	⇩	1.22	0.025
NM_030912	3261820	TRIM8	tripartite motif-containing 8	⇧	1.21	0.003
NM_018259	3327948	TTC17	tetratricopeptide repeat domain 17	⇩	1.20	5.83E-06
NM_001135993	3781980	TTC39C	tetratricopeptide repeat domain 39C	⇧	1.56	2.54E-04
NM_175852	2328713	TXLNA	taxilin alpha	⇧	1.23	4.43E-05
NM_014044	2495555	UNC50	ubiquitin specific peptidase 9, Y-linked	⇩	1.20	7.82E-04
NM_007125	4035017	UTY	ubiquitously transcribed tetratricopeptide repeat gene, Y-linked	⇧	1.49	0.043
NM_024029	3850576	YIPF2	Yip1 domain family, member 2	⇩	1.31	4.28E-04
NM_017665	2875634	ZCCHC10	zinc finger, CCHC domain containing 10	⇧	1.20	0.002
NM_016505	2328236	ZCCHC17	zinc finger, CCHC domain containing 17	⇧	1.20	9.05E-04
NM_144723	2832081	ZMAT2	zinc finger, matrin-type 2	⇧	1.23	6.85E-04

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

Transcript	Symbol	p-value	Transcript	Symbol	p-value	Transcript	Symbol	p-value	Transcript	Symbol	p-value
3173880	TJP2	4.08E-18	3346548	BIRC3	1.71E-08	3023350	SMO	3.80E-07	3604147	KIAA1199	2.20E-06
3253880	PPIF	3.77E-16	3129731	DUSP4	1.78E-08	3459120	LRIG3	4.09E-07	3064361	ACHE	2.25E-06
3666779	NFAT5	1.58E-15	2400322	HP1BP3	2.22E-08	2878726	HDAC3	4.12E-07	3303059	SLC25A28	2.29E-06
3002640	EGFR	1.69E-14	2888648	RAB24	2.41E-08	3806525	PIAS2	4.37E-07	2775214	PRKG2	2.30E-06
2622469	RBM5	4.76E-14	2456849	RAB3GAP2	2.43E-08	3064006	C7orf47	4.40E-07	3081862	PTPRN2	2.31E-06
3542207	SRSF5	8.59E-14	3233431	FBXO18	2.68E-08	3087813	PCM1	4.47E-07	3363923	COPB1	2.42E-06
3377044	SF1	6.88E-13	3847814	KHSRP	2.81E-08	3628650	HERC1	5.14E-07	2768273	NFXL1	2.48E-06
2655688	EIF4G1	1.42E-12	3393200	PCSK7	2.82E-08	2891241	DUSP22	5.50E-07	2610336	VHL	2.73E-06
3989721	STAG2	1.57E-12	3204744	TLN1	4.26E-08	2800026	ADAMTS16	5.70E-07	2546008	SUPT7L	2.73E-06
2400793	HSPG2	1.72E-12	3475717	RSRC2	4.67E-08	3724591	C17orf57	5.75E-07	2878778	FCHSD1	2.74E-06
3400034	WNK1	1.74E-12	3860208	ALKBH6	5.72E-08	3741528	TAX1BP3	7.24E-07	3835675	CEACAM19	2.88E-06
3955815	HPS4	1.95E-12	3484497	FRY	6.03E-08	2892738	PRPF4B	7.68E-07	3416256	HOXC13	2.88E-06
3708663	CHRNB1	1.82E-11	3553872	KLC1	6.90E-08	3643966	CRAMP1L	7.83E-07	2436401	JTB	2.91E-06
2964350	MDN1	3.65E-11	3602116	C15orf39	6.92E-08	3966000	TYMP	7.94E-07	3425108	C12orf29	3.13E-06
3518496	MYCBP2	1.09E-10	2639054	PARP14	9.40E-08	3536706	LGALS3	8.65E-07	3815493	HMHA1	3.14E-06
3614087	UBE3A	1.21E-10	3824395	PGLS	9.45E-08	3729834	TBX2	9.69E-07	2409344	MED8	3.30E-06
3417842	LRP1	1.24E-10	2664099	MRPS25	9.97E-08	4027176	FLNA	1.10E-06	2476219	BIRC6	3.47E-06
2704894	PHC3	1.41E-10	2842951	NSD1	1.05E-07	2545653	MPV17	1.10E-06	3719161	GGNBP2	4.17E-06
3413344	PFKM	2.78E-10	3704717	ANKRD11	1.12E-07	3430776	ISCU	1.11E-06	2548500	PRKD3	4.22E-06
2560254	AUP1	6.16E-10	2329887	NCDN	1.78E-07	2589017	PDE11A	1.12E-06	3611744	LRRK1	4.36E-06
3607447	ABHD2	1.40E-09	3880767	PYGB	1.83E-07	2881747	ANXA6	1.17E-06	3338060	MYEOV	4.46E-06
3372459	FNBP4	1.77E-09	3199790	PSIP1	2.04E-07	2673345	COL7A1	1.21E-06	2419235	FUBP1	4.65E-06
2838598	CCNG1	2.20E-09	3539724	SYNE2	2.12E-07	3631498	LARP6	1.22E-06	2647898	MED12L	4.79E-06
3607275	ISG20	3.56E-09	3552847	DYNC1H1	2.28E-07	2373336	CFH	1.25E-06	2320727	TNFRSF1B	4.80E-06
2508611	ARHGAP15	4.52E-09	3310479	NSMCE4A	2.32E-07	2698738	XRN1	1.26E-06	2986546	PDCD2	5.11E-06
3820865	CARM1	6.50E-09	2852591	ADAMTS12	2.33E-07	2866704	ARRDC3	1.26E-06	2524653	ADAM23	5.19E-06
3311269	FAM53B	8.21E-09	3923436	TRAPPC10	2.83E-07	2372781	RGS1	1.27E-06	3831831	HKR1	5.21E-06
3110999	OXR1	8.39E-09	2532699	INPP5D	2.95E-07	3387033	MRE11A	1.55E-06	3654859	ATXN2L	5.26E-06
2888485	HK3	9.27E-09	3339261	IL18BP	3.05E-07	2621122	NBEAL2	1.57E-06	2831719	ANKHD1	5.69E-06
3548346	CALM1	9.71E-09	3082248	ESYT2	3.36E-07	2789957	FBXW7	1.64E-06	2548970	SRSF7	6.17E-06
2809128	ITGA1	1.27E-08	3795680	THOC1	3.46E-07	3860003	PRODH2	1.88E-06	3498502	TM9SF2	6.66E-06
3708306	ACADVL	1.28E-08	3719883	MLLT6	3.73E-07	2434776	CDC42SE1	1.89E-06	2409970	HECTD3	6.72E-06

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

2560076	RTKN	7.21E-06
3868183	NUP62	7.63E-06
3190463	ODF2	7.71E-06
2522616	CFLAR	7.90E-06
3655140	NFATC2IP	7.95E-06
3771513	PRPSAP1	8.33E-06
3744229	TMEM107	8.81E-06
3354879	HYLS1	8.99E-06
3529601	FITM1	9.42E-06
2714132	PDE6B	9.63E-06
3693183	CIAPIN1	9.76E-06
2920962	FIG4	9.98E-06
2546795	CAPN13	1.00E-05
3741585	ITGAE	1.05E-05
3120887	ZNF517	1.07E-05
3057550	STYXL1	1.09E-05
3354174	TBRG1	1.14E-05
2692573	CCDC14	1.27E-05
3762198	COL1A1	1.28E-05
2800906	MTRR	1.33E-05
3721956	TUBG2	1.35E-05
4015602	TRMT2B	1.37E-05
2318086	KCNAB2	1.40E-05
3335600	SNX32	1.42E-05
4025339	IDS	1.42E-05
3634852	RASGRF1	1.45E-05
3770944	H3F3B	1.46E-05
3225003	PSMB7	1.50E-05
3656829	BCKDK	1.54E-05
3441941	VAMP1	1.56E-05
3535125	ATP5S	1.65E-05
3445643	HIST4H4	1.66E-05
3334025	MARK2	1.70E-05
3841157	CACNG8	1.73E-05
2340845	MIER1	1.75E-05
3335517	KAT5	1.75E-05
2520429	MYO1B	1.79E-05
3665550	FAM65A	1.89E-05
3282463	MKX	1.92E-05
3192693	CEL	1.93E-05
2414505	C8B	1.98E-05
3952360	PRODH	2.00E-05
2446198	TOR1AIP2	2.01E-05
3000984	ABCA13	2.07E-05
3986647	VSIG1	2.12E-05
2321238	PRDM2	2.13E-05
2322103	SPEN	2.22E-05
3739679	VPS53	2.32E-05
3381377	FCHSD2	2.32E-05
2673937	QARS	2.34E-05
3933999	U2AF1	2.37E-05
2992197	SP4	2.48E-05
2491615	MAT2A	2.50E-05
2877028	KLHL3	2.50E-05
2623922	STAB1	2.59E-05
2889382	PROP1	2.63E-05
3795312	CTDP1	2.64E-05
3556418	METTL3	2.66E-05
3706736	TMEM93	2.68E-05
2827709	ISOC1	2.76E-05
3273601	IDI1	2.77E-05
3449368	CAPRIN2	2.79E-05
2551327	SRBD1	2.81E-05
2402536	TRIM63	2.82E-05
2623180	RAD54L2	2.82E-05
3393536	TMPRSS13	2.84E-05
3466206	TMCC3	2.87E-05
4012511	NAP1L2	2.98E-05
2949885	GPSM3	3.01E-05
3391816	USP28	3.02E-05
3418214	MBD6	3.05E-05
2927506	TNFAIP3	3.09E-05
3551935	WDR25	3.12E-05
3976299	ARAF	3.20E-05
2363248	LY9	3.23E-05
3744263	AURKB	3.25E-05
3568310	ZBTB25	3.31E-05
3670772	CMIP	3.40E-05
3383081	INTS4	3.41E-05
3703164	COX4NB	3.49E-05
2674229	GPX1	3.57E-05
3740479	PRPF8	3.57E-05
3914072	ARFRP1	3.63E-05
2732844	ANXA3	3.78E-05
3194635	C9orf86	3.87E-05
3750740	PIGS	3.88E-05
4011464	PJA1	3.90E-05
2655387	EIF2B5	3.95E-05
2934801	MAP3K4	3.96E-05
2673312	PFKFB4	3.96E-05
2806799	NIPBL	3.97E-05
3942648	TUG1	4.03E-05
3620380	PLA2G4D	4.05E-05
3147321	UBR5	4.09E-05
3933550	TFF2	4.11E-05
3962997	EFCAB6	4.11E-05
2758978	EVC2	4.12E-05
3168415	CLTA	4.13E-05
3941907	EWSR1	4.19E-05
3063685	MCM7	4.21E-05
2619344	NKTR	4.24E-05
3703799	KLHDC4	4.27E-05
3261544	GBF1	4.42E-05
2609960	TTLL3	4.43E-05
2991233	AHR	4.68E-05
3457101	ITGA7	4.71E-05
3850859	RGL3	4.76E-05
3690388	ABCC12	4.79E-05
3042421	HNRNPA2B1	4.86E-05
3908963	B4GALT5	4.94E-05
3704299	MVD	4.95E-05
4002081	MAP7D2	4.99E-05
3417249	ERBB3	5.05E-05
3182409	ZNF189	5.07E-05
3257559	RPP30	5.24E-05
2788511	SLC10A7	5.26E-05
3284596	PARD3	5.29E-05
3119945	GRINA	5.32E-05
2406677	STK40	5.41E-05
2539125	CMPK2	5.42E-05
3190394	URM1	5.60E-05
3011861	STEAP2	5.68E-05
3961955	PHF5A	5.73E-05
2826159	SNCAIP	5.75E-05
3653317	RBBP6	5.76E-05
2362892	ATP1A2	6.01E-05
2442800	ADCY10	6.05E-05
2590452	CERKL	6.05E-05
3772581	USP36	6.14E-05
3023318	TSPAN33	6.17E-05
3334954	CAPN1	6.17E-05
3771800	SRSF2	6.22E-05

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

3141857	TPD52	6.33E-05
3743611	NEURL4	6.35E-05
3911177	ZBP1	6.45E-05
2346074	ZNF326	6.62E-05
3068519	C7orf60	6.73E-05
2957499	ICK	6.98E-05
3164181	RRAGA	7.04E-05
2905664	ZFAND3	7.36E-05
2621333	PTPN23	7.37E-05
2425118	SASS6	7.38E-05
2491386	TCF7L1	7.42E-05
2462329	ERO1LB	7.51E-05
3903836	EIF6	7.54E-05
3514639	DHRS12	7.54E-05
3034987	ADAP1	7.61E-05
2450568	CACNA1S	7.75E-05
3645549	CLDN9	7.94E-05
3663055	C16orf57	7.99E-05
3773174	CBX4	8.01E-05
3846403	MATK	8.03E-05
2903574	B3GALT4	8.19E-05
3452865	COL2A1	8.20E-05
3633890	SCAPER	8.24E-05
3387771	CCDC82	8.43E-05
3686080	NSMCE1	8.63E-05
2756673	GAK	8.71E-05
2550790	LRPPRC	8.82E-05
3036985	RNF216	8.94E-05
3822849	CLEC17A	9.41E-05
3301556	TCTN3	9.50E-05
3846238	C19orf28	9.56E-05
2881370	CD74	9.62E-05
4027708	MTCP1	9.71E-05
3620880	UBR1	9.78E-05
3490504	ALG11	9.92E-05
3261723	TMEM180	1.00E-04
2823820	WDR36	1.01E-04
3708764	TNFSF12-13	1.02E-04
3859761	DMKN	1.03E-04
3942179	MTMR3	1.03E-04
3923257	PDXK	1.04E-04
3228007	SETX	1.04E-04
2592268	STAT1	1.07E-04
3360941	ARFIP2	1.09E-04
2560625	FAM176A	1.10E-04
3118818	PTP4A3	1.11E-04
3692280	IRX3	1.11E-04
2847264	MED10	1.13E-04
3349660	HTR3B	1.15E-04
3701433	C16orf46	1.16E-04
3976766	WAS	1.16E-04
3108901	VPS13B	1.16E-04
4018080	CHRDL1	1.16E-04
3380365	SHANK2	1.19E-04
2440625	DEDD	1.19E-04
3259087	C10orf129	1.20E-04
3977651	MAGED1	1.20E-04
3335952	PACS1	1.21E-04
4000704	AP1S2	1.22E-04
3804000	INO80C	1.22E-04
3994964	GPR50	1.25E-04
3741800	ATP2A3	1.26E-04
3768015	HELZ	1.27E-04
2789266	LRBA	1.27E-04
2876011	SKP1	1.27E-04
3708704	POLR2A	1.28E-04
3029129	ZYX	1.29E-04
3260895	SEMA4G	1.30E-04
2798952	NKD2	1.31E-04
2638988	PARP15	1.31E-04
3442427	LPCAT3	1.31E-04
2475042	PLB1	1.33E-04
3960061	RAC2	1.34E-04
2775994	HPSE	1.35E-04
3625052	WDR72	1.39E-04
2903034	CYP21A2	1.40E-04
3290210	ZWINT	1.45E-04
2443335	SLC19A2	1.48E-04
3279698	CUBN	1.48E-04
3771037	WBP2	1.51E-04
3398482	SNX19	1.52E-04
3634588	WDR61	1.54E-04
2686646	SENP7	1.54E-04
3848745	FBN3	1.56E-04
3962678	PACSIN2	1.56E-04
2390489	ZNF672	1.57E-04
3304301	PSD	1.58E-04
3268669	BUB3	1.59E-04
3475679	ZCCHC8	1.59E-04
2369110	RASAL2	1.61E-04
2942432	C6orf114	1.61E-04
3866135	PRKD2	1.61E-04
3886889	PIGT	1.62E-04
3679812	GRIN2A	1.62E-04
3085874	MTMR9	1.63E-04
3867796	TEAD2	1.63E-04
2459793	C1orf96	1.64E-04
3028011	MGAM	1.65E-04
3075136	CREB3L2	1.66E-04
2326912	WDTC1	1.68E-04
2389247	KIF26B	1.69E-04
2730257	C4orf40	1.70E-04
3757690	KCNH4	1.71E-04
2442493	GPA33	1.75E-04
3655708	C16orf53	1.77E-04
2886130	PANK3	1.80E-04
3647504	PMM2	1.80E-04
3484768	PDS5B	1.81E-04
3685610	ARHGAP17	1.86E-04
3454006	FMNL3	1.86E-04
2659676	LOC152217	1.89E-04
3229741	LHX3	1.90E-04
3837081	NPAS1	1.90E-04
3010503	CD36	1.92E-04
2991395	HDAC9	1.93E-04
2332999	WDR65	1.94E-04
3040073	SNX13	1.94E-04
3398754	C11orf39	1.95E-04
3204721	TPM2	1.97E-04
3222534	ASTN2	2.09E-04
3597603	USP3	2.09E-04
2878987	PCDH12	2.09E-04
3336238	DPP3	2.10E-04
2755897	MGC39584	2.13E-04
2904788	C6orf81	2.14E-04
3276337	ITIH5	2.15E-04
3894545	SDCBP2	2.18E-04
3761395	HOXB6	2.19E-04
2426385	VAV3	2.20E-04
2342176	FPGT	2.22E-04
3281068	PIP4K2A	2.22E-04
3940001	SPECC1L	2.24E-04

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

2616596	ARPP21	2.24E-04
3754469	ACACA	2.28E-04
3639031	PRC1	2.30E-04
3846363	APBA3	2.31E-04
2870828	STARD4	2.33E-04
2769810	KDR	2.36E-04
2694817	PLXND1	2.39E-04
3326183	CAPRIN1	2.42E-04
3035464	MAD1L1	2.45E-04
3304718	PCGF6	2.47E-04
2697490	CEP70	2.51E-04
3391029	PPP2R1B	2.54E-04
2767710	KCTD8	2.58E-04
3743906	TP53	2.58E-04
2608801	EDEM1	2.60E-04
3870449	VSTM1	2.65E-04
2418000	ZRANB2	2.66E-04
3446919	ABCC9	2.69E-04
2904563	DEF6	2.72E-04
3875642	PLCB1	2.73E-04
3178611	SECISBP2	2.80E-04
2321813	CELA2A	2.81E-04
3453513	WNT10B	2.84E-04
2337147	ACOT11	2.88E-04
3305313	ITPRIP	2.88E-04
3709244	CHD3	2.89E-04
3104489	STMN2	2.89E-04
3746040	ELAC2	2.90E-04
3995975	SSR4	2.92E-04
2882897	GEMIN5	2.92E-04
2403261	IFI6	2.96E-04
3373795	PRG3	2.97E-04
3393744	CD3D	2.97E-04
3035892	GNA12	2.99E-04
2673594	CELSR3	2.99E-04
3241316	ZEB1	3.03E-04
2626097	ABHD6	3.05E-04
3939498	SLC2A11	3.07E-04
2962525	IBTK	3.09E-04
3922369	UMODL1	3.09E-04
3803194	TRAPPC8	3.10E-04
3708399	SLC2A4	3.14E-04
3699335	LDHD	3.14E-04
2978989	LATS1	3.15E-04
2832115	PCDHA12	3.20E-04
3716411	CPD	3.20E-04
3147508	KLF10	3.21E-04
2766588	PDS5A	3.21E-04
2655845	EPHB3	3.25E-04
3951719	CECR6	3.26E-04
2881165	TIGD6	3.32E-04
3815834	DAZAP1	3.36E-04
3038065	ICA1	3.38E-04
2800503	PAPD7	3.40E-04
2510713	FMNL2	3.46E-04
3308619	PDZD8	3.46E-04
3907652	NCOA5	3.47E-04
3458837	METTL1	3.47E-04
3761291	HOXB2	3.48E-04
2634965	BBX	3.50E-04
4011096	EDA2R	3.51E-04
2438657	ARHGEF11	3.53E-04
3620421	PLA2G4F	3.54E-04
3226804	SH3GLB2	3.59E-04
3380142	FGF4	3.62E-04
3816664	ZNF555	3.75E-04
2835792	GM2A	3.75E-04
3592214	DUOX1	3.84E-04
3741715	CAMKK1	3.88E-04
3240340	WAC	3.89E-04
2407496	POU3F1	3.98E-04
2580304	ORC4	3.99E-04
2326954	TMEM222	4.09E-04
2389834	LOC149134	4.10E-04
3529064	BCL2L2	4.13E-04
3470734	FOXN4	4.15E-04
3119017	BAI1	4.18E-04
3758606	SOST	4.18E-04
2909404	CD2AP	4.25E-04
2960399	C6orf155	4.26E-04
2798586	AHRR	4.27E-04
3731228	CCDC45	4.27E-04
3672455	COX4I1	4.27E-04
2570616	BUB1	4.29E-04
2544238	ITSN2	4.29E-04
3457201	SARNP	4.37E-04
3814033	MBP	4.50E-04
2817291	JMY	4.50E-04
3742627	C17orf87	4.51E-04
3927949	LTN1	4.54E-04
3461341	CPM	4.58E-04
3924674	DIP2A	4.59E-04
3436117	DNAH10	4.60E-04
3660213	CYLD	4.60E-04
3458337	STAT6	4.62E-04
2525533	MAP2	4.66E-04
3764471	MTMR4	4.67E-04
3621029	EPB42	4.69E-04
2766122	FLJ13197	4.69E-04
2319225	H6PD	4.71E-04
3662876	CCDC135	4.73E-04
3750767	ALDOC	4.74E-04
3619595	FAM82A2	4.79E-04
2742224	SPRY1	4.79E-04
2420790	C1orf52	4.80E-04
3075550	ZC3HAV1L	4.83E-04
3838757	SCAF1	4.89E-04
3907335	SPINLW1	4.90E-04
3204833	GBA2	4.92E-04
3947604	BIK	4.94E-04
3735107	SAP30BP	4.94E-04
2399908	TMCO4	4.95E-04
2935475	QKI	4.99E-04
2395245	RERE	5.01E-04
3862452	CNTD2	5.02E-04
2620538	LARS2	5.08E-04
2731257	AFM	5.09E-04
3557504	MYH7	5.12E-04
3696016	PSMB10	5.14E-04
3368054	PAX6	5.26E-04
3893033	DPH3P1	5.28E-04
3647632	C16orf72	5.30E-04
3897505	JAG1	5.31E-04
3989180	MCTS1	5.43E-04
3707990	TXNDC17	5.47E-04
3844512	THEG	5.49E-04
3494629	SCEL	5.50E-04
3548929	RIN3	5.52E-04
3779817	CEP192	5.53E-04
3405032	ETV6	5.63E-04
3017547	MLL5	5.74E-04
2853055	AGXT2	5.74E-04

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

2475911	EHD3	5.78E-04
3716113	TP53I13	5.83E-04
2706297	TBL1XR1	5.85E-04
3709010	DNAH2	5.93E-04
2392528	PANK4	5.94E-04
3274361	KLF6	5.94E-04
3249788	CCAR1	5.99E-04
3735447	FAM100B	6.02E-04
2404766	SPOCD1	6.03E-04
3393796	---	6.08E-04
3591909	CTDSPL2	6.09E-04
2331822	ZMPSTE24	6.13E-04
2636786	TIGIT	6.16E-04
3416577	NCKAP1L	6.17E-04
2955282	SUPT3H	6.24E-04
3036476	RADIL	6.24E-04
2408477	SLFNL1	6.26E-04
3456260	ATF7	6.30E-04
4029079	TBL1Y	6.31E-04
3791341	ZCCHC2	6.33E-04
3881443	TPX2	6.37E-04
2776305	NKX6-1	6.37E-04
3012213	FZD1	6.37E-04
3825260	KLHL26	6.39E-04
3474885	CAMKK2	6.41E-04
2899216	HIST1H4E	6.50E-04
2524301	NRP2	6.53E-04
3617230	C15orf24	6.54E-04
3720739	CASC3	6.58E-04
3396249	HEPACAM	6.63E-04
3815165	PTBP1	6.70E-04
3413875	TROAP	6.74E-04
3540091	ZBTB1	6.75E-04
3021158	C7orf58	6.81E-04
3934439	DNMT3L	6.87E-04
3020496	ST7	6.92E-04
3219788	EPB41L4B	7.02E-04
2927604	KIAA1244	7.04E-04
2606026	HDAC4	7.10E-04
3846076	TLE2	7.12E-04
3619773	INO80	7.18E-04
3278977	DCLRE1C	7.22E-04
3451246	GXYLT1	7.25E-04
2360310	TDRD10	7.30E-04
2359780	NPR1	7.44E-04
3836317	VASP	7.47E-04
3335751	TSGA10IP	7.47E-04
3488253	COG3	7.52E-04
3186137	ORM2	7.52E-04
4051619	EXD3	7.53E-04
3181417	ANP32B	7.54E-04
3394412	THY1	7.56E-04
3978819	RRAGB	7.57E-04
2434746	FAM63A	7.60E-04
3701297	CDYL2	7.67E-04
4002173	RPS6KA3	7.69E-04
3414390	SMARCD1	7.73E-04
2832963	KIAA0141	7.77E-04
3576812	TRIP11	7.80E-04
2489228	WDR54	7.84E-04
2428313	ST7L	7.93E-04
3976716	WDR13	7.93E-04
2413943	USP24	7.98E-04
3862661	BLVRB	7.99E-04
3859946	HSPB6	8.02E-04
3029198	TAS2R60	8.18E-04
3551407	HHIPL1	8.24E-04
3016692	PRKRIP1	8.28E-04
3750369	NOS2	8.29E-04
2360186	AQP10	8.34E-04
3119289	GML	8.37E-04
3329206	CREB3L1	8.38E-04
4041300	FAM195B	8.46E-04
3723378	FMNL1	8.48E-04
3474935	ANAPC5	8.49E-04
2968144	OSTM1	8.51E-04
3893796	DNAJC5	8.51E-04
3666897	WWP2	8.51E-04
2947889	GABBR1	8.56E-04
3454680	TFCP2	8.59E-04
2902463	BAT2	8.77E-04
2565119	DUSP2	8.84E-04
2566021	ACTR1B	8.85E-04
3455388	KRT75	8.85E-04
3886765	PI3	8.88E-04
2869124	SLCO6A1	8.91E-04
3229837	CARD9	8.92E-04
2375916	SOX13	8.93E-04
3790704	PMAIP1	8.96E-04
3132940	ANK1	8.97E-04
3146103	STK3	9.00E-04
2369843	CEP350	9.03E-04
3431553	C12orf24	9.16E-04
3902609	PDRG1	9.18E-04
3655806	TMEM219	9.21E-04
3029030	CASP2	9.21E-04
3892409	LSM14B	9.26E-04
2725332	TMEM33	9.32E-04
3201277	KLHL9	9.35E-04
3023103	CCDC136	9.39E-04
3076076	SLC37A3	9.42E-04
2543066	C2orf43	9.52E-04
3056838	WBSCR16	9.59E-04
3954545	ZNF280A	9.60E-04
3272761	PRAP1	9.77E-04
4015763	GLA	9.88E-04
2809885	SKIV2L2	9.91E-04
2954771	GTPBP2	9.94E-04
3872542	ZNF418	9.95E-04
3434681	HNF1A	1.01E-03
2363679	---	1.03E-03
2327283	C1orf38	1.03E-03
3051907	PHKG1	1.04E-03
2316953	PRDM16	1.04E-03
3088048	NSAP11	1.04E-03
2542795	SDC1	1.04E-03
2890326	TBC1D9B	1.05E-03
3154700	ZFAT	1.05E-03
3687752	SEPT1	1.06E-03
3853814	EPS15L1	1.07E-03
3155937	TRAPPC9	1.07E-03
3629811	DENND4A	1.07E-03
3352070	CBL	1.08E-03
2967249	BVES	1.09E-03
3766651	ERN1	1.09E-03
3439603	KDM5A	1.09E-03
3976930	PQBP1	1.10E-03
3045338	AAA1	1.10E-03
2327630	YTHDF2	1.10E-03
3819016	STXBP2	1.11E-03
3897280	PAK7	1.11E-03
2469252	RRM2	1.12E-03

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

3768969	ABCA5	1.12E-03	3883207	PROCR	1.31E-03	2612401	BTD	1.48E-03	3190939	PPP2R4	1.69E-03
2453881	IRF6	1.13E-03	2651671	MYNN	1.34E-03	2646818	ZIC1	1.50E-03	3569441	ZFYVE26	1.71E-03
2453370	PLXNA2	1.13E-03	2703750	SI	1.34E-03	2391255	UBE2J2	1.51E-03	3188780	GPR144	1.71E-03
3685051	USP31	1.13E-03	3000010	ZMIZ2	1.34E-03	3944129	HMOX1	1.53E-03	4007919	CACNA1F	1.71E-03
2328465	KHDRBS1	1.13E-03	2316905	ACTRT2	1.34E-03	3394315	C1QTNF5	1.54E-03	3437801	PIWIL1	1.72E-03
3726569	SPATA20	1.13E-03	3188299	RABGAP1	1.34E-03	3422231	TMEM19	1.55E-03	2609560	THUMPD3	1.73E-03
3542847	SIPA1L1	1.14E-03	2662698	ATP2B2	1.35E-03	3188111	PTGS1	1.55E-03	3165825	TEK	1.73E-03
3202421	C9orf72	1.16E-03	3773244	TBC1D16	1.35E-03	3444820	LRP6	1.56E-03	3336277	BBS1	1.74E-03
3035281	INTS1	1.19E-03	3217167	CORO2A	1.35E-03	2448232	TPR	1.56E-03	3712675	RAI1	1.75E-03
3663287	NDRG4	1.19E-03	3995885	PLXNB3	1.36E-03	3733275	KCNJ2	1.56E-03	3030799	KRBA1	1.76E-03
3707141	ZMYND15	1.20E-03	2825514	DMXL1	1.37E-03	3249738	HNRNPH3	1.56E-03	3166844	CHMP5	1.76E-03
3572278	NEK9	1.20E-03	2555277	USP34	1.38E-03	3665230	HSF4	1.57E-03	2453006	PIGR	1.80E-03
2416522	JAK1	1.20E-03	2948630	IER3	1.39E-03	3507465	SLC46A3	1.57E-03	2759654	ABLIM2	1.81E-03
3189545	LMX1B	1.21E-03	3523881	KDELC1	1.39E-03	2414958	TACSTD2	1.58E-03	3167553	IL11RA	1.81E-03
3991992	ZNF449	1.21E-03	2943434	ATXN1	1.39E-03	2774365	CCNI	1.59E-03	2726483	OCIAD1	1.81E-03
3646542	ALG1	1.22E-03	3484641	BRCA2	1.40E-03	2950384	COL11A2	1.60E-03	3995633	BGN	1.82E-03
3881874	ASXL1	1.22E-03	2845879	CLPTM1L	1.40E-03	2550542	THADA	1.60E-03	3103062	KCNB2	1.83E-03
2759158	JAKMIP1	1.22E-03	3381241	ARAP1	1.40E-03	2553282	PSME4	1.60E-03	3758615	DUSP3	1.83E-03
2845043	TRIM41	1.24E-03	3852743	GIPC1	1.42E-03	3515009	VPS36	1.61E-03	2622607	SLC38A3	1.83E-03
3627363	NARG2	1.24E-03	3833443	PLD3	1.42E-03	2437577	YY1AP1	1.61E-03	3919124	FAM165B	1.84E-03
3231774	GTPBP4	1.24E-03	2897635	CDKAL1	1.44E-03	3403045	ATN1	1.61E-03	2441386	RGS5	1.85E-03
3033209	INSIG1	1.25E-03	2415910	DOCK7	1.44E-03	2340695	SGIP1	1.61E-03	3288707	ERCC6	1.85E-03
3188050	MRRF	1.25E-03	3371303	PEX16	1.44E-03	2673684	IP6K2	1.62E-03	2622638	GNAI2	1.86E-03
3815210	AZU1	1.26E-03	2623568	PPM1M	1.44E-03	3449008	OVCH1	1.64E-03	3817116	TJP3	1.86E-03
3387469	---	1.27E-03	2334098	KIF2C	1.45E-03	2358136	C1orf51	1.65E-03	3374083	MED19	1.86E-03
3017123	PMPCB	1.27E-03	3376914	NRXN2	1.45E-03	3603199	IDH3A	1.66E-03	3924929	BAGE2	1.87E-03
2401448	E2F2	1.28E-03	2862380	ANKRA2	1.45E-03	3620590	ZFP106	1.66E-03	2953751	PGC	1.87E-03
3405748	EMP1	1.29E-03	3427820	SLC25A3	1.46E-03	2705690	GHSR	1.68E-03	3842456	NLRP4	1.87E-03
2478748	EML4	1.29E-03	2907754	CUL9	1.46E-03	4000370	FANCB	1.68E-03	3588125	C15orf55	1.88E-03
2689378	DRD3	1.30E-03	3217395	ANKS6	1.46E-03	3601889	LMAN1L	1.68E-03	3715368	NLK	1.89E-03
3847590	RFX2	1.30E-03	3866605	NAPA	1.47E-03	3624410	BCL2L10	1.69E-03	3803882	ZSCAN30	1.89E-03
2322957	ARHGEF10L	1.30E-03	2565246	TMEM127	1.48E-03	3908631	PREX1	1.69E-03	2333599	IPO13	1.89E-03
2877861	SLC23A1	1.31E-03	2376168	NFASC	1.48E-03	2946369	HIST1H3G	1.69E-03	2429147	DENND2C	1.90E-03

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

3958475	SYN3	1.90E-03
2796995	SORBS2	1.91E-03
2337392	BSND	1.92E-03
3208995	KLF9	1.94E-03
3815757	MUM1	1.94E-03
3597125	TLN2	1.94E-03
3972862	MAGEB1	1.95E-03
3833040	SUPT5H	1.95E-03
3817984	SAFB	1.96E-03
3942838	LIMK2	1.96E-03
3178952	SYK	1.96E-03
3990512	SASH3	1.97E-03
3082373	VIPR2	1.97E-03
3303774	LBX1	1.99E-03
3443464	PZP	1.99E-03
2723605	C4orf19	1.99E-03
2495555	UNC50	1.99E-03
2913123	RIMS1	1.99E-03
3870054	ZNF160	2.00E-03
2742093	BBS12	2.00E-03
3850725	DOCK6	2.00E-03
2376548	MFSD4	2.01E-03
3642060	CHSY1	2.01E-03
3521484	UGGT2	2.01E-03
3758692	MPP2	2.04E-03
3729123	DHX40	2.05E-03
3557069	CDH24	2.05E-03
3044518	NEUROD6	2.06E-03
3180880	LOC158435	2.06E-03
3083936	AGPAT5	2.08E-03
2467249	ALLC	2.10E-03
2598868	TNP1	2.12E-03
3985511	TCEAL7	2.14E-03
3406179	H2AFJ	2.14E-03
3678516	NAGPA	2.15E-03
3308489	KIAA1598	2.20E-03
2889542	COL23A1	2.20E-03
4021433	ELF4	2.20E-03
2557759	CNRIP1	2.21E-03
3013054	COL1A2	2.21E-03
3774029	NPLOC4	2.21E-03
3656665	ORAI3	2.21E-03
3278198	PHYH	2.22E-03
3420442	IRAK3	2.23E-03
2440354	CD48	2.23E-03
3766269	LIMD2	2.24E-03
3549033	GOLGA5	2.27E-03
3187577	CEP110	2.28E-03
3447798	CASC1	2.28E-03
2910364	TMEM14A	2.28E-03
2952102	MTCH1	2.29E-03
3293390	NODAL	2.30E-03
2732068	SHROOM3	2.30E-03
2692883	MUC13	2.30E-03
2858134	PDE4D	2.30E-03
3541137	EIF2S1	2.30E-03
3866117	DACT3	2.31E-03
3847356	LONP1	2.31E-03
3348891	C11orf57	2.34E-03
2437871	SSR2	2.36E-03
3358854	DUSP8	2.37E-03
3041875	OSBPL3	2.37E-03
3861738	SARS2	2.38E-03
2343823	LPHN2	2.38E-03
3489212	FNDC3A	2.38E-03
2326157	FAM54B	2.39E-03
3466110	CCDC41	2.39E-03
2948713	RDBP	2.39E-03
3345427	ENDOD1	2.40E-03
2669488	PLCD1	2.41E-03
3981164	ACRC	2.42E-03
3614305	ATP10A	2.42E-03
3988874	UBE2A	2.43E-03
2525989	CPS1	2.44E-03
3190151	SLC25A25	2.44E-03
2763805	DHX15	2.44E-03
3681377	PARN	2.45E-03
3802254	KCTD1	2.45E-03
2843163	GRK6	2.48E-03
3498589	CLYBL	2.49E-03
3416036	PCBP2	2.49E-03
3918098	C21orf119	2.49E-03
2955638	CLIC5	2.53E-03
3849044	MYO1F	2.53E-03
3778372	TWSG1	2.54E-03
3822551	IL27RA	2.54E-03
2451463	ADIPOR1	2.55E-03
2476411	TTC27	2.56E-03
4006326	EFHC2	2.56E-03
3797015	ZFP161	2.56E-03
3431483	ATP2A2	2.56E-03
3677356	HCFC1R1	2.58E-03
3278234	SEPHS1	2.58E-03
2486520	ETAA1	2.58E-03
3940124	UPB1	2.60E-03
3908786	STAU1	2.60E-03
2555490	XPO1	2.61E-03
2976417	PBOV1	2.62E-03
3418513	MARCH9	2.62E-03
2363444	USP21	2.65E-03
3362263	DENND5A	2.66E-03
3843848	ZNF544	2.67E-03
3329983	PTPRJ	2.68E-03
2428699	PHTF1	2.69E-03
3463727	LIN7A	2.72E-03
3793760	CNDP2	2.73E-03
3182019	STX17	2.74E-03
3403140	EMG1	2.75E-03
3393311	DSCAML1	2.75E-03
2793221	NEK1	2.76E-03
2699844	ZIC4	2.76E-03
3428783	DRAM1	2.77E-03
3867032	CCDC114	2.77E-03
2660648	CRBN	2.79E-03
3913821	KCNQ2	2.80E-03
2507209	CCNT2	2.81E-03
3358262	DEAF1	2.82E-03
2454532	INTS7	2.84E-03
2975385	AHI1	2.84E-03
3456212	MAP3K12	2.87E-03
3679564	USP7	2.88E-03
3707596	---	2.88E-03
3470927	TRPV4	2.88E-03
3403015	ENO2	2.89E-03
2704441	MECOM	2.90E-03
2876793	TRPC7	2.90E-03
3736087	TNRC6C	2.91E-03
3087703	PDGFRL	2.92E-03
2334986	CYP4X1	2.92E-03
3624448	GNB5	2.92E-03
2515707	PDK1	2.92E-03
3933536	TFF3	2.94E-03

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

2916502	SPACA1	2.95E-03
3063795	GAL3ST4	2.97E-03
3507798	UBL3	2.98E-03
2317512	DFFB	2.98E-03
2898971	HIST1H2BA	2.99E-03
3158190	---	3.02E-03
3652489	POLR3E	3.02E-03
3861352	GGN	3.04E-03
2334404	NASP	3.07E-03
3373962	UBE2L6	3.07E-03
4011008	VSIG4	3.08E-03
2783207	PRSS12	3.09E-03
3077004	TRYX3	3.11E-03
2746693	ARHGAP10	3.14E-03
3938175	UBE2L3	3.18E-03
3232944	AKR1E2	3.19E-03
3893910	TCEA2	3.20E-03
3571059	DPF3	3.25E-03
3716337	CCDC55	3.26E-03
2816681	PDE8B	3.27E-03
3191695	EXOSC2	3.28E-03
3871302	HSPBP1	3.28E-03
3686750	RABEP2	3.30E-03
3818596	EMR1	3.30E-03
3854311	USHBP1	3.31E-03
2573232	TMEM185B	3.35E-03
3096368	HOOK3	3.37E-03
2946146	SLC17A2	3.38E-03
3601741	CLK3	3.40E-03
3450899	SLC2A13	3.40E-03
2934089	WTAP	3.42E-03
3451814	NELL2	3.42E-03
2585236	TTC21B	3.42E-03
2951916	STK38	3.43E-03
2409507	SLC6A9	3.44E-03
3896034	RASSF2	3.46E-03
3120917	ZNF7	3.47E-03
3279108	NMT2	3.47E-03
3811339	BCL2	3.49E-03
3150715	DSCC1	3.51E-03
2887164	SH3PXD2B	3.52E-03
3698422	C16orf47	3.54E-03
3544905	C14orf118	3.55E-03
3450775	KIF21A	3.56E-03
3419239	MON2	3.57E-03
2527747	SLC11A1	3.58E-03
3401920	GALNT8	3.58E-03
3633236	RPP25	3.59E-03
3436082	DNAH10	3.60E-03
2726828	DCUN1D4	3.60E-03
2572909	EN1	3.61E-03
2473735	HADHB	3.61E-03
3915936	NCAM2	3.61E-03
3832256	SPINT2	3.62E-03
3532313	SRP54	3.62E-03
3816645	ZNF554	3.64E-03
3305081	COL17A1	3.66E-03
3290649	FAM13C	3.67E-03
3557791	FAM158A	3.69E-03
3626826	MYO1E	3.69E-03
3236448	SUV39H2	3.71E-03
3666033	NFATC3	3.71E-03
2438531	HDGF	3.75E-03
2624565	IL17RB	3.76E-03
2362351	PYHIN1	3.76E-03
3531032	SCFD1	3.77E-03
3209623	ZFAND5	3.80E-03
2967151	HACE1	3.81E-03
3820571	ATG4D	3.81E-03
3853495	PGLYRP2	3.83E-03
2896177	JARID2	3.85E-03
3865344	PPP1R13L	3.86E-03
3048517	CAMK2B	3.86E-03
2793054	CBR4	3.87E-03
2737257	MTTP	3.87E-03
2842530	ARL10	3.90E-03
3114111	FAM83A	3.95E-03
3614774	OCA2	3.96E-03
2471978	RHOB	3.99E-03
3268274	PLEKHA1	3.99E-03
2532399	CHRNG	3.99E-03
3499453	TPP2	3.99E-03
3903525	NCOA6	4.00E-03
3289948	PCDH15	4.00E-03
3444195	MAGOHB	4.01E-03
3649714	C16orf45	4.01E-03
4019486	SEPT6	4.02E-03
3458857	AVIL	4.02E-03
3699634	TMEM231	4.02E-03
3216356	CDC14B	4.04E-03
2360728	TRIM46	4.04E-03
3531163	COCH	4.04E-03
3065638	DNAJC2	4.04E-03
3845175	GAMT	4.08E-03
3656418	SRCAP	4.08E-03
3464967	GALNT4	4.08E-03
2557948	BMP10	4.09E-03
3197509	RLN1	4.10E-03
2439861	IGSF9	4.13E-03
2655438	DVL3	4.13E-03
2443476	SELE	4.15E-03
3103494	TMEM70	4.16E-03
3715489	TMEM97	4.16E-03
2663130	TIMP4	4.16E-03
2890148	HNRNPH1	4.18E-03
2618665	ZNF619	4.19E-03
3675285	WDR24	4.20E-03
2467691	TTC15	4.20E-03
3816225	IZUMO4	4.21E-03
3686339	XPO6	4.21E-03
3713627	SLC5A10	4.22E-03
3646156	VASN	4.22E-03
3853658	CYP4F11	4.22E-03
3545564	ADCK1	4.23E-03
2393654	KIAA0495	4.23E-03
2771342	EPHA5	4.25E-03
2438792	ETV3	4.25E-03
3839880	---	4.27E-03
3844656	POLRMT	4.27E-03
3464912	POC1B	4.27E-03
2762468	DCAF16	4.27E-03
4007617	PIM2	4.31E-03
2372924	TROVE2	4.32E-03
3381150	PDE2A	4.32E-03
3765299	APPBP2	4.32E-03
3471538	FAM109A	4.33E-03
3214668	IARS	4.34E-03
3693083	FAM192A	4.36E-03
2378121	TRAF3IP3	4.37E-03
2408111	TRIT1	4.38E-03
2669803	SCN11A	4.39E-03
3887049	UBE2C	4.41E-03

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

2692319	ADCY5	4.43E-03
3174121	MAMDC2	4.45E-03
3414632	DIP2B	4.47E-03
3080033	MLL3	4.47E-03
3158478	FBXL6	4.50E-03
3620741	CDAN1	4.52E-03
3016791	LRWD1	4.52E-03
3368304	WT1	4.55E-03
2635263	DZIP3	4.56E-03
3737677	---	4.59E-03
3853108	NOTCH3	4.61E-03
2497252	SLC9A2	4.65E-03
3015682	PCOLCE	4.67E-03
3619400	C15orf52	4.67E-03
3880629	CST7	4.67E-03
3918447	IFNAR2	4.68E-03
3233605	PFKFB3	4.68E-03
2767295	BEND4	4.69E-03
3351531	ARCN1	4.72E-03
3848039	C3	4.74E-03
2608469	ITPR1	4.76E-03
3710515	DNAH9	4.76E-03
3490741	SUGT1	4.77E-03
2501140	IL1F6	4.79E-03
3599669	---	4.79E-03
3973556	CXorf59	4.80E-03
2708457	CLCN2	4.80E-03
3751541	GIT1	4.81E-03
3766415	SMARCD2	4.81E-03
2734629	PTPN13	4.82E-03
2849992	FAM134B	4.84E-03
3851720	HOOK2	4.85E-03
2494537	ARID5A	4.88E-03
3713794	EPN2	4.88E-03
3715839	TRAF4	4.90E-03
3529113	CMTM5	4.91E-03
3707041	SMTNL2	4.93E-03
3777991	KIAA0802	4.93E-03
2427898	OVGP1	4.94E-03
3597421	LACTB	4.97E-03
2555174	PUS10	4.99E-03
2993206	MPP6	5.00E-03
2754673	ANKRD37	5.00E-03
3842379	EPN1	5.02E-03
3975455	DUSP21	5.05E-03
3977083	CCDC22	5.06E-03
3744377	SLC25A35	5.07E-03
3339423	INPPL1	5.08E-03
3867865	PIH1D1	5.08E-03
3824596	B3GNT3	5.08E-03
3882720	RALY	5.09E-03
3757154	KRT14	5.10E-03
3092808	NRG1	5.13E-03
3859915	U2AF1L4	5.13E-03
2462456	HEATR1	5.16E-03
3894995	SNRPB	5.19E-03
3846011	SGTA	5.22E-03
2683763	ROBO1	5.24E-03
3066751	SYPL1	5.25E-03
2441043	OLFML2B	5.27E-03
3745781	ZNF18	5.31E-03
2737220	C4orf17	5.33E-03
3972657	IL1RAPL1	5.33E-03
3573051	C14orf148	5.36E-03
3834519	ARHGEF1	5.40E-03
2548402	EIF2AK2	5.41E-03
3855701	---	5.42E-03
2866543	CETN3	5.43E-03
3948528	UPK3A	5.45E-03
2813414	CCNB1	5.46E-03
3961023	CBX7	5.47E-03
3947011	C22orf46	5.48E-03
2479560	ABCG8	5.49E-03
2544781	DTNB	5.49E-03
3430228	RFX4	5.53E-03
3762339	MRPL27	5.57E-03
2523689	ABI2	5.64E-03
3836841	CALM3	5.64E-03
2611122	TSEN2	5.64E-03
2690776	B4GALT4	5.65E-03
2585476	SCN7A	5.65E-03
3045739	HERPUD2	5.66E-03
2342475	LHX8	5.69E-03
2554018	EFEMP1	5.72E-03
3094286	PROSC	5.73E-03
3671607	LRRC50	5.75E-03
3571553	C14orf43	5.77E-03
3018535	BCAP29	5.79E-03
2560178	LBX2	5.79E-03
3568108	SGPP1	5.79E-03
2464909	SMYD3	5.81E-03
3436329	FAM101A	5.87E-03
3662750	POLR2C	5.90E-03
3474787	---	5.91E-03
3992747	ZIC3	5.91E-03
3048373	POLM	5.91E-03
2998536	CDK13	5.93E-03
3556386	RAB2B	5.98E-03
3981959	SLC16A2	5.98E-03
3620022	LTK	5.98E-03
2746645	TMEM184C	5.99E-03
3719474	TADA2A	6.04E-03
3087167	TUSC3	6.05E-03
3554104	KIF26A	6.06E-03
3522327	SLC15A1	6.06E-03
3199431	ZDHHC21	6.07E-03
3223738	TRAF1	6.08E-03
2442424	ILDR2	6.10E-03
3650953	TMC5	6.10E-03
3457824	TIMELESS	6.11E-03
2655338	HTR3E	6.12E-03
3950726	PPP6R2	6.12E-03
2993727	SNX10	6.13E-03
3229994	INPP5E	6.13E-03
3390067	NPAT	6.15E-03
3728625	OR4D2	6.16E-03
2565410	KIAA1310	6.17E-03
3409006	MED21	6.20E-03
3914327	C20orf201	6.21E-03
3456049	ITGB7	6.24E-03
2813524	RAD17	6.27E-03
2910868	TINAG	6.29E-03
2790486	DCHS2	6.36E-03
3179975	PHF2	6.36E-03
3383322	NARS2	6.38E-03
3012633	GATAD1	6.39E-03
2841802	HMP19	6.39E-03
2855963	HCN1	6.39E-03
3194896	TRAF2	6.40E-03
3280902	DNAJC1	6.41E-03
3113133	COLEC10	6.41E-03
3166718	DNAJA1	6.41E-03

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

3230490	EDF1	6.43E-03	3029900	CNTNAP2	6.88E-03	3933039	TMPRSS2	7.57E-03	2818035	CKMT2	8.10E-03
3954596	RTDR1	6.44E-03	3680583	RSL1D1	6.89E-03	2657025	RTP4	7.59E-03	3377789	RELA	8.10E-03
2673509	UQCRC1	6.45E-03	2775965	COQ2	6.89E-03	3356115	APLP2	7.65E-03	3329724	MADD	8.11E-03
3444304	TAS2R8	6.45E-03	3667281	SF3B3	6.90E-03	2675998	TLR9	7.66E-03	3934642	KRTAP12-1	8.11E-03
3911485	APCDD1L	6.48E-03	3770305	CD300C	6.94E-03	3976341	TIMP1	7.66E-03	3418249	KIF5A	8.12E-03
3825383	UPF1	6.48E-03	2421883	GBP1	6.97E-03	3318383	OR52B6	7.67E-03	2540210	NOL10	8.13E-03
2595042	ALS2	6.50E-03	3238466	COMMD3	7.00E-03	2808748	PARP8	7.70E-03	2391302	ACAP3	8.15E-03
3951927	BID	6.52E-03	3766960	SMURF2	7.00E-03	2906934	PRICKLE4	7.70E-03	3856554	ZNF100	8.16E-03
3381063	CLPB	6.53E-03	3490655	CKAP2	7.01E-03	3740462	RILP	7.70E-03	2396480	EXOSC10	8.17E-03
3434594	ACADS	6.53E-03	3429754	KIAA1033	7.04E-03	3332276	MS4A2	7.70E-03	2369252	C1orf49	8.18E-03
2816298	IQGAP2	6.53E-03	2607110	HDLBP	7.04E-03	3004768	ZNF273	7.71E-03	2599433	USP37	8.23E-03
2388794	ZNF238	6.54E-03	2443537	SCYL3	7.08E-03	2733287	PRDM8	7.72E-03	2716246	FLJ35424	8.23E-03
2662491	TMEM111	6.56E-03	3528605	OR4E2	7.17E-03	4036497	TTTY5	7.73E-03	3345157	PIWIL4	8.24E-03
3558012	TINF2	6.57E-03	3064462	VGF	7.18E-03	3715109	WSB1	7.74E-03	2382043	C1orf65	8.28E-03
3628104	C2CD4B	6.57E-03	2820893	RFESD	7.19E-03	3560711	BAZ1A	7.75E-03	2641769	RHO	8.30E-03
2899808	PRSS16	6.59E-03	2436576	C1orf43	7.23E-03	3727033	FLJ42842	7.77E-03	3581442	JAG2	8.31E-03
2532314	ALPI	6.60E-03	3707095	ARRB2	7.23E-03	3074912	DGKI	7.79E-03	3509910	FAM48A	8.31E-03
3695107	TK2	6.60E-03	3766512	GH1	7.24E-03	2973995	EPB41L2	7.79E-03	3674840	POLR3K	8.32E-03
3956781	AP1B1	6.62E-03	3971923	ZFX	7.24E-03	2317317	TP73	7.79E-03	2805786	TARS	8.32E-03
3820758	DNM2	6.64E-03	2756497	ATP5I	7.25E-03	3371339	PHF21A	7.80E-03	2350952	GSTM2	8.34E-03
3826504	ZNF431	6.66E-03	2857112	CCNO	7.28E-03	3302572	CRTAC1	7.85E-03	3816509	GADD45B	8.36E-03
2895945	---	6.69E-03	3253683	ZMIZ1	7.29E-03	3438061	GPR133	7.86E-03	3759137	ITGA2B	8.41E-03
3065740	RELN	6.71E-03	4013460	CYSLTR1	7.31E-03	3152220	KIAA0196	7.87E-03	2932219	OPRM1	8.41E-03
3428190	SLC17A8	6.73E-03	3375894	EML3	7.33E-03	2721087	GBA3	7.96E-03	3228279	C9orf98	8.42E-03
3071700	IMPDH1	6.73E-03	2358949	CGN	7.35E-03	3757433	ACLY	7.96E-03	3943101	DEPDC5	8.51E-03
3149161	CSMD3	6.74E-03	3047581	INHBA	7.38E-03	2699145	SLC9A9	7.98E-03	3011830	DPY19L2P4	8.53E-03
2593464	ANKRD44	6.74E-03	3680953	CPPED1	7.39E-03	3015276	CNPY4	7.99E-03	3899111	BFSP1	8.54E-03
3891163	GNAS	6.76E-03	3948640	FBLN1	7.41E-03	3720817	RAPGEFL1	8.02E-03	2666566	NGLY1	8.57E-03
3513147	HTR2A	6.76E-03	3113280	DEPDC6	7.43E-03	3973803	XK	8.03E-03	4027355	UBL4A	8.61E-03
2943874	KIF13A	6.80E-03	3635456	MESDC2	7.43E-03	3816815	GNA15	8.06E-03	3611126	MEF2A	8.62E-03
2454935	ANGEL2	6.82E-03	3226160	SIAT7F	7.44E-03	3836217	KLC3	8.09E-03	2809245	ITGA2	8.63E-03
3453592	MLL2	6.85E-03	2593670	SF3B1	7.51E-03	2734992	NUDT9	8.09E-03	3000276	RAMP3	8.66E-03
3751184	PHF12	6.85E-03	2954355	CUL7	7.52E-03	3013894	DLX6	8.09E-03	2667809	OSBPL10	8.68E-03

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

3817316	CREB3L3	8.68E-03	3972093	POLA1	9.35E-03	2969886	FYN	0.010	2324634	CDC42	0.011
2405192	YARS	8.69E-03	3759410	GFAP	9.37E-03	3293244	SAR1A	0.010	3003228	SUMF2	0.011
2952927	KCNK16	8.75E-03	2644418	CLDN18	9.39E-03	2779992	UBE2D3	0.010	3315712	B4GALNT4	0.011
2691798	IQCB1	8.77E-03	3986412	---	9.41E-03	2584520	FIGN	0.010	3863060	EXOSC5	0.011
3883690	EPB41L1	8.77E-03	3834439	DMRTC2	9.47E-03	3970833	PDHA1	0.010	3119572	RHPN1	0.011
3721886	MLX	8.79E-03	3379597	MTL5	9.49E-03	3354293	ROBO3	0.010	3992408	FHL1	0.011
3744300	C17orf44	8.79E-03	2661992	OXTR	9.50E-03	3343008	TMEM126A	0.010	3735392	ZACN	0.011
2523419	ALS2CR8	8.81E-03	3124353	---	9.53E-03	3406195	C12orf60	0.010	3458819	CYP27B1	0.011
3090697	CDCA2	8.84E-03	3883309	CEP250	9.56E-03	2930957	ULBP2	0.010	3815014	BSG	0.011
2343334	GIPC2	8.85E-03	3722739	G6PC3	9.57E-03	3770029	CDC42EP4	0.010	3399545	NCAPD3	0.011
2428405	RHOC	8.89E-03	3601840	CSK	9.61E-03	3131916	WHSC1L1	0.010	2880905	CSNK1A1	0.011
3437500	GLT1D1	8.90E-03	3429008	ASCL1	9.63E-03	3884922	DHX35	0.010	2379009	PPP2R5A	0.011
2777333	PPM1K	8.95E-03	2484970	EHBP1	9.64E-03	3244539	ZNF22	0.010	3042952	HOXA10	0.011
2607757	CNTN6	8.95E-03	3017068	NFE4	9.64E-03	3186191	ATP6V1G1	0.010	3478957	DDX51	0.011
2650357	ARL14	9.00E-03	2949038	BAT1	9.66E-03	2456805	BPNT1	0.010	2527856	RQCD1	0.011
3185643	RGS3	9.01E-03	4018194	CAPN6	9.67E-03	3892456	SS18L1	0.010	3978999	UBQLN2	0.011
3790259	MALT1	9.04E-03	2368840	FAM5B	9.68E-03	2689452	ZNF80	0.011	2488252	DYSF	0.011
3883819	DLGAP4	9.06E-03	2933536	TULP4	9.71E-03	3441542	ANO2	0.011	3638337	POLG	0.011
3402836	LEPREL2	9.06E-03	2622026	CCDC36	9.71E-03	3128954	TRIM35	0.011	3012677	C7orf64	0.011
3665083	B3GNT9	9.07E-03	2597552	ERBB4	9.73E-03	3631964	PKM2	0.011	2889486	AGXT2L2	0.011
3434490	CABP1	9.10E-03	3555492	TMEM55B	9.76E-03	3026495	AKR1D1	0.011	3571634	COQ6	0.011
3850990	ZNF653	9.13E-03	2460551	EGLN1	9.76E-03	3932148	BRWD1	0.011	3160500	C9orf70	0.011
3632671	STOML1	9.16E-03	2361697	C1orf66	9.77E-03	2792161	TKTL2	0.011	3829049	RGS9BP	0.011
2701081	P2RY12	9.18E-03	2925510	L3MBTL3	9.77E-03	3872733	ZNF329	0.011	3113180	MAL2	0.011
2500875	CHCHD5	9.23E-03	2889698	CLK4	9.79E-03	2903673	PHF1	0.011	3633403	SIN3A	0.011
2551189	SIX2	9.26E-03	3421897	CNOT2	9.81E-03	2648535	ARHGEF26	0.011	3005995	TYW1	0.011
3427282	C12orf63	9.28E-03	3008108	LIMK1	9.84E-03	3903952	GDF5	0.011	3205834	ANKRD18A	0.011
3887241	SLC12A5	9.28E-03	3871043	PPP1R12C	9.85E-03	3564071	NIN	0.011	3593652	USP8	0.011
3907320	WFDC6	9.30E-03	3193482	COL5A1	9.94E-03	2437801	ARHGEF2	0.011	3674960	LUC7L	0.011
3507710	SLC7A1	9.32E-03	3764103	SRSF1	9.94E-03	3723627	CRHR1	0.011	3203636	SUGT1P1	0.011
3415148	ACVR1B	9.33E-03	2892262	---	9.95E-03	3855660	SUGP1	0.011	3848651	TIMM44	0.011
2444363	SLC9A11	9.35E-03	2336585	SCP2	9.96E-03	2326463	CD52	0.011	3049522	TNS3	0.011
3556888	RBM23	9.35E-03	2999334	HECW1	9.96E-03	3182063	INVS	0.011	3842481	NLRP8	0.011

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

2730714	DCK	0.012
2614663	LRRC3B	0.012
2487082	ANTXR1	0.012
3403224	LOC283314	0.012
3415915	PFDN5	0.012
2773719	CDKL2	0.012
2434490	ENSA	0.012
2796790	KIAA1430	0.012
2894689	TMEM14C	0.012
2678526	C3orf67	0.012
2556529	SERTAD2	0.012
3320301	CTR9	0.012
2640263	ROPN1B	0.012
3838004	PPP1R15A	0.012
2487527	SNRNP27	0.012
2339139	INADL	0.012
2888385	GPRIN1	0.012
3618736	RASGRP1	0.012
2969406	SLC22A16	0.012
3741171	KIAA0664	0.012
2915268	DOPEY1	0.012
3595846	FAM63B	0.012
2843091	RGS14	0.012
2426676	C1orf59	0.012
3692735	CES5A	0.012
3753452	NLE1	0.012
2589255	FKBP7	0.012
2488732	CCT7	0.012
3377226	EHD1	0.012
3886639	YWHAB	0.012
2412529	NRD1	0.012
2697652	FOXL2	0.012
2967989	SCML4	0.012
3126191	PSD3	0.012
3842768	ZNF471	0.012
3878308	CSRP2BP	0.012
2323951	VWA5B1	0.012
3294576	USP54	0.012
3348608	SIK2	0.012
2638886	FAM162A	0.012
2435149	CELF3	0.012
2707824	MCCC1	0.012
3696697	NOB1	0.012
3360874	HPX	0.012
3652338	VWA3A	0.012
3070183	AASS	0.012
2622590	GNAT1	0.012
3580498	CDC42BPB	0.012
3638819	CIB1	0.012
3953033	TRMT2A	0.012
2410470	PIK3R3	0.012
3358049	RNH1	0.012
3260423	CUTC	0.012
4052378	SNRNP35	0.012
3630736	ITGA11	0.012
3223872	RAB14	0.012
3762040	TAC4	0.012
3007829	FZD9	0.012
3350850	RNF214	0.013
3564997	DDHD1	0.013
3441685	VWF	0.013
2620685	SACM1L	0.013
3337168	GSTP1	0.013
2419219	C1orf118	0.013
3182489	RNF20	0.013
3349918	RBM7	0.013
3401804	RAD51AP1	0.013
2358221	RPRD2	0.013
3728820	PPM1E	0.013
2929870	STXBP5	0.013
3930781	SETD4	0.013
2460817	SIPA1L2	0.013
3465274	DCN	0.013
3747288	ZNF287	0.013
3766549	SCN4A	0.013
3031383	REPIN1	0.013
3189422	FAM125B	0.013
2903507	RING1	0.013
2398193	CROCCP3	0.013
3462630	CAPS2	0.013
2586845	SLC25A12	0.013
3174224	SMC5	0.013
2988336	KIAA0415	0.013
3970338	NHS	0.013
3377091	MAP4K2	0.013
2401347	TCEA3	0.013
3916290	FLJ42200	0.013
2380991	IARS2	0.013
3261165	BTRC	0.013
2635184	HHLA2	0.013
3871935	ZNF667	0.013
2878943	PCDH1	0.013
4053462	KLHL17	0.013
2899768	HIST1H4I	0.013
2692816	ITGB5	0.013
3977067	PLP2	0.013
4026902	NAA10	0.013
3861037	ZNF607	0.013
2712906	RNF168	0.013
3056226	STX1A	0.013
2360633	EFNA4	0.013
3260957	LZTS2	0.013
3886453	HNF4A	0.013
2647109	CPA3	0.013
3822322	MRI1	0.013
3891278	TH1L	0.014
2796553	ACSL1	0.014
2593733	HSPD1	0.014
2956593	CRISP1	0.014
3455865	KRT4	0.014
3683549	UMOD	0.014
2633039	OR5AC2	0.014
3259920	ANKRD2	0.014
3682028	MYH11	0.014
2758298	LRPAP1	0.014
2547751	MYADML	0.014
3823488	FLJ25328	0.014
2672532	SETD2	0.014
3008220	CLIP2	0.014
3873777	TGM6	0.014
2527971	STK36	0.014
3415368	KRT86	0.014
3659888	HEATR3	0.014
3318186	MMP26	0.013
2835213	PPARGC1B	0.014
3888613	CEBPB	0.014
2910236	EFHC1	0.014
3075742	KLRG2	0.014
3446355	PLCZ1	0.014
3128411	EBF2	0.014
3512527	TPT1	0.014
3867538	GYS1	0.014

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

3893287	ARFGAP1	0.014
2408855	FOXJ3	0.014
3409127	ARNTL2	0.014
2997272	EEPD1	0.014
3975987	RBM10	0.014
4054437	GJB5	0.014
3828887	ZNF507	0.014
2734784	AFF1	0.014
2949148	BAT3	0.014
2674963	MON1A	0.014
3705539	RNMTL1	0.014
3936442	PEX26	0.014
3873185	RBCK1	0.014
2773872	NAAA	0.014
3564250	TRIM9	0.014
3944147	MCM5	0.014
2348702	SLC35A3	0.014
2645951	TRPC1	0.015
3906709	GTSF1L	0.015
3334304	DNAJC4	0.015
4025771	CD99L2	0.015
2462415	LGALS8	0.015
2892170	WRNIP1	0.015
2329920	TFAP2E	0.015
2812539	SREK1	0.015
3934837	C21orf122	0.015
3238761	MSRB2	0.015
4027009	IRAK1	0.015
3357237	JAM3	0.015
3632806	STRA6	0.015
2345128	SH3GLB1	0.015
2655476	AP2M1	0.015
3344990	PANX1	0.015
3394192	DPAGT1	0.015
3852880	EMR2	0.015
3399004	OPCML	0.015
3944620	MPST	0.015
3723348	HEXIM1	0.015
2324341	NBPF3	0.015
3019158	LRRN3	0.015
3976240	ZNF157	0.015
2954506	CRIP3	0.015
3049700	PKD1L1	0.015
2390050	NLRP3	0.015
3996142	OPN1LW	0.015
3642993	C16orf11	0.015
3260001	MARVELD1	0.015
3854627	JAK3	0.014
3867374	IZUMO1	0.015
2617041	GOLGA4	0.015
2874794	RAPGEF6	0.015
2914777	TTK	0.015
2515783	RAPGEF4	0.015
3175494	GCNT1	0.015
3899551	RBBP9	0.015
3687889	ZNF785	0.015
3716664	SUZ12P	0.015
3842675	ZNF542	0.015
3335643	MUS81	0.015
3020192	TES	0.015
2681195	UBA3	0.015
3157563	NAPRT1	0.015
3226644	ZDHHC12	0.016
3301713	BLNK	0.016
3747792	RASD1	0.016
3330710	OR4C6	0.016
3157132	SLURP1	0.016
3563734	SOS2	0.016
2394784	NOL9	0.016
2687255	CBLB	0.016
3386737	C11orf75	0.016
2581000	NEB	0.016
3677592	ZNF434	0.016
2626802	PTPRG	0.016
3899404	OVOL2	0.016
3841134	CACNG7	0.016
3451670	PUS7L	0.016
2653114	NAALADL2	0.016
3182930	OR13D1	0.016
2719617	BST1	0.016
2519038	FSIP2	0.016
2331771	RLF	0.016
2625546	SPATA12	0.016
2799509	C5orf38	0.016
3131720	BRF2	0.016
3347431	ELMOD1	0.016
2824872	AP3S1	0.016
2695200	PIK3R4	0.016
3972551	MAGEB10	0.016
3125116	DLC1	0.016
3643019	PIGQ	0.016
3361072	DCHS1	0.016
3203753	UBAP2	0.016
3643892	TELO2	0.016
2939034	SERPINB9	0.016
3857523	---	0.016
3800116	MC2R	0.016
2633166	OR5K2	0.016
3894337	SCRT2	0.016
3956226	MN1	0.016
3226138	AK1	0.016
4007086	ZNF41	0.016
3259253	ENTPD1	0.016
3895614	SIGLEC1	0.016
3933243	PRDM15	0.016
2416218	ITGB3BP	0.016
3168032	CCDC107	0.016
2701109	IGSF10	0.016
3868587	SHANK1	0.017
2667181	AZI2	0.017
2409820	BEST4	0.017
3980170	EFNB1	0.017
3094157	ZNF703	0.017
3832830	PAK4	0.017
3135340	OPRK1	0.017
2824483	YTHDC2	0.017
2440440	ITLN2	0.017
2356115	TXNIP	0.017
3736232	SYNGR2	0.017
3907473	ACOT8	0.017
2781138	LEF1	0.017
3191724	ABL1	0.017
2900269	ZSCAN16	0.017
2492015	MRPL35	0.017
2458921	ITPKB	0.017
2926802	MYB	0.017
3392332	CADM1	0.017
3876084	C20orf103	0.017
3630701	CLN6	0.017
3389745	CWF19L2	0.017
3843797	ZNF274	0.017
2808438	NNT	0.017

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

3168508	MELK	0.017
3501661	ARHGEF7	0.017
3391653	DRD2	0.017
2609824	CPNE9	0.017
3854066	C19orf42	0.017
3977205	GAGE12G	0.017
2390180	TRIM58	0.017
3224556	---	0.017
2623413	GPR62	0.017
3359469	NAP1L4	0.017
3963289	LDOC1L	0.017
3107661	INTS8	0.017
2362723	FCRL6	0.017
2325002	KDM1A	0.017
3677795	CREBBP	0.017
3603405	---	0.017
3688381	ZNF843	0.017
2805078	CDH6	0.017
2451419	RABIF	0.017
2620985	TMIE	0.018
2620150	ZNF660	0.018
3835467	ZNF234	0.018
2487882	VAX2	0.018
3722195	AOC3	0.018
3643100	WFIKKN1	0.018
3854297	NR2F6	0.018
2928930	PHACTR2	0.017
3734270	DNAI2	0.017
3759335	GJC1	0.017
2963929	RNGTT	0.017
3758317	BRCA1	0.017
3919952	MORC3	0.017
3558290	KHNYN	0.017
2620256	KIF15	0.018
3529237	DHRS2	0.018
3659670	FLJ44674	0.018
2583631	RBMS1	0.018
3751164	DHRS13	0.018
3190762	ENDOG	0.018
3914786	ABCC13	0.018
3855633	TM6SF2	0.018
3580769	CKB	0.018
3560403	EGLN3	0.018
2770469	IGFBP7	0.018
3832292	KCNK6	0.018
3330965	OR8U1	0.018
2455699	USH2A	0.018
2475678	LBH	0.018
3675205	C16orf13	0.018
2413685	SSBP3	0.018
3417075	DGKA	0.018
3056131	TBL2	0.018
3849267	ZNF558	0.018
3610982	SYNM	0.018
3511031	ELF1	0.018
3459801	DPY19L2	0.018
3459434	FAM19A2	0.018
3991109	MST4	0.018
2469157	GRHL1	0.018
3271687	PPP2R2D	0.018
3910724	CBLN4	0.018
2672190	LRRC2	0.018
3393622	SCN4B	0.018
2716124	HGFAC	0.019
3669092	TERF2IP	0.019
3656223	ITGAL	0.019
3815685	C19orf24	0.019
2925871	ENPP3	0.019
2360989	MSTO1	0.019
2489071	TET3	0.019
3708528	TNK1	0.019
3869714	ZNF611	0.019
3991650	PHF6	0.019
3867734	SLC6A16	0.019
2639225	PDIA5	0.019
3262490	C10orf78	0.019
3064024	C7orf61	0.019
3595315	CGNL1	0.019
3891048	NPEPL1	0.019
3757423	KLHL11	0.019
3709213	CYB5D1	0.019
3656151	MYLPF	0.019
2675457	C3orf18	0.019
2677723	ARHGEF3	0.019
3928620	KRTAP11-1	0.019
2730554	RUFY3	0.019
3526831	RASA3	0.019
3848907	KANK3	0.019
2948259	TRIM26	0.019
3791482	PHLPP1	0.019
3715614	SLC13A2	0.019
3527662	RNASE6	0.019
3743194	SLC13A5	0.019
3737140	GAA	0.019
3260636	WNT8B	0.019
3133233	PLAT	0.019
3705967	SERPINF1	0.019
2326410	CCDC21	0.019
2883541	SOX30	0.019
2717518	AFAP1	0.020
7385683	VPS41	0.020
3972025	PDK3	0.020
3330700	OR4P4	0.020
2865860	CCNH	0.020
3653398	TNRC6A	0.020
3694657	CDH11	0.020
3109191	POLR2K	0.020
2441940	LMX1A	0.020
2511603	GALNT5	0.020
3571944	LTBP2	0.020
2835576	SYNPO	0.020
3812385	CD226	0.020
4015661	TAF7L	0.020
2771839	TMPRSS11D	0.020
3920385	TTC3	0.020
3284073	EPC1	0.020
2901970	DDR1	0.020
3090053	SLC25A37	0.020
3884640	RALGAPB	0.020
3710108	GLP2R	0.020
2451309	KDM5B	0.020
3843386	ZNF530	0.020
3601348	LOXL1	0.020
3939470	MMP11	0.020
3669171	CNTNAP4	0.020
2910477	FBXO9	0.020
3869237	FPR1	0.020
3179551	FGD3	0.020
2318157	RNF207	0.020
3358174	IRF7	0.020
3198346	PTPRD	0.020
2989050	RAC1	0.020

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

2558844	CLEC4F	0.020
3709327	CNTROB	0.020
3594825	PIGB	0.020
3643431	CHTF18	0.020
3818468	TNFSF9	0.020
2362323	OR6K6	0.020
3354380	HEPN1	0.020
2732391	CCNG2	0.020
3629494	CLPX	0.020
2853642	C5orf42	0.020
3195034	PTGDS	0.021
3304746	USMG5	0.020
2345196	HS2ST1	0.021
3592109	SORD	0.021
2553192	ASB3	0.021
3553531	TNFAIP2	0.021
3593452	DTWD1	0.021
3347549	CUL5	0.021
4018436	LHFPL1	0.021
3841184	CACNG6	0.021
2456204	GPATCH2	0.021
3864286	PSG9	0.021
3683879	DNAH3	0.021
3882949	DYNLRB1	0.021
3960302	SOX10	0.021
3762625	MBTD1	0.021
3025005	EXOC4	0.021
3318961	OR10A5	0.021
3559690	HEATR5A	0.021
3820469	ICAM5	0.021
3562671	KLHL28	0.021
3127878	ENTPD4	0.021
3940901	SEZ6L	0.021
2964553	BACH2	0.021
3347658	ATM	0.021
3501999	SOX1	0.021
2757751	MXD4	0.021
2339454	ANGPTL3	0.021
3931112	HLCS	0.021
3693240	CCDC102A	0.021
3310413	ATE1	0.021
2879927	LARS	0.021
3892561	FLJ44790	0.021
3994610	MAGEA8	0.021
3587495	SCG5	0.021
3451375	PRICKLE1	0.021
3644625	E4F1	0.021
3476457	NCOR2	0.021
3810542	CCBE1	0.021
3557430	MYH6	0.021
3282016	ABI1	0.021
2527939	BCS1L	0.021
3302805	HPS1	0.022
3823982	MYO9B	0.022
3606304	AKAP13	0.022
2960146	COL9A1	0.022
3319018	NLRP14	0.022
2764478	CCKAR	0.022
3931946	---	0.022
2318455	CAMTA1	0.022
3589756	PAK6	0.022
3289392	FLJ31958	0.022
3653516	SLC5A11	0.022
3258966	CYP2C18	0.022
3252382	MYST4	0.022
2436526	TPM3	0.022
3644593	MLST8	0.022
3747966	SREBF1	0.022
3401259	TEAD4	0.022
3453882	MCRS1	0.022
3717539	RHOT1	0.022
3181302	NCBP1	0.022
2953435	C6orf130	0.022
3825713	GATAD2A	0.022
3624513	MYO5C	0.022
3354719	---	0.022
3960246	ANKRD54	0.022
2961929	HMGN3	0.022
3589212	FAM98B	0.022
3937814	AIFM3	0.022
2521479	HSPE1	0.022
2605674	ILKAP	0.022
3735847	SEPT9	0.022
2702610	SHOX2	0.022
3699178	WDR59	0.022
2880463	C5orf46	0.022
2361342	SEMA4A	0.022
3734236	TTYH2	0.022
3673600	MGC23284	0.022
3681956	KIAA0430	0.022
2606741	ANKMY1	0.022
3025740	TMEM140	0.023
3965447	IL17REL	0.023
3065244	RASA4	0.023
3614901	HERC2	0.023
3378830	CORO1B	0.023
3791254	TNFRSF11A	0.023
3607698	C15orf42	0.023
3670631	CENPN	0.023
2780143	BDH2	0.023
2695941	TOPBP1	0.023
2574984	LIMS2	0.023
3673583	IL17C	0.023
3514879	TPTE2P2	0.023
2955691	RCAN2	0.023
2343170	CCDC55	0.023
2831519	C5orf32	0.023
2323087	ACTL8	0.023
2828520	SLC22A5	0.023
3902764	C20orf112	0.023
3621080	TGM5	0.023
3874498	MAVS	0.023
3215395	BARX1	0.023
3340697	UVRAG	0.023
2476671	RASGRP3	0.023
3903999	C20orf173	0.023
3402039	KCNA5	0.023
2992243	DNAH11	0.023
3870733	LILRB2	0.023
3200762	SLC24A2	0.023
3894727	SIRPB1	0.023
2427930	WDR77	0.023
3212420	SLC28A3	0.023
3071878	KCP	0.023
3975893	PHF16	0.023
3655665	MAZ	0.023
2693569	ZXDC	0.023
2435443	TCHH	0.024
2376799	IKBKE	0.024
2712236	MUC4	0.024
3418610	XRCC6BP1	0.024
3992041	---	0.024

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

2982270	FLJ27255	0.024
3853761	CIB3	0.024
3994915	HMGB3	0.024
3250278	HK1	0.024
3896078	SLC23A2	0.024
3603408	PSMA4	0.024
2564816	ANKRD36B	0.024
3375340	CPSF7	0.024
3127745	TNFRSF10D	0.024
2970086	LAMA4	0.024
3917155	USP16	0.024
3534128	FAM179B	0.024
3239437	GPR158	0.024
4007765	PRAF2	0.024
3784783	MOCOS	0.024
2358855	ZNF687	0.024
3751625	SSH2	0.024
3863597	CNFN	0.024
3323413	HTATIP2	0.024
2530539	MFF	0.024
3772661	TIMP2	0.024
3457752	STAT2	0.024
2875685	FSTL4	0.024
3647993	CIITA	0.024
2909263	MEP1A	0.024
3957790	PIK3IP1	0.024
3527785	SLC39A2	0.024
3320123	ADM	0.024
2425212	DBT	0.024
2620894	RTP3	0.024
2649532	RSRC1	0.024
3769779	SLC39A11	0.024
3306516	SMNDC1	0.024
3719980	LASP1	0.024
3673806	ACSF3	0.025
3860737	ZNF585A	0.025
3623552	ATP8B4	0.025
3842839	ZNF470	0.025
2855542	CCL28	0.025
3164312	ACER2	0.025
3849688	ZNF266	0.025
3869396	ZNF841	0.025
3904119	CPNE1	0.025
2672016	FYCO1	0.025
2331857	SMAP2	0.025
2524743	FASTKD2	0.025
3005069	ZNF92	0.025
3755934	ORMDL3	0.025
2394817	KLHL21	0.025
3718185	CCL11	0.025
2476075	SPAST	0.025
3708462	ACAP1	0.025
2882747	HAND1	0.025
3833757	SNRPA	0.025
2609870	BRPF1	0.025
2877314	CDC23	0.025
2595560	RAPH1	0.025
2334319	TOE1	0.025
3300211	FGFBP3	0.025
2554975	BCL11A	0.025
2685944	CPOX	0.025
2675720	IQCF1	0.025
3469319	APPL2	0.025
2443575	KIFAP3	0.025
2544625	POMC	0.025
3473750	VSIG10	0.025
2906333	DAAM2	0.025
3064293	EPHB4	0.025
3869312	ZNF649	0.026
3212706	---	0.026
3258384	CYP26A1	0.026
3145149	TP53INP1	0.026
3204928	HINT2	0.026
3815649	CIRBP	0.026
3401325	TSPAN9	0.026
2791419	FAM198B	0.026
2698565	TFDP2	0.026
3499632	ERCC5	0.026
3815888	APC2	0.026
2511153	KCNJ3	0.026
2475116	PLB1	0.026
2799184	NDUFS6	0.026
3929664	TMEM50B	0.026
3072630	TSGA13	0.026
2878809	ARAP3	0.026
2534252	MLPH	0.026
2602770	DNER	0.026
3757770	STAT5B	0.026
3830320	MAG	0.026
3067250	SLC26A3	0.026
2497161	IL18RAP	0.026
3190190	LCN2	0.026
3402874	GNB3	0.026
3922100	MX1	0.026
4021508	ZNF280C	0.026
3983105	APOOL	0.026
3388631	TMEM123	0.026
2603987	NGEF	0.026
3687910	ZNF689	0.026
2654394	FXR1	0.026
4002809	APOO	0.026
3695916	CENPT	0.026
3884892	FAM83D	0.026
3359910	NUP98	0.026
2742829	INTU	0.026
3473586	KSR2	0.026
2828135	LYRM7	0.027
2924851	RSPO3	0.027
2468105	LOC150622	0.027
3248470	C10orf107	0.027
3331603	C11orf31	0.027
3833893	CYP2B7P1	0.027
3161042	INSL4	0.027
3934785	C21orf67	0.027
3212143	UBQLN1	0.027
2536531	FARP2	0.027
2841491	C5orf41	0.027
3878220	C20orf72	0.027
2496628	C2orf29	0.027
3840224	ZNF528	0.027
3742236	PELP1	0.027
3830649	COX6B1	0.027
2472054	GDF7	0.027
2522247	AOX1	0.027
2756029	FRG1	0.027
2957314	GSTA2	0.027
3216529	ZNF782	0.027
3063968	ZCWPW1	0.027
2453036	FCAMR	0.027
2461786	ARID4B	0.027
3257268	IFIT5	0.027
3318666	SMPD1	0.027

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

2920327	NR2E1	0.027
3507686	LOC728437	0.027
2440664	B4GALT3	0.027
3456688	GPR84	0.027
3452664	ENDOU	0.027
3456130	AAAS	0.027
3173974	FAM189A2	0.027
3860596	ZNF461	0.027
2452977	FAIM3	0.027
3502411	F7	0.027
2662956	VGLL4	0.027
2743370	C4orf33	0.027
2677356	WNT5A	0.027
3909777	SALL4	0.027
3834176	TMEM91	0.027
3752709	MYO1D	0.027
3251566	OIT3	0.027
2562343	GGCX	0.027
3944637	KCTD17	0.027
2880679	SH3TC2	0.027
3551566	EVL	0.027
3260829	FAM178A	0.027
2399765	CAPZB	0.027
3555736	NDRG2	0.028
3346584	BIRC2	0.028
3845120	C19orf23	0.028
3482219	NUPL1	0.028
3336652	SYT12	0.028
3553998	TDRD9	0.028
3461795	PTPRB	0.028
3715703	SUPT6H	0.028
3987029	TMEM164	0.028
2950307	HLA-DOA	0.028
4023467	ARHGEF6	0.028
3528115	TOX4	0.028
3192062	BAT2L1	0.028
3316447	AP2A2	0.028
2658595	HES1	0.028
3643143	WDR90	0.028
2901393	TRIM40	0.028
3844822	MED16	0.028
2830450	NPY6R	0.028
3381038	PHOX2A	0.028
2363784	HSPA6	0.028
3512294	TSC22D1	0.028
3159735	DMRT3	0.028
2572601	CCDC93	0.028
3604267	C15orf26	0.028
2717857	CPZ	0.028
3764199	MKS1	0.028
3577360	PRIMA1	0.028
2643901	PPP2R3A	0.028
2378019	CAMK1G	0.028
2784027	ANXA5	0.028
3646434	UBN1	0.028
3994451	CXorf40A	0.028
3455914	KRT78	0.028
2973376	PTPRK	0.029
3467720	GOLGA2B	0.029
2380440	SPATA17	0.029
2690715	IGSF11	0.029
3670918	PLCG2	0.029
2853102	PRLR	0.029
2337217	C1orf175	0.029
2796623	SLED1	0.029
3937183	DGCR8	0.029
3330685	OR4C15	0.029
3447129	KIAA0528	0.029
2652669	---	0.029
3512769	ZC3H13	0.029
3267678	WDR11	0.029
2818079	ZCCHC9	0.029
3181728	TGFBR1	0.029
3431892	SH2B3	0.029
2562685	IMMT	0.029
3533397	SIP1	0.029
2372169	OCLM	0.029
3883013	TP53INP2	0.029
3778601	VAPA	0.029
2871617	TRIM36	0.029
2319550	RBP7	0.029
2674047	LAMB2	0.029
2412834	ZCCHC11	0.029
2328750	CCDC28B	0.029
3835035	CD177	0.029
3191352	NCS1	0.029
3690470	ABCC11	0.029
3621728	FRMD5	0.029
3821079	DOCK6	0.029
3894637	NSFL1C	0.029
3377569	SLC25A45	0.030
3712835	LRRC48	0.030
3094611	LETM2	0.030
3344861	C11orf54	0.030
2629345	GPR27	0.030
3884191	SRC	0.030
3561381	NKX2-1	0.030
2587730	SP9	0.030
3676669	RNPS1	0.030
2346625	EPHX4	0.030
3319937	WEE1	0.030
3603840	C15orf37	0.030
4005392	BCOR	0.030
2617433	VILL	0.030
3845899	TIMM13	0.030
2363084	NCSTN	0.030
2709750	SST	0.030
3770361	CD300LF	0.030
3680249	PRM3	0.030
3209060	TRPM3	0.030
3693214	DOK4	0.030
3493448	PIBF1	0.030
2854824	HEATR7B2	0.030
3331217	P2RX3	0.030
2987523	CHST12	0.030
4042392	MIB2	0.030
3223776	C5	0.030
2440586	PVRL4	0.031
3119516	ZNF696	0.031
3301141	CYP2C8	0.031
3443868	CD69	0.031
3930942	CLDN14	0.031
3502259	MCF2L	0.031
3746675	CDRT4	0.031
2635741	CD96	0.031
3999148	GPR143	0.031
2663295	TMEM40	0.031
2322226	CLCNKA	0.031
3227696	RAPGEF1	0.031
3518766	EDNRB	0.031
2452754	SLC26A9	0.031
3822723	PKN1	0.031

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

3742708	C1QBP	0.031
2573326	LOC84931	0.031
2552368	LHCGR	0.031
2623662	DNAH1	0.031
3646000	DNASE1	0.031
3315584	NLRP6	0.031
3263944	PDCD4	0.031
3101851	C8orf45	0.031
4009288	HSD17B10	0.031
2338487	FGGY	0.031
3974957	GPR82	0.031
3022422	FSCN3	0.031
2669979	CX3CR1	0.031
2559849	SLC4A5	0.031
3315952	RASSF7	0.032
3973692	PRRG1	0.032
2914070	MYO6	0.032
2975867	MAP3K5	0.032
2327677	EPB41	0.032
3414029	KCNH3	0.032
3977347	CCNB3	0.032
3675101	MRPL28	0.032
3289631	CSTF2T	0.032
2770039	NMU	0.032
3819312	SNAPC2	0.032
3949229	TBC1D22A	0.032
3303109	COX15	0.032
2477438	QPCT	0.032
3603295	CRABP1	0.032
2922881	RFX6	0.032
3860793	ZNF585B	0.032
4004035	FTHL17	0.032
3895075	IDH3B	0.032
2664760	DAZL	0.032
3675266	JMJD8	0.032
3942124	CABP7	0.032
2545534	C2orf53	0.032
3870135	ZNF347	0.032
3079576	SMARCD3	0.032
3907234	SDC4	0.032
3447348	SOX5	0.032
3481296	SGCG	0.032
3363266	DKK3	0.032
2702307	CCNL1	0.032
3628832	DAPK2	0.032
3890099	MC3R	0.032
2398073	FBXO42	0.032
3476012	MPHOSPH9	0.032
3674659	GAS8	0.032
3740664	C17orf91	0.032
3913018	LAMA5	0.033
2708066	KLHL6	0.033
3111530	ENY2	0.033
2714407	IDUA	0.033
2408499	SCMH1	0.033
3578089	C14orf49	0.033
2980870	NOX3	0.033
2367154	BAT2L2	0.033
3269373	ZRANB1	0.033
2902804	C2	0.033
3316234	NS3BP	0.033
3376046	LRRN4CL	0.033
3048468	GCK	0.033
3901851	ABHD12	0.033
2621583	ZNF589	0.033
3127259	NUDT18	0.033
3335338	FAM89B	0.033
3175274	PCSK5	0.033
3149843	RAD21	0.033
2888674	MXD3	0.033
2358700	GABPB2	0.033
3418394	SLC26A10	0.033
2417016	WDR78	0.033
3818515	TRIP10	0.033
3545634	NRXN3	0.033
2876213	CDKN2AIP	0.033
2903343	BRD2	0.033
3951302	POTEM	0.033
2942306	TBC1D7	0.033
3580832	XRCC3	0.033
3176999	RMI1	0.033
3472755	TBX3	0.033
3571347	NUMB	0.033
2453365	PLXNA2	0.033
2594773	ALS2CR12	0.033
3643047	RAB40C	0.033
2464129	---	0.033
3349437	---	0.033
2998192	POU6F2	0.033
3011675	ZNF804B	0.033
3738490	GPS1	0.034
2673873	IMPDH2	0.034
3453169	LALBA	0.034
3144740	FP6628	0.034
2357845	FCGR1A	0.034
3867693	C19orf73	0.034
3753935	LYZL6	0.034
2447246	C1orf14	0.034
2821347	ERAP2	0.034
3503164	CDC16	0.034
3623865	SPPL2A	0.034
3955102	GSTT1	0.034
3704567	CBFA2T3	0.034
2856995	ESM1	0.034
3932270	HMGN1	0.034
3555461	OSGEP	0.034
2364438	NUF2	0.034
2771718	UBA6	0.034
2351854	C1orf162	0.034
2608765	ARL8B	0.034
3566383	C14orf105	0.034
3059464	SEMA3A	0.034
2974671	C6orf192	0.034
2926969	PDE7B	0.034
3312045	C10orf90	0.034
3573870	DIO2	0.034
4023006	ZNF75D	0.034
3284882	CUL2	0.034
3739162	TBCD	0.034
2738146	TET2	0.034
4007186	ELK1	0.034
3415988	AMHR2	0.035
3969455	OFD1	0.035
3324162	LUZP2	0.035
3299970	ANKRD1	0.035
3432394	RPH3A	0.035
3884830	PPP1R16B	0.035
3864390	PHLDB3	0.035
3820501	PDE4A	0.035
2644461	ARMC8	0.035
2842157	HRH2	0.035
3430462	BTBD11	0.035

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2828757	ANKRD43	0.035
2973694	ARHGAP18	0.035
3902682	PLAGL2	0.035
3015241	AP4M1	0.035
3230811	DPP7	0.035
3304116	C10orf76	0.035
2701892	C3orf33	0.035
2405576	CSMD2	0.035
2528504	SPEG	0.035
3360622	TRIM5	0.035
3150844	SNTB1	0.035
2362333	MNDA	0.035
2487639	PCBP1	0.035
4026346	PNMA5	0.035
2647647	TSC22D2	0.035
2949859	PBX2	0.035
3532353	FAM177A1	0.036
3332964	C11orf66	0.036
3429159	STAB2	0.036
2633737	GPR128	0.036
3318543	OR52E5	0.036
2908423	SLC29A1	0.036
3632037	PARP6	0.036
2964139	GABRR2	0.036
2573112	SCTR	0.036
2619480	CCBP2	0.036
3914050	STMN3	0.036
2434872	TMOD4	0.036
2713555	KIAA0226	0.036
3190420	CERCAM	0.036
3045570	TBX20	0.036
2339328	---	0.036
3190925	DOLPP1	0.036
3393257	BACE1	0.036
4001029	---	0.036
3817380	EBI3	0.036
3837866	SULT2B1	0.036
4000944	RBBP7	0.036
3806366	LOXHD1	0.036
2622359	RBM6	0.036
3870824	LAIR1	0.036
3202528	LINGO2	0.036
3397951	FLJ45950	0.036
2881923	SLC36A3	0.036
3601387	PML	0.037
2359993	CREB3L4	0.037
2318242	---	0.037
3887069	SNX21	0.037
3725779	MYST2	0.037
3788302	SMAD4	0.037
2518889	ZNF804A	0.037
3398076	NFRKB	0.037
3590498	TYRO3	0.037
3255361	RGR	0.037
2989141	C7orf26	0.037
4009667	FGD1	0.037
2830861	EGR1	0.037
3780287	RNMT	0.037
4014387	RPSA	0.037
3318390	TRIM6-34	0.037
2901503	TRIM39	0.037
3239667	GAD2	0.037
3124180	PINX1	0.037
3468103	GNPTAB	0.037
3895330	SLC4A11	0.037
2419046	ZZZ3	0.037
2727587	KIT	0.037
3139035	ARFGEF1	0.037
2340078	CACHD1	0.037
2891768	FOXC1	0.037
3437780	FZD10	0.037
2900497	ZKSCAN3	0.037
3111695	EBAG9	0.037
3543857	PTGR2	0.038
3319119	OLFML1	0.038
2321960	PLEKHM2	0.038
2897172	RNF144B	0.038
2738664	SGMS2	0.038
3726465	RSAD1	0.038
3090294	ADAMDEC1	0.038
3009520	UPK3B	0.038
3819263	MAP2K7	0.038
3989826	SH2D1A	0.038
2430762	WARS2	0.038
3241601	C10orf68	0.038
3825523	SLC25A42	0.038
2585701	STK39	0.038
3671935	CRISPLD2	0.038
3815936	REEP6	0.038
2912416	BAI3	0.038
3753568	SLFN13	0.038
4015548	XKRX	0.038
3506093	FAM123A	0.038
3015519	PILRA	0.038
3317056	TNNI2	0.038
2715476	FAM193A	0.038
3572340	TMED10	0.038
2691014	GSK3B	0.038
3294854	CAMK2G	0.038
3952880	TXNRD2	0.038
3023246	IRF5	0.038
2505779	GPR148	0.038
3783435	DSG4	0.038
2491686	RNF181	0.038
3374224	OR10W1	0.038
2790999	ACCN5	0.039
2685034	CGGBP1	0.039
3001345	VWC2	0.039
3914021	GMEB2	0.039
3070507	RNF148	0.039
2387126	RYR2	0.039
2971801	MAN1A1	0.039
3944778	GGA1	0.039
2772450	SULT1E1	0.039
3615556	NDNL2	0.039
3450234	PKP2	0.039
3755510	PLXDC1	0.039
3765580	BRIP1	0.039
2601648	DOCK10	0.039
3403539	FOXJ2	0.039
2949330	CLIC1	0.039
3533184	SSTR1	0.039
3955875	TFIP11	0.039
3695235	CCDC79	0.039
3333417	SCGB2A1	0.039
3143970	NBN	0.039
2445643	SEC16B	0.039
2383999	OBSCN	0.039
3807261	SMAD7	0.039
3890640	PCK1	0.039
3224366	RC3H2	0.039
2761285	BOD1L	0.039

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

2357961	BOLA1	0.039	2610136	CRELD1	0.041	2663396	IQSEC1	0.042	3924424	COL6A2	0.043
2970044	TUBE1	0.040	3057520	TMEM120A	0.041	2351940	DDX20	0.042	3291682	JMJD1C	0.043
3085065	ERI1	0.040	3890154	CSTF1	0.041	2746269	LSM6	0.042	2412082	FAF1	0.043
3145107	CCNE2	0.040	3767531	CCDC46	0.041	2850676	CDH18	0.042	3532560	BRMS1L	0.043
3072014	TNPO3	0.040	4010183	SPIN3	0.041	3719231	MRM1	0.042	3662723	COQ9	0.043
3944873	PDXP	0.040	2768354	TXK	0.041	3168136	RGP1	0.042	3851493	ZNF443	0.043
3589822	DISP2	0.040	2415266	CYP2J2	0.041	3869078	SIGLEC12	0.042	3786471	SETBP1	0.043
3557268	PPP1R3E	0.040	3625326	CCPG1	0.041	3224220	LHX6	0.042	2459587	TRIM17	0.043
2460189	PGBD5	0.040	3545183	C14orf166B	0.041	3527418	PARP2	0.042	3661065	RBL2	0.043
3652271	C16orf52	0.040	3947627	TSPO	0.041	3758209	LOC388387	0.042	2875954	VDAC1	0.043
3661940	GNAO1	0.040	3770588	NT5C	0.041	2966636	ASCC3	0.042	2532021	PTMA	0.043
3807965	MRO	0.040	2454343	RD3	0.041	3475764	GPR81	0.042	3266408	EMX2	0.043
3357397	GLB1L2	0.040	2322786	PADI1	0.041	2744597	NAA15	0.042	3825446	DDX49	0.043
3119213	LY6K	0.040	3952566	CLTCL1	0.041	3821159	LPPR2	0.042	2694314	GATA2	0.043
3254468	DYDC2	0.040	2632919	ARL6	0.041	4019599	RNF113A	0.042	3389566	KBTBD3	0.043
3420713	CAND1	0.040	3059667	SEMA3D	0.041	2551786	MCFD2	0.042	2427981	ADORA3	0.043
3377177	CDC42BPG	0.040	2322894	PADI6	0.041	2978050	SHPRH	0.042	3349719	ZBTB16	0.043
3880467	TMEM90B	0.040	3305017	OBFC1	0.041	3580876	PPP1R13B	0.042	3332838	DAK	0.043
2493813	ZNF2	0.040	3737430	FLJ35220	0.041	2553771	CCDC88A	0.042	3316057	DRD4	0.043
3978706	PAGE5	0.040	3768703	ABCA9	0.041	3535674	C14orf166	0.042	2498911	SULT1C2	0.043
2327572	RAB42	0.040	2404209	SDC3	0.041	3924041	ADARB1	0.042	2356300	PIAS3	0.043
3548538	C14orf159	0.040	3722060	VPS25	0.041	3645322	PRSS41	0.042	2770023	PDCL2	0.044
3086206	FDFT1	0.040	2887309	DUSP1	0.041	2340350	DNAJC6	0.043	3893338	COL20A1	0.044
2686371	TOMM70A	0.040	3309383	PRDX3	0.041	2943236	DTNBP1	0.043	2330334	THRAP3	0.044
2962998	KIAA1009	0.040	3115504	MYC	0.042	3959918	TST	0.043	3876645	BTBD3	0.044
2779823	SLC39A8	0.040	2405284	TMEM54	0.042	2460296	AGT	0.043	3129588	KIF13B	0.044
2949971	C6orf10	0.040	2503374	GLI2	0.042	3708961	WRAP53	0.043	2471316	GEN1	0.044
3359461	PHLDA2	0.040	3763656	TRIM25	0.042	3844152	ZNF324	0.043	3304797	CALHM3	0.044
2655606	ECE2	0.041	2546409	ALK	0.042	3759105	FAM171A2	0.043	3035223	MICALL2	0.044
3631517	THAP10	0.041	3456306	ATF7	0.042	3015299	MBLAC1	0.043	3848492	FCER2	0.044
3907711	CDH22	0.041	2997231	PP13004	0.042	3174643	TMC1	0.043	3838809	PRMT1	0.044
3136229	SDR16C5	0.041	2475710	LCLAT1	0.042	3743340	ASGR2	0.043	3469687	CKAP4	0.044
3273251	DIP2C	0.041	3130244	TEX15	0.042	3272834	MTG1	0.043	3237548	ARL5B	0.044

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

3363979	PSMA1	0.044	2451428	KLHL12	0.045	3285119	FZD8	0.046	3603436	CHRNA5	0.048
3924518	MCM3AP-AS	0.044	3680254	PRM2	0.045	2399718	AKR7A2	0.046	3256074	BMPR1A	0.048
3385509	FZD4	0.044	2349211	HEJ1	0.045	3873057	DEFB125	0.047	3579546	WARS	0.048
3840562	HERV-V1	0.044	2832447	PCDHB13	0.045	2400718	USP48	0.047	2324919	EPHB2	0.048
3695433	TRADD	0.044	2772160	---	0.045	3988638	LONRF3	0.047	3975869	RP2	0.048
3757602	DHX58	0.044	3861557	LGALS4	0.045	3977611	CXorf67	0.047	2840002	CCDC99	0.048
3935486	S100B	0.044	2451816	C1orf157	0.045	2374414	GPR25	0.047	3635198	BCL2A1	0.048
3351711	FOXR1	0.044	3382216	ARRB1	0.045	3066297	SRPK2	0.047	3855011	ELL	0.048
3766373	FTSJ3	0.044	3435362	KNTC1	0.045	3452417	SLC38A4	0.047	2900940	MOG	0.048
3717052	NF1	0.044	3605780	SCAND2	0.046	3923426	AGPAT3	0.047	3044597	PDE1C	0.048
2468811	ASAP2	0.044	2768056	GABRA4	0.046	2438117	VHLL	0.047	2951881	PXT1	0.048
3625234	RSL24D1	0.044	2902013	GTF2H4	0.046	2517013	MTX2	0.047	2434178	MTMR11	0.048
3715809	NEK8	0.044	3569814	ACTN1	0.046	2365872	RCSD1	0.047	3652902	SCNN1B	0.048
3016380	CUX1	0.044	2359885	SLC27A3	0.046	3118651	DENND3	0.047	2844479	SQSTM1	0.048
2644014	PCCB	0.044	3322521	KCNC1	0.046	3642875	RAB11FIP3	0.047	3743571	YBX2	0.048
2830742	KDM3B	0.044	3148582	EIF3E	0.046	2833078	NDFIP1	0.047	2953481	TREML1	0.048
3346453	YAP1	0.044	3996404	GDI1	0.046	3360333	OR51A2	0.047	2350922	GSTM4	0.048
2350741	ATXN7L2	0.044	3818732	ARHGEF18	0.046	2615060	RBMS3	0.047	3094245	ERLIN2	0.048
3756997	KRT32	0.044	2536874	GAL3ST2	0.046	3714779	KCNJ12	0.047	3448744	PTHLH	0.049
3417435	MYL6B	0.045	3113894	ZHX2	0.046	3448481	TM7SF3	0.047	3156193	EIF2C2	0.049
3375990	INTS5	0.045	2838462	GABRG2	0.046	2505833	ARHGEF4	0.047	2602304	TM4SF20	0.049
3696142	DPEP2	0.045	3361381	CYB5R2	0.046	3393993	BCL9L	0.047	4001223	RAI2	0.049
3062576	ASNS	0.045	3845944	GNG7	0.046	2435383	S100A10	0.047	3738353	ASPSCR1	0.049
3101385	MTFR1	0.045	2806517	SKP2	0.046	2429613	NHLH2	0.047	3728037	SCPEP1	0.049
3838444	CCDC155	0.045	2350316	FNDC7	0.046	2560317	C2orf65	0.047	2876897	SPOCK1	0.049
2435347	THEM4	0.045	2332144	CTPS	0.046	3421300	MDM2	0.047	2677200	LRTM1	0.049
3091000	BNIP3L	0.045	2749191	GLRB	0.046	3079336	FASTK	0.047	3837464	GLTSCR2	0.049
2443370	F5	0.045	2360850	FDPS	0.046	3843180	ZNF304	0.047	2432647	POLR3C	0.049
2659521	LRRC33	0.045	3221571	RNF183	0.046	3772158	TK1	0.048	2516853	HOXD9	0.049
3380065	CCND1	0.045	3502497	CUL4A	0.046	3764592	TEX14	0.048	2888399	SNCB	0.049
3540839	---	0.045	2961816	PHIP	0.046	2438612	INSRR	0.048	2829416	SEC24A	0.049
2404546	COL16A1	0.045	3679503	TMEM186	0.046	3885537	PLCG1	0.048	3180342	C9orf3	0.049
2675088	IFRD2	0.045	3887165	PCIF1	0.046	3544605	BATF	0.048	3359134	IGF2	0.049

Table B11: *C9ORF72*vCtrl Alternatively Spliced List (n=2,511) [Partek® p-value (alt. splicing) <0.05]

3544251	YLPM1	0.049	3217194	TBC1D2	0.049	3633578	CSPG4	0.049	3940751	MYO18B	0.049
3894365	C20orf54	0.049	2797771	TRIML2	0.049	3042001	CYCS	0.049	3743440	DVL2	0.049
3015786	ZAN	0.049	3841881	NCR1	0.049	3757840	STAT3	0.049	3095766	GINS4	0.049
2414558	DAB1	0.049	3707175	TM4SF5	0.049	2459352	WNT9A	0.049			

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

Transcript	Symbol	p-value	Transcript	Symbol	p-value	Transcript	Symbol	p-value	Transcript	Symbol	p-value
2979871	SYNE1	0.000	3928866	SFRS15	3.02E-13	3843848	ZNF544	8.80E-11	2843091	RGS14	1.70E-09
2715076	WHSC1	1.96E-38	2971267	ROS1	5.56E-13	2367963	RABGAP1L	8.88E-11	3895722	CENPB	2.12E-09
3377044	SF1	2.44E-36	2845591	BRD9	6.18E-13	2664099	MRPS25	1.02E-10	2334052	C1orf228	2.24E-09
3653317	RBBP6	8.93E-32	3509910	FAM48A	6.18E-13	3712835	LRRC48	1.10E-10	2348634	AGL	2.43E-09
2321238	PRDM2	1.51E-23	3036985	RNF216	7.43E-13	3620457	VPS39	1.11E-10	3659156	PHKB	2.52E-09
3771513	PRPSAP1	3.09E-23	3529609	PSME1	7.53E-13	2723997	KLF3	1.11E-10	2870113	FBXL17	2.54E-09
3896621	FERMT1	7.71E-23	3310479	NSMCE4A	9.13E-13	3869361	ZNF615	1.16E-10	3253683	ZMIZ1	2.80E-09
2548970	SRSF7	2.13E-22	3430776	ISCU	1.03E-12	3629811	DENND4A	1.18E-10	2871821	TMED7	3.06E-09
3081862	PTPRN2	3.72E-22	3368054	PAX6	1.10E-12	3398076	NFRKB	1.22E-10	3536706	LGALS3	3.54E-09
3194635	C9orf86	6.83E-22	2622469	RBM5	1.19E-12	2662087	SRGAP3	1.37E-10	3661559	IRX5	3.56E-09
3771800	SRSF2	2.81E-21	3816264	DOT1L	2.27E-12	3597125	TLN2	2.04E-10	3318390	TRIM6-34	4.45E-09
3868183	NUP62	6.28E-20	3249886	TET1	2.31E-12	3908149	ZMYND8	2.23E-10	3746881	NCOR1	4.63E-09
2593464	ANKRD44	6.87E-20	3604287	IL16	2.62E-12	2928930	PHACTR2	2.44E-10	3036476	RADIL	4.72E-09
3240340	WAC	8.72E-18	2967151	HACE1	2.64E-12	2927506	TNFAIP3	2.52E-10	3661065	RBL2	5.00E-09
3882012	DNMT3B	4.11E-17	2818079	ZCCHC9	5.22E-12	3470831	MMAB	2.57E-10	2610336	VHL	5.55E-09
3708663	CHRNB1	5.43E-17	2358743	SCNM1	1.09E-11	2675801	PCBP4	2.72E-10	3159946	SMARCA2	6.50E-09
3778252	ANKRD12	1.23E-16	3557268	PPP1R3E	1.20E-11	3427820	SLC25A3	2.82E-10	3228373	TSC1	6.55E-09
3962997	EFCAB6	1.82E-16	3645253	SRRM2	1.41E-11	3222534	ASTN2	2.98E-10	3553690	MARK3	7.30E-09
3764103	SRSF1	1.86E-16	3335517	KAT5	1.74E-11	2548500	PRKD3	3.21E-10	2752478	WDR17	8.06E-09
3499453	TPP2	5.02E-16	3403015	ENO2	1.79E-11	3017547	MLL5	3.41E-10	2496727	MAP4K4	8.56E-09
2520291	GLS	2.00E-15	2317512	DFFB	2.11E-11	4027708	MTCP1	3.48E-10	3341440	RN28S1	9.52E-09
3571347	NUMB	4.36E-15	3257031	STAMBPL1	2.12E-11	3737430	FLJ35220	3.58E-10	2897899	SOX4	9.75E-09
2962998	KIAA1009	4.38E-15	2708720	EHHADH	2.69E-11	2935475	QKI	3.82E-10	3500055	DAOA	9.79E-09
3249738	HNRNPH3	1.50E-14	2459793	C1orf96	3.47E-11	3168415	CLTA	3.84E-10	2617687	XYLB	1.01E-08
2943236	DTNBP1	2.25E-14	2407755	GJA9	3.73E-11	3614087	UBE3A	4.58E-10	3151473	ZHX1	1.01E-08
2575054	WDR33	2.63E-14	2705266	TNIK	3.81E-11	2662331	CAMK1	5.81E-10	3167731	UNC13B	1.02E-08
3336857	ANKRD13D	2.78E-14	3239760	APBB1IP	4.00E-11	2943874	KIF13A	6.75E-10	2343473	IFI44L	1.20E-08
2704894	PHC3	4.67E-14	3848745	FBN3	5.20E-11	2395245	RERE	7.11E-10	2524743	FASTKD2	1.31E-08
3634852	RASGRF1	5.00E-14	3517251	DACH1	6.16E-11	2785282	SCLT1	7.58E-10	2789266	LRBA	1.47E-08
3199790	PSIP1	6.47E-14	2642911	UBA5	6.65E-11	3940901	SEZ6L	9.96E-10	3907524	PLTP	1.50E-08
3543411	RBM25	1.38E-13	3933999	U2AF1	7.02E-11	3708764	TNFSF12-13	1.09E-09	3868587	SHANK1	1.63E-08
3148796	NUDCD1	2.59E-13	3847356	LONP1	8.02E-11	2488252	DYSF	1.26E-09	3155637	COL22A1	1.77E-08

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3886704	STK4	1.79E-08
3452145	SRSF2IP	1.94E-08
3154700	ZFAT	1.94E-08
3470597	SSH1	1.99E-08
2417791	ANKRD13C	2.12E-08
3282519	ARMC4	2.22E-08
3701481	PKD1L2	2.23E-08
3351531	ARCN1	2.49E-08
2909263	MEP1A	2.80E-08
2400322	HP1BP3	2.90E-08
2346074	ZNF326	2.92E-08
3893760	TPD52L2	2.99E-08
3091000	BNIP3L	3.02E-08
3741997	ANKFY1	3.13E-08
3168136	RGP1	3.18E-08
3708399	SLC2A4	3.26E-08
2404546	COL16A1	3.60E-08
3434193	CCDC64	3.65E-08
3064039	TSC22D4	3.72E-08
2927873	CCDC28A	3.77E-08
3223738	TRAF1	3.94E-08
2877314	CDC23	4.07E-08
3340913	C11orf30	4.15E-08
2419235	FUBP1	4.27E-08
3720921	RARA	4.34E-08
3740838	SMG6	4.34E-08
3471264	VPS29	4.46E-08
2612175	NR2C2	4.50E-08
3716481	GOSR1	4.57E-08
3923436	TRAPPC10	4.58E-08
3553872	KLC1	5.12E-08
2341565	SRSF11	5.16E-08
3701433	C16orf46	5.21E-08
3400034	WNK1	5.55E-08
2376548	MFSD4	5.97E-08
3304718	PCGF6	6.19E-08
3837431	EHD2	6.26E-08
3064082	LRCH4	6.27E-08
3911177	ZBP1	6.32E-08
3764592	TEX14	6.40E-08
3377358	BATF2	6.48E-08
2779163	ADH6	7.29E-08
3134034	PRKDC	7.98E-08
2424524	DPYD	8.30E-08
3839206	MYH14	8.94E-08
2488959	STAMBP	9.00E-08
2366490	BLZF1	9.01E-08
2450568	CACNA1S	9.04E-08
3978819	RRAGB	9.28E-08
3014957	ZNF498	9.32E-08
2925871	ENPP3	9.42E-08
2429147	DENND2C	9.47E-08
3605395	ADAMTSL3	9.68E-08
3430959	ACACB	1.01E-07
3529877	LTB4R2	1.02E-07
2798586	AHRR	1.04E-07
3947604	BIK	1.06E-07
2549455	THUMPD2	1.15E-07
3503164	CDC16	1.20E-07
3258671	PDE6C	1.36E-07
3510755	---	1.38E-07
2546008	SUPT7L	1.40E-07
3653398	TNRC6A	1.43E-07
3845647	MKNK2	1.55E-07
3804143	RPRD1A	1.55E-07
2476671	RASGRP3	1.65E-07
2727226	PDGFRA	1.68E-07
3251848	SEC24C	1.71E-07
3320717	MICAL2	1.72E-07
3413344	PFKM	1.75E-07
2645690	RNF7	1.93E-07
2451428	KLHL12	1.95E-07
3547696	TTC8	1.98E-07
3923257	PDXK	2.02E-07
2606574	NDUFA10	2.03E-07
2712794	TCTEX1D2	2.19E-07
3924674	DIP2A	2.22E-07
3893338	COL20A1	2.22E-07
3129731	DUSP4	2.27E-07
2904563	DEF6	2.28E-07
2531233	SP140	2.36E-07
3645881	ZNF174	2.51E-07
3125342	SGCZ	2.51E-07
2407163	SNIP1	2.55E-07
3762753	CA10	2.65E-07
3252382	MYST4	2.71E-07
3389566	KBTBD3	2.78E-07
3064204	ACTL6B	2.81E-07
3738969	FOXK2	2.98E-07
3387771	CCDC82	3.11E-07
3421446	CPSF6	3.16E-07
3989721	STAG2	3.18E-07
2678400	ACOX2	3.49E-07
3758692	MPP2	3.51E-07
3980078	STARD8	3.75E-07
3707214	PLD2	3.78E-07
3584443	SNRPN	3.80E-07
3620741	CDAN1	3.80E-07
3806525	PIAS2	3.86E-07
3851267	ZNF625	4.00E-07
3267036	GRK5	4.61E-07
3647993	CIITA	4.64E-07
3294499	PPP3CB	4.86E-07
2372924	TROVE2	4.88E-07
2452754	SLC26A9	5.40E-07
3726618	CACNA1G	5.47E-07
2360468	FLAD1	5.61E-07
3919860	DOPEY2	5.70E-07
3607275	ISG20	5.78E-07
2328320	TINAGL1	5.82E-07
3381241	ARAP1	6.04E-07
2320411	AGTRAP	6.16E-07
3188299	RABGAP1	6.27E-07
3672455	COX4I1	6.46E-07
3108901	VPS13B	6.50E-07
2853388	C5orf33	6.83E-07
3894098	C20orf96	6.86E-07
3823982	MYO9B	7.11E-07
3524999	LIG4	7.17E-07
3041875	OSBPL3	7.24E-07
3962530	CYB5R3	7.27E-07
2969677	REV3L	7.45E-07
2621705	ATRIP	7.50E-07
2333794	DMAP1	7.97E-07
2534126	COPS8	8.06E-07
2780522	PPA2	8.67E-07
3756630	KRT40	9.60E-07
2622970	DOCK3	9.71E-07
2508520	KYNU	9.93E-07
2824872	AP3S1	1.03E-06
3427352	NEDD1	1.05E-06
2793221	NEK1	1.08E-06

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3843419	ZNF211	1.23E-06	3177880	DAPK1	2.46E-06	2405576	CSMD2	4.35E-06	2369252	C1orf49	6.54E-06
3336277	BBS1	1.29E-06	3677498	ZNF200	2.50E-06	2678526	C3orf67	4.38E-06	3409605	FAR2	6.64E-06
3090326	ADAM7	1.33E-06	3347658	ATM	2.51E-06	3454006	FMNL3	4.52E-06	3674303	CDK10	6.69E-06
2929870	STXBP5	1.40E-06	3892409	LSM14B	2.60E-06	2475407	CLIP4	4.56E-06	3868857	KLK12	6.74E-06
3357885	SIGIRR	1.40E-06	3377789	RELA	2.63E-06	3820758	DNM2	4.61E-06	2559386	SFXN5	6.76E-06
3501661	ARHGEF7	1.42E-06	2821347	ERAP2	2.74E-06	3653516	SLC5A11	4.64E-06	3372253	CELF1	6.90E-06
3178952	SYK	1.42E-06	3158516	CPSF1	2.74E-06	3604006	ARNT2	4.66E-06	3644764	CCNF	7.28E-06
3878220	C20orf72	1.43E-06	3844978	SBNO2	2.76E-06	2522728	CASP8	4.68E-06	3824395	PGLS	7.36E-06
2599901	C2orf24	1.49E-06	2454935	ANGEL2	2.83E-06	3048413	POLD2	4.74E-06	3190190	LCN2	7.40E-06
2891241	DUSP22	1.59E-06	3933243	PRDM15	2.87E-06	2431886	PDE4DIP	4.76E-06	3528944	REM2	7.45E-06
3757037	KRT36	1.60E-06	2666478	TOP2B	3.07E-06	3948953	PPARA	4.84E-06	3185976	COL27A1	7.56E-06
3010503	CD36	1.64E-06	3904594	C20orf117	3.09E-06	3751323	MYO18A	4.90E-06	3601675	ARID3B	7.73E-06
3545183	C14orf166B	1.64E-06	2902326	HCP5	3.11E-06	3654111	JMJD5	4.98E-06	2724377	---	7.75E-06
3091301	PTK2B	1.67E-06	3881261	REM1	3.13E-06	2434776	CDC42SE1	4.99E-06	3914050	STMN3	7.77E-06
3870478	OSCAR	1.83E-06	3709327	CNTROB	3.18E-06	3819374	CCL25	5.17E-06	3580498	CDC42BPB	7.78E-06
2375664	BTG2	1.84E-06	3486383	COG6	3.19E-06	3371114	SYT13	5.20E-06	3918959	MRPS6	8.07E-06
3837276	DHX34	1.86E-06	3245783	WDFY4	3.20E-06	3770944	H3F3B	5.23E-06	2353988	FAM46C	8.56E-06
2666566	NGLY1	1.87E-06	3883309	CEP250	3.22E-06	3706071	DPH1	5.29E-06	2638824	CASR	8.62E-06
3710515	DNAH9	1.91E-06	2362892	ATP1A2	3.22E-06	3031181	ATP6V0E2	5.30E-06	2486811	PLEK	8.65E-06
3469319	APPL2	1.96E-06	2570238	NPHP1	3.36E-06	2474019	DPYSL5	5.35E-06	3326461	EHF	8.73E-06
3273601	IDI1	2.03E-06	3854132	CPAMD8	3.39E-06	3678231	FAM100A	5.40E-06	3016380	CUX1	8.76E-06
2692573	CCDC14	2.11E-06	3959451	MYH9	3.42E-06	3188050	MRRF	5.69E-06	3033728	RNF32	8.79E-06
3048373	POLM	2.16E-06	2758733	STX18	3.54E-06	3035795	C7orf27	5.81E-06	3758234	AARSD1	8.86E-06
2360850	FDPS	2.18E-06	3260829	FAM178A	3.58E-06	3604147	KIAA1199	6.04E-06	2550122	COX7A2L	8.91E-06
2746693	ARHGAP10	2.19E-06	2731417	MTHFD2L	3.61E-06	3471538	FAM109A	6.09E-06	2623662	DNAH1	8.95E-06
2326954	TMEM222	2.23E-06	2954678	XPO5	3.71E-06	3343202	EED	6.12E-06	2948630	IER3	9.25E-06
3226160	SIAT7F	2.23E-06	3913018	LAMA5	3.77E-06	2435005	SELENBP1	6.23E-06	2343511	IFI44	9.49E-06
3891664	CDH26	2.28E-06	3747657	FLCN	3.83E-06	3743611	NEURL4	6.25E-06	3505937	CENPJ	9.51E-06
4006841	SLC9A7	2.29E-06	3451814	NELL2	3.91E-06	2336439	GPX7	6.26E-06	3417201	IKZF4	9.72E-06
3189864	LRSAM1	2.34E-06	3309345	SFXN4	3.93E-06	2387126	RYR2	6.38E-06	2899216	HIST1H4E	9.90E-06
3147286	RRM2B	2.39E-06	2319661	KIF1B	3.98E-06	3326635	CD44	6.44E-06	3811339	BCL2	1.01E-05
3531736	NPAS3	2.40E-06	2738146	TET2	4.10E-06	3906062	ZHX3	6.47E-06	3266408	EMX2	1.03E-05
2316245	PRKCZ	2.46E-06	3182409	ZNF189	4.10E-06	3422458	TRHDE	6.48E-06	3179551	FGD3	1.05E-05

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3010439	GNAI1	1.06E-05
3557614	AP1G2	1.06E-05
2645906	PLS1	1.07E-05
3304012	MGEA5	1.11E-05
3849923	COL5A3	1.12E-05
3705911	WDR81	1.14E-05
3768791	ABCA6	1.16E-05
2350596	CELSR2	1.18E-05
2674919	MST1R	1.19E-05
2951541	TULP1	1.19E-05
3882652	ZNF341	1.25E-05
2939593	PECI	1.26E-05
3737488	RPTOR	1.29E-05
4009560	FAM120C	1.29E-05
3241601	C10orf68	1.33E-05
3130244	TEX15	1.35E-05
3349293	NCAM1	1.35E-05
3086100	GATA4	1.39E-05
2406926	GRIK3	1.40E-05
3854627	JAK3	1.50E-05
3300211	FGFBP3	1.50E-05
3883690	EPB41L1	1.50E-05
3891048	NPEPL1	1.56E-05
2951664	CLPS	1.58E-05
3282213	YME1L1	1.58E-05
3717539	RHOT1	1.61E-05
2476510	LTBP1	1.63E-05
3315114	TUBGCP2	1.63E-05
3992304	SAGE1	1.67E-05
3501219	COL4A2	1.70E-05
3855660	SUGP1	1.73E-05
2941784	NEDD9	1.77E-05
3807370	DYM	1.79E-05
3657041	ITGAX	1.80E-05
2605674	ILKAP	1.84E-05
3595846	FAM63B	1.84E-05
2892170	WRNIP1	1.86E-05
2967550	ATG5	1.88E-05
3938113	HIC2	1.95E-05
3740264	INPP5K	1.96E-05
3011317	CROT	1.98E-05
3212008	FRMD3	1.98E-05
2577482	TMEM163	2.01E-05
3314630	C10orf92	2.01E-05
2927722	HEBP2	2.04E-05
3531032	SCFD1	2.04E-05
2819779	GPR98	2.06E-05
3841949	EPS8L1	2.06E-05
2603544	NMUR1	2.07E-05
3537967	KIAA0586	2.08E-05
2840036	DOCK2	2.10E-05
3374083	MED19	2.11E-05
3815649	CIRBP	2.15E-05
3155489	FAM135B	2.16E-05
3703129	C16orf74	2.16E-05
2664288	METTL6	2.17E-05
3016791	LRWD1	2.17E-05
3338783	C11orf76	2.18E-05
2420642	MCOLN2	2.21E-05
3308378	C10orf82	2.21E-05
3936256	BCL2L13	2.26E-05
2712417	TNK2	2.27E-05
3571944	LTBP2	2.33E-05
2410158	TESK2	2.38E-05
3644593	MLST8	2.43E-05
2707045	PEX5L	2.43E-05
3590460	ITPKA	2.44E-05
3888055	ARFGEF2	2.45E-05
2939034	SERPINB9	2.47E-05
2617041	GOLGA4	2.50E-05
3244061	ZNF487P	2.56E-05
2479640	PPM1B	2.57E-05
3540862	GPHN	2.64E-05
3344861	C11orf54	2.68E-05
3071630	---	2.68E-05
3030799	KRBA1	2.70E-05
3723378	FMNL1	2.71E-05
3965314	BRD1	2.73E-05
2986546	PDCD2	2.92E-05
2553730	MTIF2	2.96E-05
3438027	RAN	2.98E-05
2787459	INPP4B	3.00E-05
2957499	ICK	3.01E-05
2581000	NEB	3.03E-05
3464589	C12orf50	3.03E-05
2326410	CCDC21	3.03E-05
2399908	TMCO4	3.07E-05
2757427	LETM1	3.08E-05
3971845	CXorf58	3.08E-05
3847112	PTPRS	3.10E-05
2401448	E2F2	3.10E-05
2374746	NAV1	3.13E-05
3018605	SLC26A4	3.17E-05
3515009	VPS36	3.19E-05
3103494	TMEM70	3.23E-05
3754797	HNF1B	3.24E-05
2404344	NKAIN1	3.26E-05
2920619	ARMC2	3.33E-05
3302360	MMS19	3.47E-05
3825650	MAU2	3.48E-05
2367495	C1orf105	3.51E-05
3697434	HYDIN	3.52E-05
2523689	ABI2	3.56E-05
2524653	ADAM23	3.62E-05
3107724	C8orf38	3.63E-05
3590853	CAPN3	3.65E-05
3378043	CATSPER1	3.74E-05
2698844	ATR	3.77E-05
2451958	PLEKHA6	3.87E-05
3676279	RPL3L	3.92E-05
3966929	GYG2	3.92E-05
3860296	COX7A1	3.97E-05
3376914	NRXN2	3.97E-05
2345239	---	3.97E-05
2749699	RAPGEF2	4.03E-05
3451318	ZCRB1	4.12E-05
3840224	ZNF528	4.34E-05
2954489	C6orf108	4.38E-05
2686727	ZBTB11	4.39E-05
3452865	COL2A1	4.42E-05
3263944	PDCD4	4.45E-05
2950384	COL11A2	4.46E-05
3427282	C12orf63	4.47E-05
2573641	CLASP1	4.47E-05
3909064	TMEM189	4.48E-05
3512527	TPT1	4.61E-05
2688180	DPPA4	4.74E-05
3437801	PIWIL1	4.92E-05
2522616	CFLAR	4.93E-05
3302886	HPSE2	5.00E-05
2548871	HNRPLL	5.16E-05
3695315	CDH16	5.23E-05

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3609592	MCTP2	5.24E-05
2560178	LBX2	5.27E-05
2528407	TUBA4B	5.28E-05
3468009	ARL1	5.29E-05
3918779	ITSN1	5.36E-05
2648991	KCNAB1	5.55E-05
2945741	FAM65B	5.69E-05
3040518	MACC1	5.70E-05
3476457	NCOR2	5.76E-05
2788366	ZNF827	5.81E-05
2778727	C4orf37	5.83E-05
3296386	DLG5	5.83E-05
2368198	CACYBP	5.88E-05
3164601	KIAA1797	5.93E-05
4018729	IL13RA2	5.94E-05
2667181	AZI2	5.96E-05
2686458	ABI3BP	5.96E-05
2403027	MAP3K6	5.98E-05
2956904	PKHD1	6.04E-05
3035281	INTS1	6.14E-05
3995885	PLXNB3	6.15E-05
3907987	SLC13A3	6.16E-05
3866845	PLA2G4C	6.18E-05
3135340	OPRK1	6.18E-05
3032243	GALNT11	6.19E-05
3902983	CDK5RAP1	6.24E-05
3250486	COL13A1	6.26E-05
3389330	CASP5	6.27E-05
2378019	CAMK1G	6.34E-05
3417249	ERBB3	6.38E-05
2585400	SCN9A	6.44E-05
2806091	RAI14	6.48E-05
3083778	MCPH1	6.56E-05
2734784	AFF1	6.66E-05
3704299	MVD	6.69E-05
3438617	EP400	6.75E-05
2637980	POGLUT1	6.83E-05
3815268	KISS1R	6.85E-05
3311157	OAT	6.95E-05
2402493	PAFAH2	7.08E-05
3713794	EPN2	7.14E-05
3867195	FAM83E	7.22E-05
3274934	CALML5	7.31E-05
2327338	XKR8	7.37E-05
3371339	PHF21A	7.39E-05
3644297	GFER	7.40E-05
2942432	C6orf114	7.41E-05
3558145	CIDEB	7.45E-05
2358520	SETDB1	7.54E-05
3777263	ARHGAP28	7.70E-05
2891556	FOXQ1	7.76E-05
3642200	PCSK6	7.79E-05
2353021	SYCP1	7.82E-05
3569441	ZFYVE26	7.82E-05
2910138	IL17A	7.85E-05
2694001	MGLL	7.87E-05
4000538	FIGF	7.88E-05
3776504	TGIF1	7.94E-05
2321813	CELA2A	8.02E-05
3549264	KIAA1409	8.12E-05
3218041	BAAT	8.24E-05
4026842	ARHGAP4	8.34E-05
3821159	LPPR2	8.48E-05
3721851	COASY	8.53E-05
2398820	PADI2	8.62E-05
2465778	OR6F1	8.76E-05
3225096	NR6A1	8.89E-05
3821183	C19orf39	8.92E-05
3191805	LAMC3	9.00E-05
2545653	MPV17	9.11E-05
3257670	PCGF5	9.19E-05
2337147	ACOT11	9.20E-05
3005363	ASL	9.21E-05
3447933	IFLTD1	9.24E-05
3795866	ENOSF1	9.51E-05
3453592	MLL2	9.51E-05
2949885	GPSM3	9.56E-05
3036844	FBXL18	9.58E-05
2786657	SETD7	9.59E-05
3760957	SCRN2	9.61E-05
2335922	CDKN2C	9.63E-05
2889382	PROP1	9.66E-05
3338552	CTTN	9.68E-05
2726396	ZAR1	9.87E-05
3672059	KIAA0513	9.94E-05
3255220	GHITM	9.98E-05
3662851	GPR97	9.99E-05
3854693	IL12RB1	1.00E-04
3393993	BCL9L	1.00E-04
3941907	EWSR1	1.01E-04
3835131	ZNF576	1.01E-04
3843947	ZSCAN22	1.03E-04
3996227	TKTL1	1.03E-04
3359171	INS	1.03E-04
3560527	C14orf147	1.03E-04
2588066	ATF2	1.04E-04
2491615	MAT2A	1.07E-04
3015865	SLC12A9	1.08E-04
2948587	FLOT1	1.08E-04
3985615	TCEAL4	1.08E-04
3258477	PLCE1	1.09E-04
2452977	FAIM3	1.11E-04
4021508	ZNF280C	1.13E-04
3802980	DSC2	1.14E-04
3542275	SMOC1	1.14E-04
2979111	LRP11	1.15E-04
2930592	TAB2	1.15E-04
3874249	ITPA	1.16E-04
3360622	TRIM5	1.16E-04
2674808	TRAIP	1.16E-04
2438892	FCRL5	1.17E-04
3903089	NECAB3	1.18E-04
3887049	UBE2C	1.20E-04
2327375	ATPIF1	1.22E-04
2755053	CYP4V2	1.22E-04
3035408	PSMG3	1.24E-04
3851589	C19orf56	1.24E-04
3293963	DNAJB12	1.25E-04
3474885	CAMKK2	1.25E-04
3059226	PCLO	1.26E-04
2537290	TMEM18	1.26E-04
3723627	CRHR1	1.27E-04
3924573	PCNT	1.29E-04
3149161	CSMD3	1.29E-04
2379863	CENPF	1.32E-04
3439268	NHP2L1	1.32E-04
2880679	SH3TC2	1.32E-04
3238962	KIAA1217	1.33E-04
3561532	SLC25A21	1.33E-04
3094286	PROSC	1.34E-04
3157751	SCRIB	1.36E-04
2545200	OTOF	1.38E-04

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3633890	SCAPER	1.38E-04	3225952	FAM129B	1.61E-04	3437500	GLT1D1	1.89E-04	2594905	ALS2CR11	2.27E-04
2401193	LUZP1	1.39E-04	3815757	MUM1	1.61E-04	4021469	AIFM1	1.89E-04	3683549	UMOD	2.28E-04
2425118	SASS6	1.39E-04	3736162	TMC8	1.61E-04	3003107	ZNF713	1.90E-04	3701297	CDYL2	2.28E-04
3726691	ABCC3	1.39E-04	3706753	GSG2	1.64E-04	3686750	RABEP2	1.90E-04	2590736	NCKAP1	2.28E-04
2483016	CCDC104	1.40E-04	3894601	FKBP1A	1.64E-04	3575567	FOXN3	1.91E-04	2363525	NDUFS2	2.30E-04
3393311	DSCAML1	1.41E-04	3711869	ADORA2B	1.64E-04	2949038	BAT1	1.91E-04	3600283	THSD4	2.30E-04
3940001	SPECC1L	1.42E-04	3489644	TRIM13	1.64E-04	3656990	ITGAM	1.92E-04	2394478	CHD5	2.31E-04
3762519	SPAG9	1.43E-04	3264391	VTI1A	1.64E-04	3952718	UFD1L	1.94E-04	3110341	DCAF13	2.33E-04
2485784	ACTR2	1.44E-04	2970086	LAMA4	1.68E-04	3988596	ZCCHC12	1.94E-04	2439314	OR10K2	2.35E-04
3671552	NECAB2	1.46E-04	2793054	CBR4	1.69E-04	2673830	DALRD3	1.96E-04	3894322	SRXN1	2.40E-04
3611126	MEF2A	1.46E-04	2413633	CYB5RL	1.72E-04	2876011	SKP1	1.96E-04	3336906	SSH3	2.40E-04
2360346	CHRNB2	1.47E-04	3620380	PLA2G4D	1.72E-04	3592755	SEMA6D	1.96E-04	2519981	PMS1	2.41E-04
3545564	ADCK1	1.47E-04	3443464	PZP	1.73E-04	3087813	PCM1	1.97E-04	2880905	CSNK1A1	2.43E-04
3502259	MCF2L	1.47E-04	3951927	BID	1.73E-04	2949859	PBX2	1.98E-04	2436283	DENND4B	2.44E-04
3146103	STK3	1.49E-04	3526378	PCID2	1.75E-04	3848651	TIMM44	1.98E-04	3685610	ARHGAP17	2.46E-04
3415668	TENC1	1.50E-04	2560881	LRRTM4	1.75E-04	2775562	HNRPDL	1.98E-04	2669803	SCN11A	2.47E-04
3724591	C17orf57	1.50E-04	3234277	GATA3	1.75E-04	3293215	TYSND1	1.99E-04	3965631	TUBGCP6	2.47E-04
3862661	BLVRB	1.50E-04	3497659	RAP2A	1.76E-04	3419585	TMEM5	2.00E-04	2905432	TBC1D22B	2.51E-04
2606859	KIF1A	1.51E-04	2926323	EYA4	1.77E-04	3765299	APPBP2	2.05E-04	3166880	NFX1	2.51E-04
2920377	LACE1	1.51E-04	3662696	CX3CL1	1.78E-04	2401994	RUNX3	2.07E-04	3465227	KERA	2.53E-04
3878972	C20orf26	1.52E-04	3450655	CPNE8	1.78E-04	3062794	TECPR1	2.09E-04	3397003	KIRREL3	2.55E-04
3712978	MYO15A	1.52E-04	3697712	TAT	1.79E-04	3617830	ZNF770	2.10E-04	3756046	NR1D1	2.55E-04
2461786	ARID4B	1.53E-04	2742829	INTU	1.80E-04	3916138	C21orf74	2.11E-04	2989050	RAC1	2.56E-04
3855633	TM6SF2	1.54E-04	3243846	RET	1.80E-04	3303652	MRPL43	2.11E-04	2816030	POLK	2.56E-04
3833323	ZNF546	1.54E-04	2810015	DDX4	1.81E-04	4005392	BCOR	2.13E-04	3608427	FES	2.58E-04
2583631	RBMS1	1.55E-04	3913960	PRIC285	1.81E-04	3478457	STX2	2.15E-04	2479746	C2orf34	2.60E-04
3589141	SPRED1	1.55E-04	3458857	AVIL	1.82E-04	3441280	AKAP3	2.17E-04	3301263	SORBS1	2.60E-04
3822100	DAND5	1.56E-04	2841699	CPEB4	1.84E-04	3913737	NKAIN4	2.17E-04	3074531	SLC13A4	2.60E-04
2900195	ZNF165	1.57E-04	3888383	SLC9A8	1.84E-04	4023006	ZNF75D	2.19E-04	3549033	GOLGA5	2.62E-04
2615808	GPD1L	1.57E-04	3646366	C16orf71	1.85E-04	2984543	PRR18	2.23E-04	3304004	NPM3	2.62E-04
2619120	TRAK1	1.58E-04	3893287	ARFGAP1	1.86E-04	3226340	PTGES2	2.23E-04	3064501	MOGAT3	2.62E-04
3049025	TBRG4	1.58E-04	3894637	NSFL1C	1.88E-04	3673892	CDH15	2.24E-04	3821377	ZNF441	2.64E-04
3945942	CACNA1I	1.58E-04	3822322	MRI1	1.88E-04	2963707	RARS2	2.27E-04	3394356	USP2	2.65E-04

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3836243	CD3EAP	2.66E-04
3490741	SUGT1	2.66E-04
3405207	BCL2L14	2.66E-04
3066496	ATXN7L1	2.66E-04
3389647	GUCY1A2	2.67E-04
2892979	CDYL	2.69E-04
2359036	SNX27	2.70E-04
3010082	PHTF2	2.71E-04
3497586	MBNL2	2.72E-04
3699335	LDHD	2.73E-04
2583014	BAZ2B	2.75E-04
2334932	CYP4B1	2.78E-04
3868998	NKG7	2.79E-04
4012299	PHKA1	2.85E-04
3695450	EXOC3L	2.88E-04
3501471	ING1	2.88E-04
2365391	FMO9P	2.89E-04
3734683	ARMC7	2.92E-04
3332449	C11orf64	2.92E-04
3904797	C20orf132	2.95E-04
3809826	ATP8B1	2.96E-04
3621417	CATSPER2	2.98E-04
2550522	ZFP36L2	2.99E-04
3632424	HCN4	3.00E-04
2320392	C1orf187	3.00E-04
2992766	NUPL2	3.01E-04
3999148	GPR143	3.03E-04
3291435	RTKN2	3.03E-04
3089597	KIAA1967	3.04E-04
3707041	SMTNL2	3.04E-04
2716025	RGS12	3.05E-04
3442785	CLEC4C	3.06E-04
3768412	SLC16A6	3.06E-04
3638607	ANPEP	3.06E-04
2913123	RIMS1	3.07E-04
2359664	S100A9	3.08E-04
2771718	UBA6	3.10E-04
3537884	ARID4A	3.10E-04
3421706	RAB3IP	3.10E-04
3627363	NARG2	3.10E-04
3278057	CCDC3	3.11E-04
3272027	LRRC27	3.13E-04
2672016	FYCO1	3.15E-04
3531355	NUBPL	3.15E-04
3572975	NGB	3.17E-04
3268222	BTBD16	3.17E-04
3095223	IDO1	3.18E-04
3838845	CPT1C	3.19E-04
3752258	EVI2B	3.22E-04
2740067	ANK2	3.24E-04
2469825	GREB1	3.26E-04
3528994	ACIN1	3.27E-04
3853108	NOTCH3	3.31E-04
4021149	SMARCA1	3.32E-04
3499585	BIVM	3.36E-04
3847858	SLC25A41	3.37E-04
2491386	TCF7L1	3.45E-04
3863606	LIPE	3.45E-04
2569649	EDAR	3.46E-04
2340529	PDE4B	3.46E-04
2327630	YTHDF2	3.46E-04
3881404	COX4I2	3.53E-04
3154263	SLA	3.55E-04
3246141	CHAT	3.57E-04
3864375	LYPD3	3.57E-04
2465519	ZNF669	3.59E-04
3874023	PTPRA	3.60E-04
3903836	EIF6	3.62E-04
3742212	ALOX15	3.62E-04
2631556	CADM2	3.63E-04
3856554	ZNF100	3.64E-04
2539387	C2orf46	3.64E-04
2925013	C6orf58	3.66E-04
2438042	SMG5	3.66E-04
3823681	KLF2	3.67E-04
3456666	NFE2	3.68E-04
2599670	CRYBA2	3.72E-04
3661684	MMP2	3.81E-04
2407496	POU3F1	3.90E-04
2799184	NDUFS6	3.90E-04
2655955	VPS8	3.92E-04
2627390	ATXN7	3.95E-04
3894047	PCMTD2	3.95E-04
3390195	EXPH5	3.99E-04
3676421	PKD1	4.00E-04
2772968	COX18	4.02E-04
3438847	FBRSL1	4.04E-04
3325052	EIF2AK2	4.09E-04
3833620	LTBP4	4.12E-04
2381368	HLX	4.13E-04
2953435	C6orf130	4.13E-04
2879927	LARS	4.15E-04
3835855	TOMM40	4.16E-04
2367743	PRDX6	4.16E-04
2449559	ASPM	4.17E-04
3697933	PKD1L3	4.17E-04
3226138	AK1	4.28E-04
2332999	WDR65	4.28E-04
2624074	GNL3	4.29E-04
2712236	MUC4	4.30E-04
3375894	EML3	4.31E-04
3715642	FOXN1	4.35E-04
2459837	ACTA1	4.36E-04
3194284	GPSM1	4.38E-04
3696194	DDX28	4.38E-04
2901552	RPP21	4.39E-04
2813060	PIK3R1	4.39E-04
3289631	CSTF2T	4.41E-04
2479698	SLC3A1	4.42E-04
3230760	C9orf140	4.44E-04
2360728	TRIM46	4.45E-04
2339139	INADL	4.46E-04
3157647	PYCRL	4.51E-04
3662723	COQ9	4.52E-04
3846709	STAP2	4.55E-04
3743440	DVL2	4.57E-04
3126191	PSD3	4.58E-04
2875454	SEPT8	4.59E-04
3739668	VPS53	4.60E-04
3518086	TBC1D4	4.62E-04
3838809	PRMT1	4.63E-04
3848020	TNFSF14	4.67E-04
2664452	ANKRD28	4.68E-04
3853658	CYP4F11	4.68E-04
3615579	TJP1	4.71E-04
2585236	TTC21B	4.72E-04
3361811	STK33	4.72E-04
3089740	RHOBTB2	4.73E-04
3261723	TMEM180	4.76E-04
2556017	C2orf86	4.76E-04
2380055	KCTD3	4.78E-04
2745220	ZNF330	4.83E-04

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

2652027	CLDN11	4.88E-04
2946324	HIST1H3D	4.90E-04
2593796	RFTN2	4.91E-04
3227070	PTGES	4.95E-04
3741875	ZZEF1	4.97E-04
2610732	ATG7	5.01E-04
3406880	PIK3C2G	5.06E-04
3865776	IRF2BP1	5.12E-04
2777333	PPM1K	5.12E-04
3120613	PPP1R16A	5.13E-04
2641263	RAB7A	5.14E-04
2422612	HFM1	5.14E-04
3981027	TAF1	5.15E-04
2423422	BCAR3	5.16E-04
3645683	ZNF213	5.16E-04
3396726	PATE2	5.17E-04
3062868	BAIAP2L1	5.17E-04
2346738	RPAP2	5.17E-04
3651509	ERI2	5.18E-04
3015299	MBLAC1	5.19E-04
2356181	RBM8A	5.25E-04
3642875	EFERIN	5.28E-04
2730531	UTP3	5.34E-04
2725779	GUF1	5.37E-04
2326993	SYTL1	5.51E-04
2877171	FAM13B	5.51E-04
2326912	WDTC1	5.58E-04
3417184	SUOX	5.62E-04
3158581	SLC39A4	5.62E-04
3868659	C19orf48	5.66E-04
2669888	GORASP1	5.77E-04
3179669	C9orf89	5.84E-04
3771037	WBP2	5.91E-04
2675088	IFRD2	5.91E-04
2812273	PPWD1	5.92E-04
3504526	LATS2	6.01E-04
2676182	NT5DC2	6.05E-04
2618702	ZNF620	6.07E-04
3487360	C13orf30	6.11E-04
3644810	C16orf59	6.13E-04
3204833	GBA2	6.14E-04
3644249	TBL3	6.15E-04
3062193	SLC25A13	6.21E-04
3944543	NCF4	6.21E-04
2474791	BRE	6.22E-04
2860666	TAF9	6.22E-04
2437577	YY1AP1	6.25E-04
2353396	C1orf161	6.31E-04
3379644	CPT1A	6.32E-04
3985169	NXF4	6.32E-04
3861372	RASGRP4	6.40E-04
2321911	DDI2	6.43E-04
2479433	PLEKHH2	6.44E-04
3352040	PDZD3	6.44E-04
2429277	CSDE1	6.44E-04
3820727	QTRT1	6.45E-04
3559690	HEATR5A	6.46E-04
2845450	TPPP	6.47E-04
2964553	BACH2	6.48E-04
3102372	SULF1	6.49E-04
3884612	SNHG11	6.53E-04
3947227	SEPT3	6.55E-04
2697490	CEP70	6.55E-04
3236958	VIM	6.59E-04
3299578	CH25H	6.59E-04
2610044	JAGN1	6.60E-04
2377332	CR1	6.66E-04
3357397	GLB1L2	6.77E-04
3513147	HTR2A	6.80E-04
2891644	FOXF2	6.83E-04
3409432	CCDC91	6.85E-04
3680213	SOCS1	6.87E-04
2592356	STAT4	6.87E-04
3421579	FRS2	6.89E-04
2601995	IRS1	6.89E-04
2717059	LOC93622	6.90E-04
3480508	IL17D	6.90E-04
2950823	IP6K3	6.93E-04
3192525	GTF3C4	6.95E-04
3893642	LIME1	6.95E-04
2714132	PDE6B	7.00E-04
2796790	KIAA1430	7.03E-04
3100166	RAB2A	7.03E-04
2328767	IQCC	7.04E-04
3946146	FAM83F	7.08E-04
2875555	AFF4	7.11E-04
3622176	DUOX2	7.15E-04
2952497	BTBD9	7.21E-04
3669552	VAT1L	7.24E-04
3687277	SEZ6L2	7.25E-04
3715558	SARM1	7.28E-04
3474831	OASL	7.37E-04
2622696	SEMA3B	7.38E-04
2574646	BIN1	7.39E-04
2694314	GATA2	7.41E-04
3644510	RAB26	7.48E-04
2756630	CPLX1	7.55E-04
3409127	ARNTL2	7.56E-04
3374934	MS4A6A	7.57E-04
2915268	DOPEY1	7.58E-04
3020804	NAA38	7.64E-04
3126368	PSD3	7.64E-04
3910347	SUMO1P1	7.70E-04
3484768	PDS5B	7.80E-04
3895702	SPEF1	7.83E-04
3534923	KLHDC2	7.87E-04
3867458	PLEKHA4	7.89E-04
2817731	ZFYVE16	7.91E-04
3831620	ZNF568	7.92E-04
3091699	PNOC	7.93E-04
2769182	SCFD2	7.94E-04
3734609	KCTD2	7.99E-04
3835318	ZNF155	8.03E-04
2949488	SLC44A4	8.04E-04
3489350	CDADC1	8.05E-04
3726465	RSAD1	8.05E-04
3350908	CEP164	8.06E-04
2799758	IRX1	8.12E-04
3730161	EFCAB3	8.24E-04
3015241	AP4M1	8.26E-04
3557350	SLC22A17	8.31E-04
3475926	PITPNM2	8.32E-04
3339812	ARHGEF17	8.33E-04
3761127	CBX1	8.34E-04
3744965	GAS7	8.40E-04
3322700	SAA1	8.42E-04
2375144	LGR6	8.45E-04
3269939	DOCK1	8.48E-04
3932524	DSCAM	8.56E-04
3597914	SNX22	8.59E-04
2486520	ETAA1	8.61E-04
2574798	MAP3K2	8.62E-04

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3887210	MMP9	8.89E-04
3976299	ARAF	9.01E-04
2491089	DNAH6	9.01E-04
2327542	TRNAU1AP	9.08E-04
2333195	KIAA0467	9.10E-04
2779527	DDIT4L	9.12E-04
2988726	FSCN1	9.15E-04
3723005	FZD2	9.15E-04
2828564	RAD50	9.17E-04
3873480	RAD21L1	9.21E-04
3851150	ZNF433	9.25E-04
3830789	LIN37	9.28E-04
3119656	GSDMD	9.28E-04
2648535	ARHGEF26	9.31E-04
3629125	CSNK1G1	9.41E-04
2397847	ZBTB17	9.42E-04
2500275	BCL2L11	9.44E-04
3721956	TUBG2	9.49E-04
3863597	CNFN	9.51E-04
4006210	MAOB	9.54E-04
3065740	RELN	9.55E-04
3151970	MTSS1	9.56E-04
2826159	SNCAIP	9.58E-04
2332812	ERMAP	9.63E-04
2992197	SP4	9.63E-04
3446297	RERGL	9.65E-04
3065963	ORC5	9.67E-04
3806366	LOXHD1	9.70E-04
3204721	TPM2	9.70E-04
2969886	FYN	9.72E-04
2508611	ARHGAP15	9.76E-04
2904329	ANKS1A	9.76E-04
2489606	POLE4	9.91E-04
2811812	LRRC70	9.91E-04
3638590	MESP1	9.92E-04
3308489	KIAA1598	9.93E-04
3085270	TNKS	9.93E-04
3067250	SLC26A3	9.99E-04
3651294	ACSM5	9.99E-04
3897431	MKKS	1.00E-03
4027135	TEX28	1.00E-03
2777447	NAP1L5	1.01E-03
2459042	CDC42BPA	1.01E-03
3046739	AMPH	1.01E-03
4011464	PJA1	1.01E-03
3281703	PRTFDC1	1.01E-03
3733911	SSTR2	1.02E-03
2700828	SIAH2	1.02E-03
2864118	DMGDH	1.02E-03
3652867	SCNN1G	1.03E-03
3984702	DRP2	1.03E-03
2353773	TTF2	1.04E-03
2950199	PSMB8	1.04E-03
2779992	UBE2D3	1.04E-03
3779950	C18orf1	1.04E-03
4027639	F8	1.04E-03
3320604	USP47	1.05E-03
3770923	GALK1	1.05E-03
3913335	C20orf166	1.05E-03
2874920	ACSL6	1.06E-03
2404958	MTMR9LP	1.06E-03
3190242	DNM1	1.06E-03
3639601	RGMA	1.07E-03
2910477	FBXO9	1.07E-03
3882413	C20orf114	1.07E-03
2700780	FAM194A	1.07E-03
3853036	SLC1A6	1.07E-03
3606682	AGBL1	1.07E-03
2687840	IFT57	1.08E-03
3655687	PRRT2	1.08E-03
3865618	SIX5	1.08E-03
2830450	NPY6R	1.08E-03
3466110	CCDC41	1.08E-03
3336197	NPAS4	1.09E-03
3990727	RAB33A	1.10E-03
3382830	GDPD4	1.10E-03
3138978	COPS5	1.10E-03
2669732	SCN10A	1.11E-03
2558150	AAK1	1.13E-03
3235293	C10orf47	1.13E-03
3858993	CEBPA	1.14E-03
2984655	RPS6KA2	1.15E-03
3651672	ANKS4B	1.15E-03
3259503	DNTT	1.15E-03
3893520	RTEL1	1.15E-03
3329404	ATG13	1.16E-03
2743800	PCDH10	1.16E-03
2969289	WASF1	1.16E-03
3269694	FANK1	1.16E-03
3989678	XIAP	1.18E-03
3078520	ZNF746	1.19E-03
3762339	MRPL27	1.19E-03
3509677	C13orf38	1.19E-03
2604138	USP40	1.19E-03
3849044	MYO1F	1.19E-03
3416996	MMP19	1.20E-03
3893973	MYT1	1.20E-03
2625793	SLMAP	1.21E-03
2792161	TKTL2	1.21E-03
2519756	WDR75	1.21E-03
3941623	HSCB	1.22E-03
2768197	CORIN	1.22E-03
3731228	CCDC45	1.22E-03
3902674	TSPY26P	1.23E-03
2408855	FOXJ3	1.23E-03
3238231	MLLT10	1.23E-03
2486178	MEIS1	1.23E-03
4023467	ARHGEF6	1.24E-03
3954729	---	1.24E-03
3742130	MYBBP1A	1.24E-03
2993727	SNX10	1.24E-03
3019793	FOXP2	1.24E-03
2902013	GTF2H4	1.24E-03
3267314	BAG3	1.25E-03
2571457	CKAP2L	1.25E-03
4027176	FLNA	1.25E-03
3521372	DZIP1	1.25E-03
2807686	CARD6	1.25E-03
3316834	BRSK2	1.26E-03
3900091	RALGAPA2	1.26E-03
3168210	TMEM8B	1.26E-03
2929168	UTRN	1.26E-03
2614369	RARB	1.27E-03
2554975	BCL11A	1.27E-03
2391255	UBE2J2	1.28E-03
3995105	CNGA2	1.28E-03
2756309	ABCA11P	1.31E-03
3319352	TUB	1.31E-03
3624697	ARPP19	1.31E-03
2837232	ITK	1.32E-03
2772450	SULT1E1	1.32E-03
3318115	OR52K2	1.33E-03

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

2579439	GTDC1	1.34E-03
3944690	CYTH4	1.35E-03
3435548	HIP1R	1.35E-03
3896594	LRRN4	1.35E-03
2826343	SNX24	1.35E-03
3027538	NDUFB2	1.35E-03
3000342	ADCY1	1.36E-03
2388794	ZNF238	1.36E-03
3899404	OVOL2	1.36E-03
3377226	EHD1	1.37E-03
2618940	CTNNB1	1.37E-03
3200762	SLC24A2	1.37E-03
3209060	TRPM3	1.37E-03
3768627	ABCA8	1.38E-03
3204019	C9orf25	1.38E-03
3815888	APC2	1.38E-03
3846982	TICAM1	1.39E-03
2369713	FAM163A	1.40E-03
2388525	SDCCAG8	1.40E-03
3429754	KIAA1033	1.41E-03
3929325	SYNJ1	1.41E-03
2491523	ELMOD3	1.41E-03
3629610	IGDCC3	1.41E-03
2810395	C5orf35	1.42E-03
3790704	PMAIP1	1.42E-03
3012064	CDK14	1.42E-03
3015338	STAG3	1.42E-03
3378895	PITPNM1	1.42E-03
2585972	ABCB11	1.43E-03
2359453	SMCP	1.43E-03
3942502	SLC35E4	1.44E-03
3601229	CD276	1.44E-03
3930235	RCAN1	1.44E-03
3223425	CDK5RAP2	1.46E-03
3666542	HAS3	1.46E-03
3357723	BET1L	1.46E-03
2589011	TTC30A	1.47E-03
3098378	RGS20	1.47E-03
2453006	PIGR	1.47E-03
3746040	ELAC2	1.47E-03
2638676	EAF2	1.48E-03
3216476	ZNF510	1.48E-03
3258221	HHEX	1.49E-03
3807965	MRO	1.49E-03
3021377	PTPRZ1	1.49E-03
2782822	NDST4	1.50E-03
4025339	IDS	1.51E-03
2988410	RNF216L	1.54E-03
2634153	ZPLD1	1.54E-03
3852407	RFX1	1.55E-03
2970044	TUBE1	1.55E-03
3738138	HGS	1.56E-03
3940631	ADRBK2	1.56E-03
2753732	WWC2	1.57E-03
3675020	RGS11	1.57E-03
3452417	SLC38A4	1.57E-03
2406579	COL8A2	1.57E-03
2849056	DNAH5	1.58E-03
3000010	ZMIZ2	1.58E-03
3418610	XRCC6BP1	1.58E-03
3655826	TAOK2	1.59E-03
2995811	C7orf16	1.59E-03
3772437	DNAH17	1.59E-03
3761395	HOXB6	1.59E-03
3472755	TBX3	1.60E-03
3418249	KIF5A	1.60E-03
4026119	MAGEA10	1.60E-03
3833827	EGLN2	1.60E-03
2648677	MME	1.61E-03
2888385	GPRIN1	1.61E-03
4008427	NUDT11	1.62E-03
2480619	SOCS5	1.62E-03
3871302	HSPBP1	1.62E-03
3132940	ANK1	1.62E-03
3469865	CRY1	1.64E-03
2342176	FPGT	1.65E-03
3591650	SERF2	1.65E-03
3458735	AGAP2	1.65E-03
3381540	FAM168A	1.66E-03
2320048	TARDBP	1.66E-03
3861037	ZNF607	1.67E-03
2877028	KLHL3	1.67E-03
3697632	ZNF23	1.68E-03
3455344	KRT82	1.69E-03
2474637	C2orf16	1.69E-03
2559849	SLC4A5	1.69E-03
3676669	RNPS1	1.70E-03
2383859	GUK1	1.70E-03
2766893	APBB2	1.70E-03
3241316	ZEB1	1.70E-03
3571553	C14orf43	1.70E-03
3667508	CALB2	1.71E-03
3602264	COMMD4	1.73E-03
3016070	MUC17	1.74E-03
3838185	SNRNP70	1.74E-03
3457947	BAZ2A	1.74E-03
2901503	TRIM39	1.75E-03
3267678	WDR11	1.75E-03
3415937	C12orf10	1.75E-03
3986291	TBC1D8B	1.76E-03
2889916	ADAMTS2	1.76E-03
2467691	TTC15	1.77E-03
3651152	IQCK	1.78E-03
4018218	DCX	1.79E-03
3337042	CARNS1	1.80E-03
3318239	OR51F2	1.80E-03
3657168	ARMC5	1.81E-03
3623717	FLJ10038	1.81E-03
3957429	GAL3ST1	1.82E-03
2434925	PI4KB	1.82E-03
3916290	FLJ42200	1.82E-03
3343452	PRSS23	1.82E-03
3976406	ZNF81	1.83E-03
3642687	HBQ1	1.83E-03
3567050	RTN1	1.83E-03
2913983	SENP6	1.85E-03
3151719	ANXA13	1.87E-03
3260700	PAX2	1.87E-03
2476075	SPAST	1.87E-03
3743074	PITPNM3	1.87E-03
3753760	MMP28	1.88E-03
3293469	C10orf27	1.88E-03
2509740	MBD5	1.88E-03
3803917	ZNF24	1.89E-03
3315802	PKP3	1.89E-03
3779817	CEP192	1.90E-03
2801694	ROPN1L	1.91E-03
3021009	KCND2	1.91E-03
3956909	NIPSNAP1	1.91E-03
3865344	PPP1R13L	1.91E-03
3965784	MAPK11	1.92E-03
3851840	KLF1	1.93E-03

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

2982319	SOD2	1.93E-03	2973694	ARHGAP18	2.11E-03	3704939	C16orf7	2.26E-03	2759038	CRMP1	2.47E-03
3332276	MS4A2	1.95E-03	2340078	CACHD1	2.11E-03	2900074	HIST1H2BN	2.26E-03	3380126	FGF19	2.47E-03
3581442	JAG2	1.95E-03	2386867	LGALS8	2.11E-03	2513758	XIRP2	2.27E-03	3456081	RARG	2.48E-03
3647504	PMM2	1.96E-03	3190420	CERCAM	2.12E-03	3608787	SLCO3A1	2.27E-03	3360941	ARFIP2	2.49E-03
3282601	MPP7	1.96E-03	3339774	P2RY6	2.12E-03	3042001	CYCS	2.28E-03	2424740	MIR137	2.49E-03
3721989	CNTNAP1	1.97E-03	3839910	FPR2	2.12E-03	2495279	VWA3B	2.30E-03	2620641	LIMD1	2.49E-03
3082874	ARHGEF10	1.97E-03	3334659	SLC22A12	2.12E-03	2532894	DGKD	2.30E-03	3887479	EYA2	2.50E-03
3529725	REC8	1.98E-03	2328750	CCDC28B	2.13E-03	3827427	ZNF254	2.31E-03	2439801	CCDC19	2.51E-03
3781654	RIOK3	1.98E-03	3838683	PRRG2	2.13E-03	2435443	TCHH	2.32E-03	2962113	ELOVL4	2.52E-03
3031383	REPIN1	1.99E-03	2734270	CDS1	2.13E-03	3962469	RRP7B	2.32E-03	3498589	CLYBL	2.52E-03
2430422	SPAG17	2.00E-03	2947283	ZSCAN12	2.14E-03	3181976	NR4A3	2.32E-03	3719231	MRM1	2.53E-03
3743734	C17orf61	2.00E-03	3761551	TTLL6	2.14E-03	3335751	TSGA10IP	2.33E-03	3367788	DCDC5	2.54E-03
3489212	FNDC3A	2.00E-03	3599432	FEM1B	2.15E-03	3543857	PTGR2	2.33E-03	2318656	PER3	2.54E-03
3403482	NANOGP1	2.00E-03	3851493	ZNF443	2.15E-03	3603932	FAH	2.34E-03	3442322	CDCA3	2.54E-03
3842481	NLRP8	2.01E-03	3182063	INVS	2.16E-03	3217194	TBC1D2	2.34E-03	4014191	POF1B	2.54E-03
3934652	UBE2G2	2.01E-03	3242839	ANKRD30A	2.17E-03	3225560	LOC51145	2.34E-03	2854737	PRKAA1	2.55E-03
3506093	FAM123A	2.01E-03	3788560	DCC	2.17E-03	2428855	AP4B1	2.36E-03	3986647	VSIG1	2.56E-03
3185522	SLC31A1	2.02E-03	2368590	PAPPA2	2.18E-03	3520934	DCT	2.37E-03	2584712	GRB14	2.57E-03
2620160	ZNF197	2.02E-03	3738842	HEXDC	2.18E-03	3120917	ZNF7	2.39E-03	3829857	ZNF302	2.57E-03
3918535	IL10RB	2.03E-03	3298557	GRID1	2.18E-03	3532313	SRP54	2.39E-03	3914786	ABCC13	2.58E-03
2977949	EPM2A	2.03E-03	3940124	UPB1	2.19E-03	3976930	PQBP1	2.40E-03	2674963	MON1A	2.59E-03
3767169	LRRC37A3	2.04E-03	2901660	PRR3	2.20E-03	3662876	CCDC135	2.41E-03	3608520	UNC45A	2.59E-03
3882343	BASE	2.04E-03	2936564	FGFR1OP	2.20E-03	3483468	MTUS2	2.41E-03	3532785	---	2.60E-03
3695235	CCDC79	2.04E-03	2325593	CLIC4	2.20E-03	2439960	KCNJ10	2.44E-03	3879699	PAX1	2.60E-03
3633048	EDC3	2.05E-03	2552643	NRXN1	2.20E-03	3469597	NUAK1	2.45E-03	3549757	SERPINA3	2.60E-03
2640485	C3orf46	2.07E-03	3347533	RAB39	2.22E-03	2582562	ACVR1	2.45E-03	3841881	NCR1	2.61E-03
3203753	UBAP2	2.07E-03	2808308	MGC42105	2.23E-03	2987843	SDK1	2.45E-03	4011637	PDZD11	2.62E-03
3957699	PLA2G3	2.07E-03	2317317	TP73	2.23E-03	3458451	R3HDM2	2.45E-03	3671448	HSBP1	2.62E-03
3633109	ULK3	2.08E-03	3990927	ARHGAP36	2.24E-03	2768981	SGCB	2.45E-03	3880629	CST7	2.63E-03
2757751	MXD4	2.09E-03	3645901	NAT15	2.24E-03	2394588	ICMT	2.46E-03	3791254	RANK	2.63E-03
3542847	SIPA1L1	2.09E-03	3490073	FAM124A	2.24E-03	3738439	LRRC45	2.46E-03	3682182	ABCC6	2.64E-03
3746809	CDRT1	2.09E-03	3952880	TXNRD2	2.25E-03	3646613	RBFOX1	2.47E-03	3358262	DEAF1	2.66E-03
3818842	ZNF358	2.10E-03	3867660	NTF4	2.25E-03	3901955	NINL	2.47E-03	2968232	SNX3	2.66E-03

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3861617	HNRNPL	2.67E-03
3637818	NTRK3	2.67E-03
3027915	SSBP1	2.67E-03
2916502	SPACA1	2.67E-03
3132927	NKX6-3	2.68E-03
3761348	HOXB4	2.68E-03
3965536	MLC1	2.68E-03
2754673	ANKRD37	2.68E-03
3673723	TRAPPC2L	2.69E-03
2771342	EPHA5	2.69E-03
3315549	PSMD13	2.70E-03
3331487	CTNND1	2.70E-03
2486927	ARHGAP25	2.71E-03
2677388	ERC2	2.71E-03
2964092	GABRR1	2.71E-03
2655511	ABCF3	2.72E-03
3816424	SPPL2B	2.72E-03
2708066	KLHL6	2.72E-03
2907568	KLHDC3	2.72E-03
2556215	VPS54	2.73E-03
3268059	TACC2	2.75E-03
3945815	TAB1	2.75E-03
2949830	AGER	2.76E-03
3594129	MAPK6	2.77E-03
2485433	AFTPH	2.77E-03
3612763	POTEB	2.80E-03
3458551	ARHGAP9	2.81E-03
3593408	FGF7	2.81E-03
3495968	SLITRK5	2.82E-03
3866958	CARD8	2.82E-03
2589017	PDE11A	2.83E-03
3836614	IGFL2	2.83E-03
3707498	USP6	2.83E-03
2385797	KIAA1804	2.84E-03
3652902	SCNN1B	3.20E-03
3842456	NLRP4	3.21E-03
2739792	ALPK1	3.22E-03
3335643	MUS81	3.22E-03
2832325	PCDHB5	3.22E-03
3873017	MZF1	3.24E-03
3101851	C8orf45	3.24E-03
3861948	GMFG	3.25E-03
3141809	MRPS28	3.25E-03
3832256	SPINT2	3.28E-03
2724338	LIAS	3.30E-03
2643312	TF	3.31E-03
3557791	FAM158A	3.34E-03
3775808	CLUL1	3.37E-03
3459120	LRIG3	3.37E-03
2458082	WDR26	3.38E-03
3839057	TBC1D17	3.39E-03
3862785	C19orf54	3.40E-03
2987038	GPER	3.40E-03
2905469	RNF8	3.41E-03
3062576	ASNS	3.41E-03
3307580	NRAP	3.41E-03
3993515	MAGEC1	3.42E-03
3219788	EPB41L4B	3.42E-03
3259978	PI4K2A	3.42E-03
3643431	CHTF18	3.45E-03
3016692	PRKRIP1	3.45E-03
2623821	PHF7	3.46E-03
2895841	CD83	3.46E-03
3026834	TTC26	3.49E-03
2369339	RALGPS2	3.49E-03
3445908	EPS8	3.50E-03
3548929	RIN3	3.50E-03
3726537	EPN3	3.50E-03
2672774	C3orf75	3.51E-03
2876213	CDKN2AIP	3.51E-03
2621122	NBEAL2	3.52E-03
3792273	CDH7	3.53E-03
3522644	GPR18	3.54E-03
2647216	HPS3	3.55E-03
3724360	GOSR2	3.56E-03
3203086	DDX58	3.56E-03
2551651	ATP6V1E2	3.56E-03
3379597	MTL5	3.56E-03
2835715	GPX3	3.57E-03
2817708	SPZ1	3.57E-03
3748188	FLII	3.60E-03
2809245	ITGA2	3.61E-03
3352485	TMEM136	3.61E-03
3332334	MS4A14	3.61E-03
3387537	MAML2	3.65E-03
3464622	CEP290	3.65E-03
2488114	ZNF638	3.67E-03
3872945	SLC27A5	3.68E-03
2521239	CCDC150	3.68E-03
3535515	FRMD6	3.69E-03
3364878	ABCC8	3.69E-03
2845043	TRIM41	3.70E-03
3878373	ZNF133	3.70E-03
3479355	GOLGA3	3.71E-03
2528020	TTLL4	3.71E-03
2720584	SLIT2	3.75E-03
3755198	SRCIN1	3.75E-03
3318354	OR52D1	3.76E-03
3775425	B3GNTL1	3.77E-03
2447066	GLUL	3.77E-03
3271687	PPP2R2D	3.78E-03
3359267	TRPM5	3.78E-03
3379708	MRPL21	3.78E-03
3376023	UBXN1	3.79E-03
2442800	ADCY10	3.80E-03
3004628	ZNF107	3.81E-03
2998192	POU6F2	3.81E-03
3771259	EVPL	3.85E-03
3051907	PHKG1	3.85E-03
3079313	CDK5	3.87E-03
3799415	AFG3L2	3.87E-03
2348992	VCAM1	3.89E-03
2516967	HOXD1	3.90E-03
2328936	ZBTB8A	3.91E-03
2436576	C1orf43	3.92E-03
3304624	NT5C2	3.93E-03
3597702	FBXL22	3.93E-03
3389529	KIAA1826	3.94E-03
3302240	RRP12	3.94E-03
3952825	C22orf29	3.96E-03
3315217	C10orf125	3.97E-03
2451918	KISS1	3.97E-03
3872678	ZSCAN18	3.98E-03
3852966	OR7A10	3.99E-03
3771160	FBF1	3.99E-03
3927446	ADAMTS1	4.00E-03
3274898	TUBAL3	4.00E-03
3687839	ZNF747	4.00E-03
3095766	GINS4	4.00E-03
2363876	FCRLB	4.01E-03
3266583	CASC2	4.02E-03
3553337	TRAF3	4.02E-03

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

2807621	PTGER4	4.02E-03
3679959	EMP2	4.05E-03
2746164	MMAA	4.06E-03
3757770	STAT5B	4.06E-03
3103187	TERF1	4.06E-03
4011889	ZMYM3	4.06E-03
3743167	MED31	4.07E-03
3485292	NBEA	4.07E-03
3762198	COL1A1	4.08E-03
2519577	COL3A1	4.10E-03
3643580	CACNA1H	4.10E-03
3607510	FANCI	4.13E-03
3166718	DNAJA1	4.13E-03
2556010	ELP1P	4.13E-03
3834732	PRR19	4.13E-03
2757621	POLN	4.14E-03
2654394	FXR1	4.16E-03
3571059	DPF3	4.17E-03
3723348	HEXIM1	4.18E-03
2393538	WDR8	4.18E-03
2542816	PUM2	4.19E-03
2794792	VEGFC	4.20E-03
2688955	CD200R1	4.24E-03
2812539	SREK1	4.24E-03
2752725	NEIL3	4.28E-03
2493858	MAL	4.28E-03
3872584	C19orf18	4.29E-03
3760894	OSBPL7	4.30E-03
3512948	C13orf18	4.30E-03
2772805	GC	4.32E-03
3378433	SPTBN2	4.34E-03
2971692	MCM9	4.35E-03
2387006	MTR	4.35E-03
3950846	MIOX	4.36E-03
2871801	FEM1C	4.36E-03
2823326	FER	4.36E-03
2520533	OBFC2A	4.38E-03
3676328	NOXO1	4.40E-03
2351572	CD53	4.42E-03
2469910	LPIN1	4.45E-03
3177563	NAA35	4.46E-03
3818596	EMR1	4.46E-03
2515783	RAPGEF4	4.48E-03
3899173	RRBP1	4.49E-03
3843690	ZSCAN1	4.50E-03
3132333	TM2D2	4.51E-03
3407683	SLCO1B1	4.51E-03
2707909	MCF2L2	4.51E-03
3455388	KRT75	4.52E-03
3352813	TBCEL	4.53E-03
2358092	CA14	4.53E-03
3380080	ORAOV1	4.54E-03
3723204	CCDC103	4.55E-03
2515276	DYNC1I2	4.60E-03
3982689	TBX22	4.61E-03
2643592	EPHB1	4.61E-03
3726114	DLX4	4.62E-03
3189311	PBX3	4.64E-03
3920385	TTC3	4.64E-03
3643360	HAGHL	4.66E-03
2445876	---	4.67E-03
2999334	HECW1	4.67E-03
2436973	PYGO2	4.68E-03
2988336	KIAA0415	4.69E-03
3681705	RRN3	4.71E-03
3557430	MYH6	4.71E-03
2332091	KCNQ4	4.71E-03
3794458	ZNF236	4.71E-03
2436985	SHC1	4.73E-03
3063727	TAF6	4.73E-03
3070873	GPR37	4.74E-03
3920566	DYRK1A	4.79E-03
3221633	HDHD3	4.81E-03
3695157	CMTM4	4.81E-03
4041300	FAM195B	4.82E-03
3895679	C20orf27	4.84E-03
3725517	IGF2BP1	4.84E-03
2780143	BDH2	4.84E-03
3467720	GOLGA2B	4.85E-03
3833728	ITPKC	4.87E-03
3870990	GP6	4.87E-03
3774883	CD7	4.87E-03
3973768	LANCL3	4.88E-03
2545509	PREB	4.93E-03
2888399	SNCB	4.97E-03
3887241	SLC12A5	4.97E-03
3961325	ENTHD1	4.99E-03
2866704	ARRDC3	4.99E-03
2448232	TPR	5.01E-03
2811145	PART1	5.03E-03
3240095	RAB18	5.03E-03
3753729	GAS2L2	5.04E-03
2613386	RAB5A	5.05E-03
3894288	TCF15	5.06E-03
2489440	DOK1	5.06E-03
3234083	ITIH2	5.07E-03
2528476	DES	5.08E-03
2911226	BEND6	5.09E-03
2657250	LPP	5.13E-03
3555272	TTC5	5.15E-03
4024493	SPANXE	5.16E-03
2522247	AOX1	5.18E-03
3188478	CRB2	5.18E-03
2531310	SP140L	5.18E-03
2356115	TXNIP	5.20E-03
3071700	IMPDH1	5.20E-03
3439549	SLC6A13	5.21E-03
2489035	DGUOK	5.22E-03
2541944	SMC6	5.23E-03
3529467	CPNE6	5.24E-03
3461121	IL26	5.26E-03
2517588	OSBPL6	5.27E-03
3379452	C11orf24	5.28E-03
3276421	KIN	5.30E-03
3934903	---	5.30E-03
3726298	TMEM92	5.31E-03
2348854	RTCD1	5.32E-03
3417988	NXPH4	5.32E-03
3179706	WNK2	5.34E-03
2880361	JAKMIP2	5.35E-03
3634682	CHRNB4	5.35E-03
3522398	DOCK9	5.35E-03
2817212	BHMT2	5.37E-03
2442587	CD247	5.38E-03
3762040	TAC4	5.38E-03
3846860	SEMA6B	5.38E-03
2584957	SCN3A	5.38E-03
2397948	EPHA2	5.39E-03
3581404	GPR132	5.39E-03
3315341	SYCE1	5.40E-03
3744094	ALOXE3	5.40E-03
4023907	FGF13	5.41E-03

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

2943434	ATXN1	5.41E-03
2487918	ATP6V1B1	5.41E-03
3390860	POU2AF1	5.42E-03
2601414	SERPINE2	5.43E-03
3737192	CARD14	5.44E-03
2509900	KIF5C	5.46E-03
3526831	RASA3	5.48E-03
2772876	ADAMTS3	5.51E-03
3224650	DENND1A	5.52E-03
3767230	LRRC37A3	5.52E-03
2527747	SLC11A1	5.53E-03
3376367	SLC22A8	5.53E-03
3661940	GNAO1	5.53E-03
3721010	IGFBP4	5.55E-03
3906709	GTSF1L	5.55E-03
3403140	EMG1	5.58E-03
3985305	GPRASP2	5.63E-03
2853275	CAPSL	5.63E-03
2390253	OR2L8	5.64E-03
3303059	SLC25A28	5.64E-03
3628650	HERC1	5.65E-03
3037944	RPA3	5.66E-03
3464276	SLC6A15	5.67E-03
2830504	PKD2L2	5.67E-03
3085933	C8orf12	5.68E-03
3251068	CDH23	5.68E-03
2817464	CMYA5	5.68E-03
2382467	CNIH3	5.70E-03
3624513	MYO5C	5.71E-03
2837029	SGCD	5.71E-03
3131916	WHSC1L1	5.74E-03
3182229	TMEFF1	5.74E-03
3599495	CORO2B	5.76E-03
3982975	POU3F4	5.77E-03
3655012	SH2B1	5.80E-03
2989493	MIOS	5.80E-03
2416522	JAK1	5.80E-03
3284302	NRP1	5.82E-03
2339511	ATG4C	5.83E-03
3947434	SERHL	5.83E-03
2827057	GRAMD3	5.84E-03
2556302	PELI1	5.85E-03
2735362	HERC6	5.85E-03
3159132	COMMD5	5.85E-03
3941076	CRYBA4	5.89E-03
3784670	C18orf21	5.92E-03
3908901	KCNB1	5.93E-03
3479438	CHFR	5.94E-03
2374414	GPR25	5.98E-03
2378584	RCOR3	5.99E-03
3127505	---	6.00E-03
2487063	GKN1	6.00E-03
2323347	PAX7	6.01E-03
3928070	CCT8	6.01E-03
2907943	ABCC10	6.02E-03
3544562	JDP2	6.05E-03
3934479	C21orf2	6.06E-03
3031399	ZNF775	6.08E-03
3845081	C19orf26	6.10E-03
2379974	KCNK2	6.11E-03
2736060	GRID2	6.11E-03
3560403	EGLN3	6.12E-03
3023825	C7orf45	6.13E-03
3774535	DCXR	6.14E-03
2527672	PNKD	6.16E-03
3144859	CDH17	6.17E-03
3772581	USP36	6.18E-03
3353914	VWA5A	6.20E-03
2759582	AFAP1	6.21E-03
3406015	ATF7IP	6.22E-03
2369609	C1orf125	6.23E-03
3758845	HDAC5	6.24E-03
3851250	ZNF20	6.26E-03
3683584	PDILT	6.27E-03
3527831	RNASE7	6.27E-03
3227634	BAT2L1	6.31E-03
3813840	ZNF516	6.34E-03
2677922	ASB14	6.35E-03
3032446	ACTR3B	6.38E-03
3574121	STON2	6.43E-03
3113352	COL14A1	6.43E-03
2364438	NUF2	6.45E-03
3771068	TRIM47	6.47E-03
2327283	C1orf38	6.50E-03
2607020	MTERFD2	6.52E-03
2591643	COL5A2	6.55E-03
2412082	FAF1	6.56E-03
2621032	PTH1R	6.56E-03
3815416	ABCA7	6.59E-03
3336117	TMEM151	6.60E-03
3414326	AQP6	6.61E-03
3597338	TPM1	6.62E-03
3070543	SLC13A1	6.63E-03
3575241	KCNK10	6.64E-03
3840562	HERV-V1	6.65E-03
3560575	EAPP	6.65E-03
3257268	IFIT5	6.67E-03
2924081	NKAIN2	6.70E-03
3693837	GOT2	6.71E-03
2883440	ADAM19	6.71E-03
3756546	KRT12	6.72E-03
3914181	UCKL1	6.72E-03
3120682	MFSD3	6.76E-03
3662774	GPR114	6.79E-03
2988594	SLC29A4	6.79E-03
2830818	REEP2	6.80E-03
3033307	EN2	6.80E-03
3789680	ST8SIA3	6.80E-03
3072546	TSGA14	6.80E-03
3082990	MYOM2	6.82E-03
3214749	NOL8	6.82E-03
2955076	NFKBIE	6.83E-03
3085403	MSRA	6.83E-03
2413879	PARS2	6.84E-03
4002011	CXorf23	6.85E-03
3614774	OCA2	6.85E-03
3259400	CCNJ	6.87E-03
3191877	AIF1L	6.89E-03
3498315	UBAC2	6.92E-03
2324084	CDA	6.93E-03
3934623	KAP12.2	6.93E-03
2359885	SLC27A3	6.94E-03
2964350	MDN1	6.95E-03
3601889	LMAN1L	6.98E-03
4035017	UTY	6.99E-03
3551029	C14orf177	7.00E-03
3550139	TCL1B	7.01E-03
2594569	ORC2	7.01E-03
3363091	GALNTL4	7.03E-03
2585129	GALNT3	7.04E-03
3096271	C8orf40	7.10E-03
3227482	FIBCD1	7.12E-03

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

2891015	TRIM7	7.16E-03
2606643	MYEOV2	7.17E-03
2396781	MAD2L2	7.17E-03
3715839	TRAF4	7.18E-03
2742935	HSPA4L	7.18E-03
2345128	SH3GLB1	7.18E-03
2417008	INSL5	7.20E-03
3000276	RAMP3	7.23E-03
3913483	TCFL5	7.24E-03
3955102	GSTT1	7.25E-03
2774365	CCNI	7.26E-03
3851911	PRG6	7.27E-03
3391029	PPP2R1B	7.27E-03
3089102	EPB49	7.27E-03
4017747	GUCY2F	7.29E-03
3636216	AP3B2	7.29E-03
2903507	RING1	7.29E-03
2906872	MDFI	7.30E-03
3545403	GSTZ1	7.30E-03
2956586	PGK2	7.30E-03
2633773	TFG	7.31E-03
4003017	PCYT1B	7.31E-03
2890148	HNRNPH1	7.33E-03
2681044	FAM19A4	7.38E-03
3904119	CPNE1	7.38E-03
2435410	S100A11	7.41E-03
3360874	HPX	7.41E-03
3272566	KNDC1	7.45E-03
2373406	CFHR3	7.46E-03
2475678	LBH	7.52E-03
4020655	ODZ1	7.55E-03
2837499	LSM11	7.56E-03
2601341	WDFY1	7.62E-03
3145586	MTERFD1	7.64E-03
3712582	MED9	7.64E-03
3089049	NPM2	7.66E-03
3188780	GPR144	7.67E-03
3918104	C21orf63	7.69E-03
2550175	KCNG3	7.69E-03
3698081	PMFBP1	7.71E-03
3455186	KRT5	7.72E-03
2704188	PDCD10	7.72E-03
3883013	TP53INP2	7.75E-03
2672629	KIF9	7.75E-03
2951916	STK38	7.76E-03
3757399	NT5C3L	7.77E-03
2653902	ZNF639	7.78E-03
3523156	TMTC4	7.79E-03
3230697	NPDC1	7.80E-03
3815097	FSTL3	7.82E-03
3867796	TEAD2	7.86E-03
3283920	ARHGAP12	7.88E-03
3952956	ARVCF	7.88E-03
3374189	OR9I1	7.89E-03
3136229	SDR16C5	7.92E-03
3305313	ITPRIP	7.92E-03
3467637	SHIP164	7.93E-03
3216529	ZNF782	7.94E-03
2405469	PHC2	7.95E-03
3084950	CLDN23	7.98E-03
3597603	USP3	7.99E-03
2497082	IL1RL1	8.00E-03
3995765	DUSP9	8.00E-03
2791419	FAM198B	8.06E-03
2721777	PI4K2B	8.11E-03
2422517	ZNF644	8.12E-03
3742236	PELP1	8.13E-03
2324594	CELA3A	8.13E-03
2401493	ID3	8.13E-03
3886576	WISP2	8.14E-03
2511432	GPD2	8.15E-03
2867836	GLRX	8.17E-03
2922246	FLJ34503	8.17E-03
3826542	ZNF738	8.19E-03
3521484	UGGT2	8.24E-03
3791341	ZCCHC2	8.26E-03
3743038	AIPL1	8.26E-03
2586038	LRP2	8.26E-03
3796335	LPIN2	8.26E-03
3291682	JMJD1C	8.30E-03
3336220	PELI3	8.34E-03
3075742	KLRG2	8.34E-03
3468888	GLT8D2	8.35E-03
2622435	RBM6	8.35E-03
3538403	LRRC9	8.35E-03
3591327	CCNDBP1	8.37E-03
2682088	EIF4E3	8.37E-03
3341137	B3GNT6	8.38E-03
3529799	GMPR2	8.38E-03
3722060	VPS25	8.40E-03
3359601	OSBPL5	8.40E-03
3638871	ATG8D	8.41E-03
3695631	TPPP3	8.42E-03
3964049	CELSR1	8.42E-03
2717014	MAN2B2	8.43E-03
2975680	BCLAF1	8.48E-03
3589905	IVD	8.48E-03
2337407	PCSK9	8.48E-03
3534248	FANCM	8.49E-03
2461531	IRF2BP2	8.50E-03
2501178	IL1F10	8.53E-03
3543756	DNAL1	8.57E-03
2985781	THBS2	8.58E-03
3632037	PARP6	8.59E-03
3665049	CES4A	8.61E-03
3579458	DEGS2	8.62E-03
2742581	FAT4	8.64E-03
3659691	C16orf78	8.65E-03
2580635	MMADHC	8.67E-03
3420497	HELB	8.67E-03
3457872	MIP	8.72E-03
3066297	SRPK2	8.73E-03
2566764	REV1	8.76E-03
2949118	LTB	8.77E-03
3675369	NARFL	8.79E-03
3513794	RCBTB1	8.80E-03
2827177	C5orf48	8.82E-03
3824666	KCNN1	8.85E-03
2950515	VPS52	8.89E-03
3931112	HLCS	8.90E-03
3190796	PHYHD1	8.90E-03
2532626	C2orf82	8.91E-03
2713382	BDH1	8.91E-03
3138929	LRRC67	8.92E-03
3339406	FOLR1	8.93E-03
3642747	ARHGDIG	8.94E-03
2379399	RPS6KC1	8.94E-03
3621117	TGM7	8.97E-03
2602653	PID1	8.97E-03
3680223	PRM1	8.99E-03
2343289	DNAJB4	8.99E-03
3380142	FGF4	9.01E-03

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3699133	FA2H	9.02E-03	2489322	TTC31	9.63E-03	3984840	ARMCX4	0.010	3865586	FBXO46	0.011
2439373	SPTA1	9.03E-03	2632832	EPHA6	9.67E-03	3541073	MPP5	0.010	3831774	ZNF383	0.011
3625234	RSL24D1	9.05E-03	2371346	RGL1	9.72E-03	3678279	ANKS3	0.010	2688499	ZBED2	0.011
3936442	PEX26	9.05E-03	2832431	PCDHB11	9.73E-03	2758658	TMEM128	0.010	2577106	NCKAP5	0.011
2896177	JARID2	9.05E-03	2955164	---	9.74E-03	2501120	IL1F9	0.010	2439101	FCRL1	0.011
2612100	FGD5	9.05E-03	2781387	AGXT2L1	9.75E-03	2322211	C1orf64	0.010	4036497	TTTY5	0.011
3173673	PIP5K1B	9.08E-03	2769095	---	9.75E-03	2892734	---	0.010	3501999	SOX1	0.011
2441386	RGS5	9.09E-03	3029646	ARHGEF5	9.77E-03	3913272	GATA5	0.010	3361021	TAF10	0.011
2892393	BPHL	9.09E-03	2783916	TNIP3	9.80E-03	3625823	ZNF280D	0.010	3146898	YWHAZ	0.011
3408966	FGFR1OP2	9.10E-03	2906105	GLP1R	9.86E-03	3219215	KLF4	0.010	3840406	ZNF137P	0.011
2377094	PFKFB2	9.14E-03	2772614	GRSF1	9.87E-03	3811000	RNF152	0.010	3794341	FLJ44313	0.011
3714779	KCNJ12	9.19E-03	3461496	BEST3	9.90E-03	2545869	IFT172	0.010	3754227	MYO19	0.011
3972025	PDK3	9.19E-03	3683879	DNAH3	9.92E-03	3977651	MAGED1	0.010	3289445	A1CF	0.011
2925237	LAMA2	9.20E-03	2412690	KTI12	9.93E-03	3642060	CHSY1	0.010	3910980	BMP7	0.011
2408111	TRIT1	9.21E-03	3680249	PRM3	9.94E-03	3413643	CCDC65	0.011	3433929	SRRM4	0.011
3548538	C14orf159	9.25E-03	2946106	SLC17A3	9.97E-03	3278401	FRMD4A	0.011	3416651	PDE1B	0.011
3808745	CCDC68	9.26E-03	3654175	IL4R	9.98E-03	3000984	ABCA13	0.011	3643679	TPSD1	0.011
3633081	CYP1A1	9.27E-03	3553998	TDRD9	9.99E-03	3866117	DACT3	0.011	2689286	KIAA1407	0.011
3760137	KIAA1267	9.30E-03	3329537	C11orf49	0.010	2532852	SAG	0.011	3023103	CCDC136	0.011
2632051	C3orf38	9.30E-03	3817437	FSD1	0.010	2325358	GRHL3	0.011	3259631	LCOR	0.011
2985368	FRMD1	9.31E-03	2924898	RNF146	0.010	2436754	ADAR	0.011	2673312	PFKFB4	0.011
3082373	VIPR2	9.34E-03	3376121	ZBTB3	0.010	3235516	CAMK1D	0.011	3800779	ESCO1	0.011
4009990	USP51	9.34E-03	2913564	DDX43	0.010	2832403	PCDHB9	0.011	3249788	CCAR1	0.011
3923537	C21orf33	9.36E-03	3042973	HOXA11	0.010	3738081	TSPAN10	0.011	2761503	---	0.011
2980870	NOX3	9.38E-03	3209726	ALDH1A1	0.010	3871792	ZSCAN5A	0.011	3596263	FOXB1	0.011
2389130	EFCAB2	9.38E-03	2494064	FAHD2A	0.010	3987228	PAK3	0.011	2623568	PPM1M	0.011
3195238	GRIN1	9.39E-03	3760552	RPRML	0.010	3012381	AKAP9	0.011	3722681	C17orf88	0.011
3417767	GPR182	9.41E-03	3981592	CDX4	0.010	2378662	TRAF5	0.011	2536531	FARP2	0.011
2776305	NKX6-1	9.43E-03	3602526	FBXO22	0.010	3663287	NDRG4	0.011	2670481	ULK4	0.011
3576014	C14orf102	9.46E-03	3613725	NDN	0.010	3555088	KIAA0125	0.011	3252577	VDAC2	0.011
3815710	EFNA2	9.47E-03	2939213	TUBB2A	0.010	3711165	COX10	0.011	2400027	PLA2G2A	0.011
2440625	DEDD	9.51E-03	3262715	SORCS3	0.010	3147985	LRP12	0.011	3636956	WDR73	0.011
3697125	COG4	9.59E-03	2623922	STAB1	0.010	3577160	ITPK1	0.011	2414505	C8B	0.011

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3011454	DBF4	0.011	2522693	CASP10	0.012	2829562	TXNDC15	0.013	2334986	CYP4X1	0.013
3086181	NEIL2	0.011	2521278	CCDC150	0.012	2739308	EGF	0.013	2623611	GLYCTK	0.013
3958157	SLC5A4	0.011	4016955	TEX13A	0.012	3922793	PDE9A	0.013	3984468	SRPX2	0.013
2465753	OR2C3	0.011	3669092	TERF2IP	0.012	3862650	SERTAD3	0.013	2460487	C1orf131	0.013
3951302	POTEM	0.011	2437417	ASH1L	0.012	3994610	MAGEA8	0.013	3623552	ATP8B4	0.013
3602423	ODF3L1	0.011	3107661	INTS8	0.012	3201144	IFNB1	0.013	2473026	C2orf84	0.013
2318398	PHF13	0.011	3655723	MVP	0.012	3598199	ANKDD1A	0.013	3023279	TPI1P2	0.013
2405192	YARS	0.011	2678029	DNAH12	0.012	3934187	HSF2BP	0.013	2361241	ROBLD3	0.013
3378758	CLCF1	0.011	2458701	ACBD3	0.012	3819880	ZNF317	0.013	3883236	MMP24	0.013
3190762	ENDOG	0.011	3307795	C10orf118	0.012	2647647	TSC22D2	0.013	3157217	CYP11B1	0.013
3042730	HOXA1	0.011	3677268	PRSS22	0.012	3204174	C9orf23	0.013	2374126	NR5A2	0.013
3333595	GNG3	0.011	3256689	PTEN	0.012	3392973	APOA4	0.013	3020646	CFTR	0.013
3474104	CIT	0.012	2609608	SETD5	0.012	2783715	MAD2L1	0.013	3063463	CYP3A7	0.013
3830712	MLL4	0.012	3583638	CYFIP1	0.012	2468351	RSAD2	0.013	2829275	UBE2B	0.013
3310041	FGFR2	0.012	2961647	HTR1B	0.012	3359529	CARS	0.013	2789957	FBXW7	0.013
3203996	C9orf24	0.012	3884524	BPI	0.012	2778440	UNC5C	0.013	3343252	C11orf73	0.013
3863380	GRIK5	0.012	3030873	ZNF862	0.012	3554452	KIAA0284	0.013	3893891	---	0.013
2709235	DGKG	0.012	3974838	DDX3X	0.012	3257559	RPP30	0.013	3959918	TST	0.013
3336951	RAD9A	0.012	2669184	LRRFIP2	0.012	2921086	CDC40	0.013	2845362	SLC9A3	0.013
2663785	CHCHD4	0.012	3301713	BLNK	0.012	2533670	AGAP1	0.013	3850331	CDC37	0.014
3934529	C21orf29	0.012	2440664	B4GALT3	0.012	3638337	POLG	0.013	3317569	---	0.014
2429069	TRIM33	0.012	2910364	TMEM14A	0.012	3379777	MRGPRF	0.013	2831719	ANKHD1	0.014
2743315	PHF17	0.012	2376799	IKBKE	0.012	3169043	RG9MTD3	0.013	3028011	MGAM	0.014
3786471	SETBP1	0.012	3200648	PLIN2	0.012	3023835	CPA2	0.013	2764678	FLJ45721	0.014
2987410	NUDT1	0.012	2567167	LONRF2	0.012	3067644	THAP5	0.013	2867392	C5orf36	0.014
3272455	GPR123	0.012	3593014	SLC24A5	0.012	2713837	ZNF718	0.013	2874794	RAPGEF6	0.014
2324820	EPHA8	0.012	2953481	TREML1	0.012	3334749	PPP2R5B	0.013	3660075	NKD1	0.014
3665722	PARD6A	0.012	3551407	HHIPL1	0.013	3869215	HAS1	0.013	3061046	KRIT1	0.014
3414029	KCNH3	0.012	2905296	PI16	0.013	2666807	NEK10	0.013	3393536	TMPRSS13	0.014
3553947	ZFYVE21	0.012	3474495	TRIAP1	0.013	3335465	SIPA1	0.013	3819968	ZNF177	0.014
3642837	DECR2	0.012	2717757	C4orf23	0.013	3680524	ZC3H7A	0.013	2946056	SLC17A1	0.014
3436544	BRI3BP	0.012	3846076	TLE2	0.013	2878943	PCDH1	0.013	2947219	ZKSCAN4	0.014
2518889	ZNF804A	0.012	3939470	MMP11	0.013	3752097	C17orf42	0.013	2632919	ARL6	0.014

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3555736	NDRG2	0.014
3948590	RIBC2	0.014
3689981	MYLK3	0.014
3376235	WDR74	0.014
2840393	GABRP	0.014
3820458	ICAM4	0.014
2947248	ZNF323	0.014
3984125	RPA4	0.014
3929237	TCP10L	0.014
3332530	MS4A10	0.014
3015786	ZAN	0.014
3090006	SLC25A37	0.014
2638988	PARP15	0.014
3015682	PCOLCE	0.014
3950629	TRABD	0.014
3105749	ATP6V0D2	0.014
3079257	ATG9B	0.014
3965447	IL17REL	0.014
3555492	TMEM55B	0.014
3347118	GRIA4	0.014
3504213	GJB6	0.014
3152558	FAM84B	0.014
2708457	CLCN2	0.014
3527390	OR11H4	0.014
3269328	ZRANB1	0.014
3934245	CSTB	0.014
3852586	LPHN1	0.014
2420681	MCOLN3	0.014
2783316	SEC24D	0.014
2521574	PLCL1	0.014
2602304	TM4SF20	0.014
3311694	MMP21	0.014
3934785	C21orf67	0.014
3788976	RAB27B	0.014
3415763	SOAT2	0.014
3445768	ERP27	0.014
3208640	PRKACG	0.014
2535976	AGXT	0.014
2809793	GZMK	0.014
2382781	DNAH14	0.014
2693682	TXNRD3	0.014
3766013	MARCH10	0.014
3835911	APOC4	0.014
2909404	CD2AP	0.015
2549092	SOS1	0.015
3223157	DBC1	0.015
2975867	MAP3K5	0.015
2671422	ZNF445	0.015
3882214	BPIL3	0.015
2954527	ZNF318	0.015
2837192	PPP1R2P3	0.015
3846507	DAPK3	0.015
4051619	EXD3	0.015
3836217	KLC3	0.015
3259836	ZDHHC16	0.015
3401878	NDUFA9	0.015
3729569	BCAS3	0.015
2481308	KLRAQ1	0.015
3699581	TMEM170A	0.015
2819044	RASA1	0.015
2600155	DNPEP	0.015
3458837	METTL1	0.015
3388696	MMP20	0.015
2855285	SEPP1	0.015
2946219	HIST1H2AB	0.015
2761842	PROM1	0.015
3182019	STX17	0.015
3146723	SNX31	0.015
3352159	---	0.015
2546054	RBKS	0.015
2330133	EIF2C3	0.015
3377474	SYVN1	0.015
3568534	SPTB	0.015
3562557	FSCB	0.015
3953033	TRMT2A	0.015
2947681	OR2W1	0.015
2650357	ARL14	0.015
3336094	CNIH2	0.015
2371255	SMG7	0.015
3014808	ZNF789	0.015
3079172	TMEM176B	0.015
3371719	CKAP5	0.016
3851801	RTBDN	0.016
3474418	PXN	0.016
2968652	SESN1	0.016
3715512	TNFAIP1	0.016
3414440	C12orf62	0.016
3693141	PLLP	0.016
3371225	CHST1	0.016
3075531	ZC3HAV1L	0.016
3322638	MRGPRX3	0.016
3957679	SELM	0.016
2722291	TBC1D19	0.016
3842130	TMEM190	0.016
3978999	UBQLN2	0.016
2951567	FKBP5	0.016
2687255	CBLB	0.016
2794704	ASB5	0.016
2743370	C4orf33	0.016
3334325	VEGFB	0.016
3913220	C20orf151	0.016
2333707	CCDC24	0.016
2479510	DYNC2LI1	0.016
3927105	MRPL39	0.016
2674646	AMIGO3	0.016
2981976	OSTCL	0.016
3781245	GATA6	0.016
3359134	IGF2	0.016
2851511	CDH9	0.016
2769810	KDR	0.016
2775994	HPSE	0.016
3371928	ARFGAP2	0.016
3862188	FCGBP	0.016
3991006	OR13H1	0.016
3835361	ZNF222	0.016
2626802	PTPRG	0.016
2362950	ATP1A4	0.016
3619690	PPP1R14D	0.016
2716124	HGFAC	0.016
3238702	ARMC3	0.016
2622359	RBM6	0.016
3718401	LIG3	0.016
3332729	CD5	0.016
3526544	DCUN1D2	0.017
3992148	DDX26B	0.017
3387033	MRE11A	0.017
3754677	SYNRG	0.017
2628081	SLC25A26	0.017
3726252	SGCA	0.017
3334604	---	0.017
2333574	ARTN	0.017
3920512	DSCR9	0.017

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3976716	WDR13	0.017	3950452	CRELD2	0.017	2840789	FGF18	0.018	3994100	FMR1	0.019
2767159	PHOX2B	0.017	3678542	C16orf89	0.017	3459604	PPM1H	0.018	2476219	BIRC6	0.019
3742627	C17orf87	0.017	3834341	CEACAM5	0.017	3468743	NT5DC3	0.018	3867400	FUT1	0.019
2669533	ACAA1	0.017	3268274	PLEKHA1	0.017	3221205	SLC46A2	0.018	3655060	ATP2A1	0.019
3455651	KRT72	0.017	3197231	C9orf68	0.017	3759704	MAP3K14	0.018	3753538	SLFN12	0.019
3296046	KCNMA1	0.017	3951493	CCT8L2	0.017	2397999	ARHGEF19	0.018	2686213	FILIP1L	0.019
2623308	GRM2	0.017	2607757	CNTN6	0.018	3833793	RAB4B	0.019	2351763	CHIA	0.019
4054204	APOD	0.017	3746625	TEKT3	0.018	3903952	GDF5	0.019	2716246	FLJ35424	0.019
3239667	GAD2	0.017	3986087	NRK	0.018	2529782	MRPL44	0.019	3362191	SCUBE2	0.019
3762185	HILS1	0.017	3545022	ESRRB	0.018	2868265	LIX1	0.019	2610972	SYN2	0.019
3741040	MNT	0.017	2953262	FLJ41649	0.018	2800477	SRD5A1	0.019	3456212	MAP3K12	0.019
2528198	CDK5R2	0.017	2321960	PLEKHM2	0.018	3631397	UACA	0.019	3486096	FREM2	0.020
3033397	RBM33	0.017	2418700	ASB17	0.018	3968303	SHROOM2	0.019	2990043	PHF14	0.020
3408733	RASSF8	0.017	2446567	STX6	0.018	2746507	---	0.019	3740479	PRPF8	0.020
3289948	PCDH15	0.017	3928559	KRTAP6-1	0.018	3791782	SERPINB5	0.019	3649811	NDE1	0.020
3345940	CNTN5	0.017	2716432	ZBTB49	0.018	2854445	DAB2	0.019	2977510	FUCA2	0.020
3509473	DCLK1	0.017	3414846	DAZAP2	0.018	3157441	MAFA	0.019	3658561	MGC34800	0.020
3220846	SUSD1	0.017	3675620	C1QTNF8	0.018	2907444	PTCRA	0.019	3127610	PEBP4	0.020
3826306	ZNF85	0.017	2726828	DCUN1D4	0.018	3198974	MPDZ	0.019	3185643	RGS3	0.020
2318212	C1orf211	0.017	3974708	USP9X	0.018	2992243	DNAH11	0.019	3969713	MOSPD2	0.020
2827299	MEGF10	0.017	3444195	MAGOHB	0.018	3217361	ANKS6	0.019	2558736	ADD2	0.020
3432798	SDSL	0.017	2337217	C1orf175	0.018	2735459	HERC3	0.019	3541497	RAD51L1	0.020
2592598	TMEFF2	0.017	3226237	DPM2	0.018	3901401	CST5	0.019	3693788	SLC38A7	0.020
3202421	C9orf72	0.017	2389718	CNST	0.018	2500919	SLC20A1	0.019	3664952	PDP2	0.020
3339971	PLEKHB1	0.017	2635812	PLCXD2	0.018	3936992	SEPT5	0.019	2542990	HS1BP3	0.020
3825292	CRTC1	0.017	4014251	CHM	0.018	2762468	DCAF16	0.019	3340066	PAAF1	0.020
2443305	C1orf114	0.017	3773558	FLJ90757	0.018	2352275	MOV10	0.019	2409847	PTCH2	0.020
3744127	HES7	0.017	3864414	PHLDB3	0.018	3075778	HIPK2	0.019	3272795	PAOX	0.020
4008078	PAGE1	0.017	3980867	GJB1	0.018	3621276	PPIP5K1	0.019	3229449	C9orf116	0.020
3540155	C14orf50	0.017	2790626	FGA	0.018	3752709	MYO1D	0.019	2510485	RIF1	0.020
2734421	ARHGAP24	0.017	3854477	TMEM221	0.018	3662750	POLR2C	0.019	3418153	MARS	0.020
2894790	SYCP2L	0.017	3125915	MTUS1	0.018	3231846	WDR37	0.019	3697005	EXOSC6	0.020
3334087	NAA40	0.017	3399004	OPCML	0.018	2421121	ODF2L	0.019	4026010	GABRE	0.020

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3079576	SMARCD3	0.020
3475511	DIABLO	0.020
3654956	LAT	0.020
3375840	TUT1	0.020
2863964	ARSB	0.020
3835085	ZNF575	0.020
3755089	GPR179	0.020
3886444	R3HDML	0.020
3481890	ATP12A	0.020
2420790	C1orf52	0.020
3192609	GFI1B	0.020
2709402	CRYGS	0.020
3718185	CCL11	0.020
3177111	NTRK2	0.020
3666146	SLC7A6	0.020
3688120	STX1B	0.020
2641769	RHO	0.020
3581373	---	0.020
2413484	YIPF1	0.020
3818395	ALKBH7	0.020
3842059	BRSK1	0.021
3851545	MAN2B1	0.021
2884727	ATP10B	0.021
3676356	ZNF598	0.021
3717052	NF1	0.021
2427500	HBXIP	0.021
3662612	RSPRY1	0.021
3731543	RGS9	0.021
3938215	CCDC116	0.021
3323413	HTATIP2	0.021
4015440	SYTL4	0.021
2447107	TEDDM1	0.021
3966891	XG	0.021
3922921	NDUFV3	0.021
2333481	ST3GAL3	0.021
2399988	RNF186	0.021
3231010	PNPLA7	0.021
2681195	UBA3	0.021
3139035	ARFGEF1	0.021
3840253	ZNF534	0.021
2392095	C1orf86	0.021
3987876	HTR2C	0.021
3959411	APOL2	0.021
2567669	RFX8	0.021
3963990	PKDREJ	0.021
2523540	NBEAL1	0.021
3341221	MYO7A	0.021
3320819	MICALCL	0.021
3899495	C20orf12	0.021
2597273	C2orf67	0.021
3039247	DGKB	0.021
2326846	TRNP1	0.021
3094980	HTRA4	0.021
3157563	NAPRT1	0.021
3226097	ENG	0.021
3824497	MAP1S	0.021
3373630	APLNR	0.021
4030162	DDX3Y	0.021
3975893	PHF16	0.021
3923608	AIRE	0.021
3852079	STX10	0.021
3402899	USP5	0.021
3917549	KAP13-1	0.021
2514304	DHRS9	0.021
3351688	UPK2	0.022
3103745	CRISPLD1	0.022
3589972	CHST14	0.022
3664779	---	0.022
2641232	---	0.022
3179646	SUSD3	0.022
3072014	TNPO3	0.022
3851630	FBXW9	0.022
3996289	EMD	0.022
2452571	ELK4	0.022
2405036	BSDC1	0.022
3434594	ACADS	0.022
2953711	TFEB	0.022
3947627	TSPO	0.022
3214050	---	0.022
3697183	MTSS1L	0.022
3000953	UPP1	0.022
3300115	PPP1R3C	0.022
3969115	TLR8	0.022
2773545	BTC	0.022
4011189	OPHN1	0.022
3162529	C9orf150	0.022
2924514	NCOA7	0.022
3932397	C21orf88	0.022
2349211	HEJ1	0.022
3048886	PURB	0.022
2793441	AADAT	0.022
3753966	CCL14-15	0.022
3709540	PFAS	0.022
3774906	SECTM1	0.022
3381682	CHCHD8	0.022
3720402	ERBB2	0.022
3817933	ZNRF4	0.022
2339454	ANGPTL3	0.022
3255311	CDHR1	0.023
3384718	DLG2	0.023
3939125	GNAZ	0.023
2565082	ADRA2B	0.023
3994451	CXorf40A	0.023
2788195	OTUD4	0.023
3526772	FAM70B	0.023
3720695	THRA	0.023
3955940	CRYBB1	0.023
3242425	CCNY	0.023
2644619	ESYT3	0.023
2413943	USP24	0.023
2759857	ACOX3	0.023
3939450	C22orf15	0.023
2468138	---	0.023
2887164	SH3PXD2B	0.023
3239437	GPR158	0.023
2316953	PRDM16	0.023
3572929	ZDHHC22	0.023
3702499	KIAA1609	0.023
2782292	C4orf21	0.023
2757278	FAM53A	0.023
2400247	KIF17	0.023
4051723	ENTPD8	0.023
3557504	MYH7	0.023
3828067	PLEKHF1	0.023
2613293	KCNH8	0.023
3851776	PRDX2	0.023
3822122	NFIX	0.023
3326826	FJX1	0.023
2908052	POLR1C	0.023
2535859	CAPN10	0.024
3242555	GJD4	0.024
2900143	OR2B6	0.024

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3783481	DSG3	0.024	2322036	FBLIM1	0.024	2545144	GPR113	0.025	2545144	GPR113	0.025
2814527	BDP1	0.024	3071304	PAX4	0.024	2700727	SERP1	0.025	2700727	SERP1	0.025
2456687	SLC30A10	0.024	3837193	CCDC9	0.024	3269587	C10orf137	0.025	3269587	C10orf137	0.025
2926437	MGC34034	0.024	3362096	C11orf16	0.024	3791815	SERPINB12	0.025	3791815	SERPINB12	0.025
2466002	SH3BP5L	0.024	3168309	RECK	0.024	3872542	ZNF418	0.025	3872542	ZNF418	0.025
3887069	SNX21	0.024	2852742	AMACR	0.024	3180342	C9orf3	0.025	3180342	C9orf3	0.025
3835544	ZNF227	0.024	3846363	APBA3	0.024	3026969	C7orf55	0.025	3026969	C7orf55	0.025
3607927	SEMA4B	0.024	3352948	SORL1	0.024	3334484	ESRRA	0.025	3334484	ESRRA	0.025
2640449	CHST13	0.024	3820906	C19orf52	0.025	3491948	TDRD3	0.025	3491948	TDRD3	0.025
3143575	DCAF4L2	0.024	3402150	NTF3	0.025	2735759	MMRN1	0.025	2735759	MMRN1	0.025
3468473	PAH	0.024	2887048	STK10	0.025	3187834	DAB2IP	0.025	3187834	DAB2IP	0.025
3516228	PCDH20	0.024	2591614	DIRC1	0.025	3193725	OLFM1	0.025	3193725	OLFM1	0.025
3860261	THAP8	0.024	3799461	SPIRE1	0.025	3907040	LOC79015	0.025	3907040	LOC79015	0.025
2752085	---	0.024	3334831	ZFPL1	0.025	2438792	ETV3	0.025	2438792	ETV3	0.025
2976768	CITED2	0.024	3957738	RNF185	0.025	2495446	INPP4A	0.025	2495446	INPP4A	0.025
2843283	B4GALT7	0.024	3931765	ERG	0.025	2672966	MAP4	0.025	2672966	MAP4	0.025
3747522	TNFRSF13	0.024	3189800	SLC2A8	0.025	2730933	NPFFR2	0.025	2730933	NPFFR2	0.025
3830065	HPN	0.024	2911413	PRIM2	0.025	3836705	HIF3A	0.025	3836705	HIF3A	0.025
3114365	FAM91A1	0.024	2493992	KCNIP3	0.025	3911217	PMEPA1	0.025	3911217	PMEPA1	0.025
3594825	PIGB	0.024	4003155	ARX	0.025	3706736	TMEM93	0.026	3706736	TMEM93	0.026
3106539	OTUD6B	0.024	3457667	CNPY2	0.025	3869030	SIGLEC10	0.026	3869030	SIGLEC10	0.026
3422215	THAP2	0.024	3246046	C10orf71	0.025	2745067	ELMOD2	0.026	2745067	ELMOD2	0.026
2631940	HTR1F	0.024	2366156	SFT2D2	0.025	2415910	DOCK7	0.026	2415910	DOCK7	0.026
2655845	EPHB3	0.024	3344897	MED17	0.025	3976670	EBP	0.026	3976670	EBP	0.026
3261063	TLX1	0.024	2888800	DBN1	0.025	3961955	PHF5A	0.026	3961955	PHF5A	0.026
2550542	THADA	0.024	3015395	PVRIG	0.025	2726234	NIPAL1	0.026	2726234	NIPAL1	0.026
3138618	CRH	0.024	3049522	TNS3	0.025	2923868	PKIB	0.026	2923868	PKIB	0.026
3611744	LRRK1	0.024	3029475	OR6B1	0.025	3153961	HHLA1	0.026	3153961	HHLA1	0.026
2850071	MYO10	0.024	2812690	MAST4	0.025	2887633	BOD1	0.026	2887633	BOD1	0.026
3007960	CLDN4	0.024	3180142	PTPDC1	0.025	4037778	DMBT1	0.026	4037778	DMBT1	0.026
2717253	SORCS2	0.024	3333942	RTN3	0.025	2380440	SPATA17	0.026	2380440	SPATA17	0.026
2362323	OR6K6	0.024	2830698	FAM53C	0.025	2769346	LNX1	0.026	2769346	LNX1	0.026
2662657	SEC13	0.024	2377165	C4BPA	0.025	3839499	ACPT	0.026	3839499	ACPT	0.026

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3645656	ZNF205	0.026
3444086	KLRK1	0.026
2902609	C6orf25	0.026
3832865	NCCRP1	0.026
3258713	LGI1	0.026
3747812	PEMT	0.026
3866491	MEIS3	0.026
2750476	TRIM60	0.026
3345593	CEP57	0.026
3123541	MFHAS1	0.026
2404122	MATN1	0.026
3770422	GRIN2C	0.027
3037535	ZNF12	0.027
3535186	ATL1	0.027
3592054	TRIM69	0.027
3610804	IGF1R	0.027
2897453	ID4	0.027
3982721	FAM46D	0.027
3858285	TSHZ3	0.027
3934837	C21orf122	0.027
3945014	GCAT	0.027
3721485	KLHL10	0.027
3273578	IDI2	0.027
3529775	TSSK4	0.027
2930418	UST	0.027
3930942	CLDN14	0.027
3096368	HOOK3	0.027
2390335	OR2M2	0.027
3833238	LGALS14	0.027
2439052	FCRL2	0.027
3915569	CHODL	0.027
3696524	COG8	0.027
2606959	C2orf54	0.027
2336585	SCP2	0.027
2442397	TADA1	0.027
3819130	CLEC4M	0.027
2700332	TM4SF18	0.027
3812074	DSEL	0.027
3292169	CTNNA3	0.027
2874686	HINT1	0.027
3415068	ANKRD33	0.027
3735089	---	0.027
3675101	MRPL28	0.027
3774516	STRA13	0.027
3270224	FOXI2	0.027
3852133	CACNA1A	0.028
3048134	C7orf44	0.028
2423017	EVI5	0.028
3588346	ZNF770	0.028
2542651	WDR35	0.028
2620410	EXOSC7	0.028
2962525	IBTK	0.028
2823880	CAMK4	0.028
2472651	KLHL29	0.028
3371964	PACSIN3	0.028
3688254	PRSS8	0.028
2576526	NOC2L	0.028
3061319	CDK6	0.028
3249641	MYPN	0.028
3575371	EML5	0.028
2427898	OVGP1	0.028
3722700	NAGS	0.028
2713664	IQCG	0.028
2940987	SLC35B3	0.028
2322103	SPEN	0.028
3523318	NALCN	0.028
2721809	ZCCHC4	0.028
3841862	FCAR	0.028
3511031	ELF1	0.028
3158011	PARP10	0.028
2376168	NFASC	0.028
2772341	UGT2B4	0.028
2900453	PGBD1	0.028
2797393	FAT1	0.028
2651989	SKIL	0.028
4054414	GJB3	0.028
3001345	VWC2	0.028
3674349	ZNF276	0.028
3978518	MAGED2	0.028
2711957	C3orf21	0.028
3941793	KREMEN1	0.028
3046197	ELMO1	0.028
2433432	GJA5	0.028
3961042	FLJ23865	0.028
3632107	CELF6	0.028
2459487	TRIM11	0.028
2950753	BAK1	0.028
2881165	TIGD6	0.028
3544071	VSX2	0.028
2359504	SPRR3	0.029
3480013	MPP8	0.029
3431143	UBE3B	0.029
2754538	SLC25A4	0.029
3458248	MYO1A	0.029
2360541	DCST1	0.029
3970714	PPEF1	0.029
2612278	CAPN7	0.029
3443206	AICDA	0.029
3258772	TMEM20	0.029
2756497	ATP5I	0.029
3323052	NAV2	0.029
3743937	---	0.029
2398040	C1orf89	0.029
2318157	RNF207	0.029
2957314	GSTA2	0.029
3354719	---	0.029
2409344	MED8	0.029
3293537	PCBD1	0.029
3331355	SERPING1	0.029
2324634	CDC42	0.029
3836401	GIPR	0.029
4009751	ITIH5L	0.029
3840194	ZNF880	0.029
3359224	ASCL2	0.029
3922602	UBASH3A	0.029
2604223	DNAJB3	0.029
3265918	PNLIPRP1	0.029
3757020	KRT35	0.029
2771839	TMPRSS11D	0.029
3094778	TACC1	0.029
3026988	LUC7L2	0.029
3848907	KANK3	0.029
3408831	SSPN	0.029
2516332	SCRN3	0.029
3954596	RTDR1	0.029
2400373	EIF4G3	0.030
3790259	MALT1	0.030
3448744	PTHLH	0.030
3824713	ARRDC2	0.030
3330864	OR5AS1	0.030
2462511	HEATR1	0.030
2532699	INPP5D	0.030

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3442579	RBP5	0.030	3949097	TRMU	0.032	2888341	RNF44	0.033	3826504	ZNF431	0.033
3843452	ZSCAN4	0.030	2434233	OTUD7B	0.032	2437205	GBAP1	0.033	3727449	TOM1L1	0.033
3449910	AMN1	0.030	2617276	CTDSPL	0.032	3695541	FHOD1	0.033	3906390	PTPRT	0.033
2874371	FBN2	0.030	2432851	NBPF11	0.032	3446845	GYS2	0.033	2448382	PTGS2	0.033
3366519	FANCF	0.030	2953852	MED20	0.032	3421824	C12orf28	0.033	3701000	MAF	0.034
2375596	ADORA1	0.030	3821410	ZNF440	0.032	2475911	EHD3	0.033	2566504	C2orf55	0.034
3942940	FLJ20464	0.030	2431031	HMGCS2	0.032	2857204	PPAP2A	0.033	3873086	DEFB129	0.034
2673594	CELSR3	0.030	2565410	KIAA1310	0.032	3352847	TECTA	0.033	3430086	TCP11L2	0.034
2443575	KIFAP3	0.030	3822976	CASP14	0.032	3882949	DYNLRB1	0.033	2906990	BYSL	0.034
3770345	CD300E	0.030	3935374	C21orf58	0.032	3110171	ATP6V1C1	0.033	2332711	PPIH	0.034
2892277	NQO2	0.030	3444820	LRP6	0.032	2910680	LRRC1	0.033	3063273	PTCD1	0.034
4019412	CXorf56	0.030	2448710	FAM5C	0.032	3105506	CA13	0.033	3455890	KRT79	0.034
3067890	IMMP2L	0.030	2699145	SLC9A9	0.032	3607332	ACAN	0.033	3679643	---	0.034
3734399	C17orf77	0.030	2623859	NISCH	0.032	3845944	GNG7	0.033	2491745	GNLY	0.034
2602403	SLC19A3	0.030	2697372	TXNDC6	0.032	3869062	SIGLEC8	0.033	3717635	ZNF207	0.034
3230610	ABCA2	0.030	2460817	SIPA1L2	0.032	2731782	C4orf26	0.033	3935192	FTCD	0.034
2808438	NNT	0.030	2807195	EGFLAM	0.032	3111375	TTC35	0.033	2783207	PRSS12	0.034
2672333	PRSS45	0.030	3184408	PALM2	0.032	2731542	AREG	0.033	4007009	NDUFB11	0.034
3108859	OSR2	0.030	3870449	VSTM1	0.032	2875491	SHROOM1	0.033	3843058	ZNF264	0.034
2524016	PARD3B	0.030	2586603	TLK1	0.032	3053312	---	0.033	3868816	KLK9	0.034
2403446	PTAFR	0.030	3219547	IKBKAP	0.032	2503257	INHBB	0.033	3303392	BLOC1S2	0.034
3190514	GLE1	0.030	3643196	WDR90	0.032	3644664	DNASE1L2	0.033	2407224	RSPO1	0.034
3354380	HEPN1	0.030	2674168	C3orf62	0.032	3023211	ATP6V1F	0.033	3860793	ZNF585B	0.034
3300597	MYOF	0.030	4007550	PCSK1N	0.032	2504595	PROC	0.033	3564620	NID2	0.034
3579114	BCL11B	0.030	2724671	RHOH	0.032	2329386	HMGB4	0.033	2452859	LGTN	0.034
3660858	CHD9	0.031	3248470	C10orf107	0.032	2404254	PUM1	0.033	3934263	---	0.034
3391653	DRD2	0.031	3677516	MEFV	0.032	3332465	MS4A8B	0.033	3579969	DIO3-OS	0.034
3331822	GLYATL1	0.031	2443370	F5	0.032	3378228	B3GNT1	0.033	3354293	ROBO3	0.034
3713951	SLC47A1	0.031	3977347	CCNB3	0.032	3233605	PFKFB3	0.033	3091403	EPHX2	0.034
2816506	S100Z	0.031	2662956	VGLL4	0.032	3657219	SLC5A2	0.033	2952198	TMEM217	0.034
2871241	MCC	0.031	3960440	HS5O6A	0.032	3416740	OR6C74	0.033	3899346	SNX5	0.034
2756404	ZNF721	0.031	3699178	WDR59	0.033	3956670	C22orf31	0.033	2673902	QRICH1	0.034
2723752	TBC1D1	0.031	3709244	CHD3	0.033	2749484	RXFP1	0.033	3515109	PCDH8	0.034

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

2772160	---	0.034	2443235	NME7	0.036	2375795	LAX1	0.036	3638699	C15orf38	0.037
3352438	POU2F3	0.035	3314720	C10orf93	0.036	3642993	C16orf11	0.036	3454157	FAIM2	0.037
3194567	FAM69B	0.035	3551566	EVL	0.036	3512719	SIAH3	0.036	3026495	AKR1D1	0.037
2985342	C6orf54	0.035	3873744	TGM3	0.036	3391724	TMPRSS5	0.036	3506936	MTIF3	0.037
3554315	INF2	0.035	3900833	FOXA2	0.036	3715460	PYY2	0.036	2708203	MAP6D1	0.037
3461105	IFNG	0.035	3886810	RBPJL	0.036	3223687	PHF19	0.036	2383639	PRSS38	0.037
2502686	MARCO	0.035	3017080	ARMC10	0.036	3592420	C15orf21	0.036	3263624	MXI1	0.037
3737697	BAIAP2	0.035	4054639	NOC2L	0.036	3635198	BCL2A1	0.037	3830825	C19orf55	0.037
3527722	RNASE2	0.035	3079336	FASTK	0.036	3914021	GMEB2	0.037	3515088	LECT1	0.037
3400730	CACNA1C	0.035	3807474	C18orf32	0.036	3874198	OXT	0.037	2685304	PROS1	0.037
3348990	TEX12	0.035	2754937	TLR3	0.036	3864107	PSG7	0.037	3656318	PRR14	0.037
2383524	ZNF678	0.035	2902884	SKIV2L	0.036	3953879	MGC16703	0.037	3436987	---	0.038
2547114	XDH	0.035	2932593	CLDN20	0.036	3994158	FMR1NB	0.037	3220740	C9orf84	0.038
4054690	HES4	0.035	2536965	FLJ38379	0.036	2934801	MAP3K4	0.037	2326774	SFN	0.038
2843855	ZFP2	0.035	2515471	DLX1	0.036	3268548	PSTK	0.037	3936009	IL17RA	0.038
2805939	RXFP3	0.035	2322848	PADI4	0.036	2755111	KLKB1	0.037	2875685	FSTL4	0.038
3729910	TBX4	0.035	2422967	GFI1	0.036	2503109	EPB41L5	0.037	2427688	C1orf103	0.038
3461883	PTPRR	0.035	3838004	PPP1R15A	0.036	4015693	TIMM8A	0.037	2638017	C3orf1	0.038
3441190	FGF6	0.035	3462567	KCNC2	0.036	2656598	AHSG	0.037	3330769	OR5D13	0.038
2577958	DARS	0.035	3882265	C20orf186	0.036	2905664	ZFAND3	0.037	3839718	CD33	0.038
2752006	SAP30	0.035	4026624	PNCK	0.036	2600881	PAX3	0.037	2343418	PTGFR	0.038
3660213	CYLD	0.035	3773742	SLC38A10	0.036	2577028	NCKAP5	0.037	2373511	CFHR5	0.038
3907514	NEURL2	0.035	2906824	FOXP4	0.036	2941546	C6orf218	0.037	3371003	TP53I11	0.038
3877892	PCSK2	0.035	3939875	SUSD2	0.036	3351931	HINFP	0.037	3292779	SLC25A16	0.038
3033127	HTR5A	0.035	3377569	SLC25A45	0.036	3540839	---	0.037	3779612	SLMO1	0.038
3945314	KDELR3	0.035	3048212	MRPS24	0.036	3070658	NDUFA5	0.037	3662150	MT1M	0.038
2322598	CROCC	0.035	2899756	H2AFP	0.036	3806711	IER3IP1	0.037	3376155	NXF1	0.038
3581221	AHNAK2	0.035	3807261	SMAD7	0.036	3837934	FUT2	0.037	3971451	PHEX	0.038
3471769	TMEM116	0.035	3727583	HLF	0.036	3549605	PPP4R4	0.037	3332663	CD6	0.038
3376193	STX5	0.035	2443952	MYOC	0.036	3221571	RNF183	0.037	3450775	KIF21A	0.038
3121751	CSMD1	0.035	2336809	DMRTB1	0.036	3934642	KAP12-1	0.037	3674659	GAS8	0.038
3863723	CEACAM8	0.036	3360277	OR52R1	0.036	3186191	ATP6V1G1	0.037	2982524	SLC22A2	0.038
3995035	PASD1	0.036	3821937	MAST1	0.036	2395418	---	0.037	3456840	PPP1R1A	0.038

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

2440413	ITLN1	0.038
3335697	CTSW	0.038
3810413	RAX	0.038
4002394	SMPX	0.038
2889753	ZNF354A	0.038
3041294	FAM126A	0.038
2911303	ZNF451	0.039
3846214	DOHH	0.039
3749432	RNFT1	0.039
3507134	CDX2	0.039
3349719	ZBTB16	0.039
2624639	CACNA2D3	0.039
2551284	UNQ6975	0.039
3425108	C12orf29	0.039
2521556	MARS2	0.039
3288707	ERCC6	0.039
2561182	REG1B	0.039
3377826	RNASEH2C	0.039
3650861	SYT17	0.039
3551485	EML1	0.039
3190151	SLC25A25	0.039
3362159	NRIP3	0.039
3836057	LRRC68	0.039
2394699	TNFRSF25	0.039
3589570	EIF2AK4	0.039
2514745	MYO3B	0.039
3708938	ATP1B2	0.039
3970476	SCML1	0.039
3680130	DEXI	0.039
2548699	CYP1B1	0.039
3749767	TMEM11	0.039
2671936	SLC6A20	0.040
3455692	KRT2	0.040
2528645	ACCN4	0.040
3603295	CRABP1	0.040
3602634	ISL2	0.040
2577644	YSK4	0.040
3537030	RPL13AP3	0.040
3807809	CXXC1	0.040
2334319	TOE1	0.040
3044938	RP9P	0.040
3675205	C16orf13	0.040
2410574	LRRC41	0.040
2916307	C6orf165	0.040
3321592	CALCB	0.040
2638869	CSTA	0.040
2416218	ITGB3BP	0.040
3837707	ZNF114	0.040
3533435	PNN	0.040
3145509	GDF6	0.040
2379314	VASH2	0.040
3097580	C8orf22	0.040
3371660	HARBI1	0.041
2453370	PLXNA2	0.041
3191113	PRRX2	0.041
3352130	RNF26	0.041
3644887	TBC1D24	0.041
2358646	BNIPL	0.041
3551935	WDR25	0.041
3865635	DMPK	0.041
2491572	SH2D6	0.041
3845439	ATP8B3	0.041
3490433	CCDC70	0.041
3445741	MGP	0.041
2773997	NUP54	0.041
2330687	ZC3H12A	0.041
3471753	C12orf47	0.041
3752424	C17orf79	0.041
3351975	ABCG4	0.041
3004768	ZNF273	0.041
3333572	C11orf83	0.041
3373392	OR8H1	0.041
3502475	PROZ	0.041
3712922	C17orf39	0.041
2766492	C4orf34	0.041
3461795	PTPRB	0.041
3549517	OTUB2	0.041
3765642	INTS2	0.041
2500875	CHCHD5	0.041
3357346	GLB1L3	0.042
3969802	BMX	0.042
2926447	TCF21	0.042
3315584	NLRP6	0.042
2501204	IL1RN	0.042
2326237	EXTL1	0.042
3379269	UNC93B1	0.042
3638068	DET1	0.042
3673661	FAM38A	0.042
3450180	YARS2	0.042
2437645	GON4L	0.042
2359646	LOR	0.042
3039177	ETV1	0.042
3164181	RRAGA	0.042
2493813	ZNF2	0.042
3159330	DOCK8	0.042
2360677	EFNA1	0.042
3980614	GDPD2	0.042
3829471	KCTD15	0.042
2918388	POU3F2	0.043
3611684	LRRK1	0.043
2852712	SLC45A2	0.043
2831897	TMCO6	0.043
3661645	IRX6	0.043
2649182	LEKR1	0.043
3398145	PRDM10	0.043
3736204	C17orf99	0.043
3815936	REEP6	0.043
3664924	CA7	0.043
3543355	DCAF4	0.043
3559936	C14orf128	0.043
3318329	OR51M1	0.043
3210497	PRUNE2	0.043
2790999	ACCN5	0.043
3074362	CNOT4	0.043
3341539	KCTD21	0.043
2315739	PUSL1	0.043
2617659	SLC22A14	0.043
2877257	BRD8	0.043
3159483	KANK1	0.043
3654699	NUPR1	0.043
3059258	PCLO	0.043
2829864	SLC25A48	0.043
3250602	H2AFY2	0.043
3165780	IFT74	0.043
2453065	C1orf116	0.043
3318329	OR51M1	0.043
3210497	PRUNE2	0.043
2790999	ACCN5	0.043
3074362	CNOT4	0.043
3341539	KCTD21	0.043
2315739	PUSL1	0.043
2617659	SLC22A14	0.043

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

2877257	BRD8	0.043
3159483	KANK1	0.043
3654699	NUPR1	0.043
3059258	PCLO	0.043
2829864	SLC25A48	0.043
3250602	H2AFY2	0.043
3165780	IFT74	0.043
2453065	C1orf116	0.043
3283613	ZNF438	0.044
3917555	KAP13-4	0.044
3816686	ZNF556	0.044
2988536	WIPI2	0.044
3186324	DEC1	0.044
3451708	TWF1	0.044
2986906	GET4	0.044
3630378	---	0.044
2521997	C2orf69	0.044
3355860	KCNJ5	0.044
3358425	LRDD	0.044
2326327	CNKSR1	0.044
3559570	HECTD1	0.044
2436526	TPM3	0.044
3540398	FNTB	0.044
3734903	LLGL2	0.044
3577545	IFI27L2	0.044
3642390	TARSL2	0.044
3679564	USP7	0.044
3830925	KIRREL2	0.044
2676471	TMEM110	0.044
2817291	JMY	0.044
2825514	DMXL1	0.044
4015884	ARMCX2	0.044
2791197	PDGFC	0.044
3630378	---	0.044
2521997	C2orf69	0.044
3355860	KCNJ5	0.044
3358425	LRDD	0.044
2326327	CNKSR1	0.044
3559570	HECTD1	0.044
2436526	TPM3	0.044
3540398	FNTB	0.044
3734903	LLGL2	0.044
3577545	IFI27L2	0.044
3642390	TARSL2	0.044
3308560	VAX1	0.044
3740704	SMYD4	0.044
3911485	APCDD1L	0.044
3302693	LOXL4	0.044
2827772	ADAMTS19	0.044
3679564	USP7	0.044
3830925	KIRREL2	0.044
2676471	TMEM110	0.044
2817291	JMY	0.044
2825514	DMXL1	0.044
4015884	ARMCX2	0.044
2791197	PDGFC	0.044
3816686	ZNF556	0.044
2988536	WIPI2	0.044
3186324	DEC1	0.044
3451708	TWF1	0.044
2986906	GET4	0.044
3308560	VAX1	0.044
3740704	SMYD4	0.044
3911485	APCDD1L	0.044
3302693	LOXL4	0.044
2827772	ADAMTS19	0.044
3283613	ZNF438	0.044
3917555	KAP13-4	0.044
2954324	MEA1	0.045
2906934	PRICKLE4	0.045
3042994	HOXA13	0.045
2607055	PASK	0.045
3830649	COX6B1	0.045
3606034	PDE8A	0.045
3996467	PLXNA3	0.045
3834046	AXL	0.045
3490892	OLFM4	0.045
3750685	SLC46A1	0.045
2883541	SOX30	0.045
2620985	TMIE	0.045
3664664	CDH5	0.045
3932917	PLAC4	0.045
3339423	INPPL1	0.045
3214451	NFIL3	0.045
3373411	OR5R1	0.045
3834046	AXL	0.045
3490892	OLFM4	0.045
3750685	SLC46A1	0.045
2883541	SOX30	0.045
2620985	TMIE	0.045
3664664	CDH5	0.045
3932917	PLAC4	0.045
3339423	INPPL1	0.045
3214451	NFIL3	0.045
3373411	OR5R1	0.045
2954324	MEA1	0.045
2906934	PRICKLE4	0.045
3042994	HOXA13	0.045
2607055	PASK	0.045
3830649	COX6B1	0.045
3606034	PDE8A	0.045
3996467	PLXNA3	0.045
3256669	CFLP1	0.045
3330943	OR8K1	0.045
3938792	VPREB1	0.046
3759587	PLCD3	0.046
3095114	ADAM5P	0.046
2958325	DST	0.046
2966496	MCHR2	0.046
2401581	GALE	0.046
3260265	CNNM1	0.046
2695453	CPNE4	0.046
3250806	ADAMTS14	0.046
3413852	PRPH	0.046
2834579	SPINK6	0.046
3751625	SSH2	0.046
3128372	KCTD9	0.046
2603844	ECEL1	0.046
2317686	AJAP1	0.046
3403841	RIMKLB	0.046
3737677	---	0.046
3318639	CCKBR	0.046
2656627	FETUB	0.046
4046481	ING5	0.046
2611504	HDAC11	0.046
3871142	C19orf51	0.046
2435323	THEM5	0.046
3064024	C7orf61	0.046
3852735	PTGER1	0.047
3658925	ORC6	0.047
3042063	NPVF	0.047
2642441	NEK11	0.047

Table B12: Non*C9ORF72*-Related_SALSvCtrl Alternatively Spliced List (n=3,163) [Partek® p-value (alt. splicing) <0.05]

3437780	FZD10	0.047	3065684	SLC26A5	0.047	2385146	TRIM67	0.048	3067592	PNPLA8	0.049
3815610	ATP5D	0.047	2351465	PROK1	0.047	3194613	TMEM141	0.048	2545007	KIF3C	0.049
3174816	ANXA1	0.047	2675315	CACNA2D2	0.048	3449008	OVCH1	0.048	3133233	PLAT	0.049
3902081	ZNF337	0.047	2661992	OXTR	0.048	3552083	DLK1	0.048	4054481	GABRD	0.049
3379091	ALDH3B2	0.047	3566176	OTX2	0.048	3148463	ANGPT1	0.048	3945781	SYNGR1	0.049
3552847	DYNC1H1	0.047	3945006	H1F0	0.048	3857171	ZNF675	0.048	2467855	SOX11	0.049
3614012	---	0.047	3262535	GSTO2	0.048	3105467	E2F5	0.048	3393704	MPZL3	0.049
3581090	TMEM179	0.047	3688362	COX6A2	0.048	3849117	ADAMTS10	0.048	2599798	IHH	0.049
3959953	TMPRSS6	0.047	2426840	WDR47	0.048	2615360	TGFBR2	0.048	3691193	SNX20	0.049
2317434	TPRG1L	0.047	3382216	ARRB1	0.048	2353749	CD101	0.048	3120653	GPT	0.049
3854836	KIAA1683	0.047	3977646	GSPT2	0.048	2448073	IVNS1ABP	0.049	2730281	ODAM	0.049
2652217	---	0.047	2702724	LXN	0.048	2460551	EGLN1	0.049	3416483	HNRNPA1	0.049
2562729	REEP1	0.047	2919399	LIN28B	0.048	2518743	NUP35	0.049	3576411	GPR68	0.049
3576284	RPS6KA5	0.047	2715580	SH3BP2	0.048	3625391	DYX1C1	0.049			

Table B13: C9-LongvShort Gene List (n=628) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value
3718555	SLFN5	⇧	2.49	5.10E-03	2423175	FAM69A	⇩	1.65	0.034	2734047	AGPAT9	⇩	1.48	0.045
2548699	CYP1B1	⇩	2.30	0.042	3507282	FLT1	⇧	1.65	0.026	2459173	PRO2012	⇧	1.48	0.029
2940202	F13A1	⇧	2.21	0.020	3945314	KDELR3	⇩	1.65	0.011	3838094	FTL	⇩	1.47	0.048
2940145	NRN1	⇧	2.17	0.022	2378068	G0S2	⇩	1.63	0.019	2522094	SPATS2L	⇧	1.47	0.028
3174510	GDA	⇧	2.13	1.87E-03	3494137	LMO7	⇧	1.62	1.09E-03	3018866	DNAJB9	⇩	1.47	0.033
2678298	DNASE1L3	⇩	2.08	9.05E-03	3496409	GPC5	⇧	1.61	0.011	3309602	RGS10	⇧	1.47	0.018
2738378	NPNT	⇩	1.97	0.045	3065244	RASA4	⇩	1.60	0.010	2582124	NR4A2	⇩	1.47	1.25E-03
3445908	EPS8	⇧	1.95	0.015	3020496	ST7	⇩	1.60	7.63E-04	3663074	MMP15	⇧	1.46	9.89E-03
3409605	FAR2	⇧	1.93	5.93E-03	3403841	RIMKLB	⇧	1.60	0.041	3925639	NRIP1	⇧	1.46	0.031
3560403	EGLN3	⇧	1.91	1.52E-03	3273667	ADARB2	⇧	1.59	4.10E-03	2375212	PPP1R12B	⇩	1.46	1.86E-03
2902707	HSPA1A	⇩	1.91	2.29E-04	3969946	ZRSR2	⇧	1.59	1.56E-03	3316344	CD151	⇩	1.46	0.010
3141755	HEY1	⇧	1.89	0.013	2902725	HSPA1B	⇩	1.58	2.16E-03	3958658	LARGE	⇩	1.46	0.015
2523801	CD28	⇧	1.88	0.021	3450899	SLC2A13	⇧	1.58	1.60E-03	3215146	NINJ1	⇩	1.46	0.038
3972929	GK	⇧	1.84	3.19E-04	3856646	ZNF208	⇧	1.58	0.024	3202316	MOBKL2B	⇧	1.46	0.012
2665199	SATB1	⇧	1.81	0.049	2761837	FGFBP2	⇩	1.56	9.43E-03	2877939	DNAJC18	⇩	1.46	9.36E-03
2399743	AKR7A3	⇩	1.79	4.55E-03	2474240	KHK	⇩	1.55	0.033	2950145	HLA-DOB	⇩	1.46	0.027
3566383	C14orf105	⇧	1.78	0.049	3540552	FUT8	⇩	1.54	0.027	2471978	RHOB	⇧	1.45	0.022
3382216	ARRB1	⇧	1.77	0.040	3705151	DBNDD1	⇧	1.54	0.024	2363248	LY9	⇩	1.45	0.031
3214451	NFIL3	⇧	1.76	2.01E-03	3447863	KRAS	⇧	1.54	3.00E-05	2902574	LY6G5B	⇩	1.45	3.43E-03
3449068	TMTC1	⇧	1.75	0.018	3263944	PDCD4	⇧	1.53	6.53E-04	2469910	LPIN1	⇩	1.45	2.99E-03
2816459	F2R	⇩	1.72	0.019	3623031	FBN1	⇧	1.53	0.023	3434490	CABP1	⇧	1.45	1.50E-03
2452691	SLC41A1	⇩	1.70	1.34E-03	3141589	IL7	⇧	1.52	0.016	3507798	UBL3	⇧	1.45	1.47E-03
2781138	LEF1	⇧	1.69	0.020	3703885	SLC7A5	⇩	1.52	7.95E-03	3945545	APOBEC3B	⇩	1.45	0.023
2664209	SH3BP5	⇩	1.68	7.17E-03	3944129	HMOX1	⇩	1.51	0.017	3824993	GDF15	⇩	1.45	0.042
2973376	PTPRK	⇧	1.68	0.040	3841621	LILRB4	⇩	1.51	0.034	3216276	SLC35D2	⇧	1.45	8.79E-03
2400518	ECE1	⇩	1.67	0.015	2768981	SGCB	⇩	1.51	0.049	2820865	ARSK	⇩	1.45	0.021
2362333	MNDA	⇩	1.67	0.022	3892812	SLCO4A1	⇩	1.50	9.17E-04	2324634	CDC42	⇩	1.44	6.43E-03
3369249	APIP	⇧	1.66	0.025	3385175	PICALM	⇧	1.50	0.018	3208355	CBWD3	⇧	1.44	0.032
2626097	ABHD6	⇩	1.65	2.18E-03	2845274	CCDC127	⇩	1.49	1.92E-03	3257204	IFIT3	⇧	1.44	0.023
3896078	SLC23A2	⇩	1.65	0.016	3887210	MMP9	⇧	1.49	0.026	3936442	PEX26	⇧	1.44	7.27E-04
3797295	L3MBTL4	⇧	1.65	2.51E-03	2957227	TRAM2	⇩	1.48	0.030	4005859	CASK	⇧	1.44	0.014

Table B13: C9-LongvShort Gene List (n=628) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3876645	BTBD3	⇧	1.44	0.022
3851072	ACP5	⇩	1.44	0.015
4035833	CD24	⇧	1.43	0.038
3409211	PPFIBP1	⇧	1.43	0.015
3727712	PCTP	⇧	1.43	0.010
2775909	PLAC8	⇧	1.43	7.86E-03
3055608	TYW1B	⇩	1.43	0.015
2990342	TMEM106B	⇩	1.43	0.029
3103523	LY96	⇩	1.43	0.011
3101153	BHLHE22	⇧	1.43	0.039
2638988	PARP15	⇩	1.43	0.047
2970897	FRK	⇧	1.42	3.99E-03
2437247	GBA	⇩	1.42	0.046
2361342	SEMA4A	⇩	1.42	3.30E-03
2327677	EPB41	⇩	1.42	6.09E-03
3893849	PRPF6	⇧	1.42	4.30E-03
3466284	NDUFA12	⇧	1.41	1.48E-04
3900091	RALGAPA2	⇧	1.41	0.015
3916527	JAM2	⇩	1.41	0.011
2420467	CTBS	⇩	1.41	0.016
3624145	DMXL2	⇧	1.41	1.27E-03
3166844	CHMP5	⇧	1.41	0.036
2626167	PXK	⇩	1.41	8.78E-03
2454661	TMEM206	⇩	1.41	8.47E-03
3081525	C7orf13	⇩	1.41	0.030
3005684	KCTD7	⇩	1.41	7.87E-04
3023883	CPA4	⇩	1.41	0.033
3845352	UQCR11	⇧	1.41	4.96E-03
3175119	OSTF1	⇧	1.40	8.46E-03
3538213	DAAM1	⇧	1.40	0.041
2766492	C4orf34	⇧	1.40	0.041
2604254	HJURP	⇩	1.40	2.28E-03
2604390	ARL4C	⇩	1.40	0.011
3761632	SNF8	⇧	1.40	2.35E-03
3969422	RAB9A	⇧	1.40	4.33E-03
3409127	ARNTL2	⇧	1.40	2.19E-03
3447694	BCAT1	⇧	1.40	0.032
2948169	HCG8	⇩	1.40	7.97E-03
2932508	TIAM2	⇩	1.39	0.024
3464967	GALNT4	⇧	1.39	3.48E-05
3167383	NUDT2	⇧	1.39	9.11E-03
2320727	TNFRSF1B	⇩	1.39	4.13E-03
2877893	MGC29506	⇩	1.39	0.044
2764192	SEL1L3	⇩	1.39	0.042
3450655	CPNE8	⇧	1.39	0.010
3149528	TRPS1	⇧	1.39	0.031
2351004	GSTM5	⇩	1.39	9.83E-03
2888879	DOK3	⇩	1.38	1.57E-04
3812385	CD226	⇩	1.38	7.26E-03
3375091	SLC15A3	⇩	1.37	0.026
3382061	XRRA1	⇧	1.37	0.047
2902178	TCF19	⇩	1.37	7.96E-03
2866590	LYSMD3	⇩	1.37	0.012
3132940	ANK1	⇧	1.37	0.049
2425118	SASS6	⇩	1.37	9.10E-04
2371346	RGL1	⇩	1.37	0.035
2452977	FAIM3	⇩	1.37	0.012
3089360	SLC39A14	⇩	1.37	0.044
2603320	GPR55	⇩	1.37	0.048
3242425	CCNY	⇧	1.37	2.03E-03
2892277	NQO2	⇩	1.37	1.93E-03
3994451	CXorf40A	⇧	1.37	3.29E-03
3344861	C11orf54	⇧	1.37	3.95E-03
3460584	LLPH	⇧	1.37	6.02E-03
2500919	SLC20A1	⇩	1.37	0.028
3434393	DYNLL1	⇧	1.36	9.68E-03
3204243	SIGMAR1	⇩	1.36	0.044
3981735	NCRNA00183	⇧	1.36	0.012
3397589	ETS1	⇧	1.36	1.50E-03
3594031	TMOD2	⇧	1.36	0.018
3293537	PCBD1	⇧	1.36	0.016
3517793	KLF12	⇧	1.36	3.20E-03
2330773	CDCA8	⇩	1.36	0.015
2841699	CPEB4	⇩	1.36	5.10E-03
3791482	PHLPP1	⇧	1.36	0.041
2714376	TMEM175	⇩	1.36	0.022
2997376	ANLN	⇩	1.36	8.35E-03
3645836	ZNF75A	⇧	1.36	9.21E-03
3577246	MOAP1	⇧	1.36	0.011
2360633	EFNA4	⇩	1.36	0.025
2780172	CENPE	⇩	1.35	0.014
2621583	ZNF589	⇩	1.35	0.011
3927081	NCRNA00158	⇧	1.35	0.017
2331679	MFSD2A	⇩	1.35	3.48E-03
3390641	ARHGAP20	⇧	1.35	3.77E-03
3004768	ZNF273	⇩	1.35	0.025
2601414	SERPINE2	⇩	1.35	0.012
2360989	MSTO1	⇩	1.35	3.63E-03
3540353	CHURC1	⇧	1.35	9.26E-03
2492496	NCRNA00152	⇩	1.35	0.020
2830638	KIF20A	⇩	1.35	0.010
2446198	TOR1AIP2	⇩	1.35	1.58E-04
3824666	KCNN1	⇧	1.35	0.012
2914777	TTK	⇩	1.34	5.24E-03
2957462	GSTA4	⇩	1.34	7.95E-03
3177111	NTRK2	⇧	1.34	6.03E-03

Table B13: C9-LongvShort Gene List (n=628) ALL SAMPLES COMBINED [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

2829562	TXNDC15	⇩	1.34	6.58E-03
3824212	DDA1	⇧	1.34	0.021
3518169	COMMD6	⇧	1.34	4.11E-03
2413423	TMEM48	⇩	1.34	0.030
2841491	C5orf41	⇩	1.34	0.043
2571457	CKAP2L	⇩	1.34	1.30E-03
2442698	CREG1	⇩	1.34	0.026
3441941	VAMP1	⇩	1.33	0.027
2838656	HMMR	⇩	1.33	0.039
3332615	TMEM109	⇩	1.33	0.044
2336302	ZFYVE9	⇧	1.33	8.56E-04
3462843	NAP1L1	⇧	1.33	0.031
2638789	CD86	⇩	1.33	0.048
3139580	SLCO5A1	⇧	1.33	0.027
3712041	UBB	⇧	1.33	0.011
2925724	AKAP7	⇧	1.33	5.53E-03
3476330	CCDC92	⇧	1.33	0.029
3413950	SPATS2	⇧	1.33	9.23E-04
2612401	BTD	⇩	1.33	0.019
2956438	MUT	⇩	1.33	6.14E-03
2334098	KIF2C	⇩	1.32	9.72E-03
3513995	DLEU2	⇧	1.32	0.031
3016636	SH2B2	⇩	1.32	0.024
3869954	ZNF321	⇧	1.32	0.017
2835792	GM2A	⇩	1.32	8.90E-03
3774096	PDE6G	⇧	1.32	7.04E-03
3936550	USP18	⇧	1.32	0.028
2495446	INPP4A	⇩	1.32	0.017
3147020	ZNF706	⇧	1.32	0.027
3142932	C8orf59	⇧	1.32	2.16E-03
3417457	MYL6	⇧	1.32	0.016
4005627	CXorf38	⇧	1.32	0.030
3860101	NFKBID	⇩	1.32	0.021
3403077	C12orf57	⇧	1.32	3.61E-03
3706659	ASPA	⇧	1.32	0.013
2436826	KCNN3	⇩	1.31	0.011
3827218	RPSAP58	⇧	1.31	0.031
3706651	OR3A3	⇩	1.31	9.19E-03
3111695	EBAG9	⇩	1.31	2.33E-03
3978169	TSPYL2	⇩	1.31	8.45E-03
2639225	PDIA5	⇩	1.31	0.032
2820893	RFESD	⇩	1.31	0.016
2411799	BEND5	⇧	1.31	2.84E-03
3892452	LSM14B	⇧	1.31	0.046
3820370	P2RY11	⇩	1.31	0.047
3332886	TMEM138	⇩	1.31	0.026
3451264	YAF2	⇧	1.31	5.03E-03
2317317	TP73	⇩	1.31	0.033
2411228	STIL	⇩	1.31	0.020
2899413	BTN3A3	⇩	1.31	5.82E-03
2515050	GORASP2	⇩	1.31	0.014
3072435	TMEM209	⇩	1.31	0.026
3427014	SNRPF	⇧	1.31	0.043
3435980	TCTN2	⇩	1.30	0.046
2950277	HLA-DMA	⇩	1.30	0.047
2749560	ETFDH	⇩	1.30	0.020
3584728	SNRPN	⇧	1.30	0.017
3254488	C10orf58	⇩	1.30	0.045
3272205	INPP5A	⇧	1.30	0.020
2949801	AGPAT1	⇩	1.30	3.58E-03
3726406	ACSF2	⇩	1.30	0.022
4002148	EIF1AX	⇧	1.30	0.015
3870135	ZNF347	⇧	1.30	0.023
3825013	SSBP4	⇧	1.30	0.035
3882949	DYNLRB1	⇧	1.30	3.62E-03
3666649	VPS4A	⇧	1.30	3.22E-03
2676182	NT5DC2	⇩	1.30	0.018
3494102	UCHL3	⇧	1.30	6.78E-03
3485292	NBEA	⇧	1.29	0.031
2946845	ZNF204P	⇩	1.29	3.94E-03
3426257	SOCS2	⇧	1.29	0.010
2444842	KIAA0040	⇩	1.29	0.039
2402431	PAQR7	⇩	1.29	0.032
3726498	MYCBPAP	⇩	1.29	0.024
3066818	NAMPT	⇩	1.29	0.025
2579572	ZEB2	⇧	1.29	0.032
3894098	C20orf96	⇩	1.29	5.77E-04
3353914	VWA5A	⇩	1.29	0.011
3611049	LRRC28	⇧	1.29	4.86E-03
3067592	PNPLA8	⇩	1.29	0.036
2681157	TMF1	⇩	1.29	1.30E-03
2494484	NCAPH	⇩	1.29	0.019
2757319	SLBP	⇩	1.29	0.028
2437401	FDPS	⇩	1.29	2.74E-03
4003895	CXorf21	⇧	1.29	0.042
3487432	DNAJC15	⇩	1.29	0.036
3382698	GUCY2E	⇩	1.29	0.014
3807595	MYO5B	⇧	1.29	0.014
2375664	BTG2	⇩	1.29	0.029
3753538	SLFN12	⇧	1.29	0.013
3705412	C17orf97	⇧	1.29	1.09E-03
3846742	SH3GL1	⇧	1.29	0.011
2955061	SLC35B2	⇩	1.29	0.041
2610241	FANCD2	⇩	1.29	0.015
2690850	TMEM39A	⇩	1.29	0.036
2902207	HCG27	⇩	1.29	0.018

Table B13: C9-LongvShort Gene List (n=628) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3005956	C7orf42	⇩	1.28	2.20E-03
2784113	CCNA2	⇩	1.28	0.013
3670700	BCMO1	⇧	1.28	0.031
2949471	NEU1	⇩	1.28	9.42E-03
3058156	TMEM60	⇩	1.28	0.015
3512050	CCDC122	⇧	1.28	0.010
2940551	SSR1	⇩	1.28	0.031
3244539	ZNF22	⇧	1.28	0.032
2379863	CENPF	⇩	1.28	0.036
3998632	PNPLA4	⇧	1.28	1.55E-04
2435251	LINGO4	⇧	1.28	0.040
2428796	PTPN22	⇩	1.28	1.51E-03
2364438	NUF2	⇩	1.28	0.011
3609592	MCTP2	⇧	1.28	0.016
3486728	SLC25A15	⇧	1.28	9.00E-03
2475407	CLIP4	⇩	1.28	0.011
3101385	MTFR1	⇩	1.28	0.025
3168700	ZCCHC7	⇧	1.28	5.84E-03
2716655	MSX1	⇧	1.28	0.022
3126504	CSGALNACT1	⇧	1.28	0.038
3373487	OR5M1	⇧	1.28	3.63E-03
2608419	SETMAR	⇩	1.28	0.013
3656760	STX4	⇧	1.28	3.83E-03
2499158	RANBP2	⇩	1.27	4.30E-03
3740432	SCARF1	⇧	1.27	0.026
2862380	ANKRA2	⇩	1.27	0.014
3421762	RAB3IP	⇧	1.27	3.33E-03
3454680	TFCP2	⇧	1.27	1.24E-03
4027532	GAB3	⇧	1.27	0.011
3421706	RAB3IP	⇧	1.27	3.39E-03
2722377	STIM2	⇩	1.27	0.028
3406493	DERA	⇧	1.27	0.027
2690900	CD80	⇩	1.27	0.020
2367843	DARS2	⇩	1.27	0.014
2487549	MXD1	⇩	1.27	0.035
3571542	PNMA1	⇧	1.27	6.05E-04
3283920	ARHGAP12	⇧	1.27	2.94E-03
3088213	SH2D4A	⇧	1.27	0.022
2599433	USP37	⇩	1.27	4.63E-03
3624273	LYSMD2	⇧	1.27	0.017
3120358	HSF1	⇩	1.27	0.040
2611848	SLC6A6	⇩	1.27	0.026
2773348	PF4	⇧	1.27	0.034
3210179	C9orf95	⇧	1.27	0.013
3406421	STRAP	⇧	1.27	5.70E-03
2673547	SLC26A6	⇩	1.27	5.17E-03
4000132	TRAPPC2	⇧	1.27	0.011
2570616	BUB1	⇩	1.27	0.018
2366184	TBX19	⇩	1.27	4.17E-03
3830216	FXYD5	⇩	1.27	0.048
3383227	GAB2	⇩	1.27	0.041
3191338	GPR107	⇩	1.27	0.013
3869714	ZNF611	⇧	1.27	8.48E-03
3289235	SGMS1	⇧	1.27	0.024
2384562	RAB4A	⇧	1.27	0.024
3945376	TOMM22	⇧	1.27	0.013
2908179	VEGFA	⇩	1.27	0.047
2708407	ALG3	⇩	1.27	0.015
2522509	NIF3L1	⇩	1.26	1.86E-03
2482230	ERLEC1	⇩	1.26	0.042
2390976	NCRNA00115	⇩	1.26	0.041
3470964	GLTP	⇧	1.26	0.015
2486927	ARHGAP25	⇩	1.26	0.036
2620538	LARS2	⇩	1.26	0.041
3829768	UBA2	⇧	1.26	7.29E-03
3840224	ZNF528	⇧	1.26	0.046
3633699	NRG4	⇧	1.26	0.049
2608765	ARL8B	⇩	1.26	2.95E-03
3725083	SNX11	⇧	1.26	0.021
2546008	SUPT7L	⇩	1.26	3.01E-03
3665230	HSF4	⇩	1.26	0.037
3348189	FDX1	⇧	1.26	1.78E-04
2645579	RASA2	⇩	1.26	0.019
3756344	SMARCE1	⇧	1.26	5.22E-04
3521174	ABCC4	⇧	1.26	0.032
2909723	CENPQ	⇩	1.26	0.017
3227454	QRFP	⇧	1.26	0.036
3750685	SLC46A1	⇩	1.26	0.010
2816298	IQGAP2	⇩	1.26	0.046
3053691	GUSB	⇩	1.26	0.016
3832292	KCNK6	⇩	1.26	9.77E-03
3693511	C16orf80	⇧	1.26	0.014
3710870	ARHGAP44	⇩	1.25	0.043
2872471	DTWD2	⇧	1.25	0.021
3341440	RN28S1	⇧	1.25	0.047
4009288	HSD17B10	⇧	1.25	0.037
3914286	SOX18	⇧	1.25	0.045
2633587	TBC1D23	⇩	1.25	0.016
2639309	SEC22A	⇩	1.25	0.017
3490251	WDFY2	⇧	1.25	2.41E-03
3010082	PHTF2	⇩	1.25	0.019
3756856	KRTAP17-1	⇧	1.25	0.036
2913594	MTO1	⇩	1.25	4.97E-03
3782166	IMPACT	⇧	1.25	0.038
2988882	AIMP2	⇩	1.25	0.045
2815965	HMGCR	⇩	1.25	0.026

Table B13: C9-LongvShort Gene List (n=628) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2829416	SEC24A	⇩	1.25	0.014	3978706	PAGE5	⇩	1.24	0.039	3781124	MIB1	⇧	1.23	2.96E-03
3708826	EIF4A1	⇧	1.25	0.047	3978819	RRAGB	⇧	1.24	0.013	3851441	ZNF442	⇧	1.23	0.022
3868905	CTU1	⇧	1.25	0.033	3037385	KDELR2	⇩	1.24	0.034	3948590	RIBC2	⇧	1.23	6.13E-03
2712906	RNF168	⇩	1.25	0.026	2841184	ERGIC1	⇩	1.24	0.011	3911814	SLMO2	⇧	1.23	0.021
2694397	RPN1	⇩	1.25	0.017	3514849	NEK3	⇧	1.24	0.026	2360158	HAX1	⇩	1.23	0.040
2478748	EML4	⇩	1.25	0.043	2436228	GATAD2B	⇩	1.24	2.41E-05	2316245	PRKCZ	⇩	1.23	0.032
3439063	ZNF26	⇧	1.25	4.42E-03	3828162	C19orf2	⇧	1.24	4.12E-03	3890109	C20orf108	⇧	1.23	7.28E-03
2782292	C4orf21	⇩	1.25	0.039	3707481	ZFP3	⇧	1.24	0.030	2883609	CLINT1	⇩	1.23	0.037
3186207	C9orf91	⇧	1.25	0.041	3822805	TECR	⇩	1.24	0.023	3535780	PTGER2	⇧	1.23	0.032
3335070	CDC42EP2	⇧	1.25	0.011	2974188	MED23	⇩	1.24	4.06E-03	3017795	RINT1	⇩	1.23	0.027
3471264	VPS29	⇧	1.25	0.035	2456746	EPRS	⇩	1.24	3.55E-03	3078656	ZNF767	⇩	1.23	0.047
3082824	CLN8	⇩	1.25	6.03E-03	2623515	ALAS1	⇩	1.24	4.96E-03	3488942	NUDT15	⇧	1.23	0.015
2559494	C2orf7	⇩	1.25	0.049	3042603	KIAA0087	⇧	1.24	8.01E-03	2708817	TMEM41A	⇩	1.23	0.039
2651782	SEC62	⇩	1.25	0.047	3099561	T1560	⇧	1.24	0.042	3859622	ZNF792	⇧	1.23	5.87E-03
3048778	TMED4	⇩	1.25	8.52E-03	2750594	SC4MOL	⇩	1.24	0.046	3489481	PHF11	⇧	1.23	7.69E-03
2687739	CD47	⇩	1.25	0.024	3670918	PLCG2	⇩	1.24	0.030	3499585	BIVM	⇧	1.23	5.27E-03
3540862	GPHN	⇧	1.25	5.28E-03	3854954	LRRC25	⇩	1.24	0.026	3969455	OFD1	⇧	1.23	0.031
3181193	TDRD7	⇧	1.25	7.08E-03	2949210	BAT4	⇩	1.24	0.012	2353773	TTF2	⇩	1.23	0.044
2652675	ECT2	⇩	1.25	0.029	2353881	MAN1A2	⇩	1.24	0.042	2678367	PDHB	⇩	1.23	0.017
2738146	TET2	⇩	1.25	4.34E-03	3490741	SUGT1	⇧	1.24	0.039	3428088	ACTR6	⇧	1.23	0.029
3089740	RHOBTB2	⇩	1.25	0.013	2962767	PGM3	⇩	1.24	0.049	2356181	RBM8A	⇩	1.23	0.017
3697563	FTSJD1	⇧	1.25	0.011	3347549	CUL5	⇧	1.24	1.01E-03	3040073	SNX13	⇩	1.23	0.022
3531479	ARHGAP5	⇧	1.25	0.038	2813414	CCNB1	⇩	1.24	0.044	3319613	RPL27A	⇩	1.23	2.92E-03
3407926	CMAS	⇧	1.24	0.027	2984655	RPS6KA2	⇧	1.24	0.046	2772968	COX18	⇩	1.23	0.018
3845647	MKNK2	⇧	1.24	0.010	2608469	ITPR1	⇩	1.24	9.91E-03	2617041	GOLGA4	⇩	1.23	0.041
3713575	PRPSAP2	⇧	1.24	0.037	2908423	SLC29A1	⇩	1.24	0.026	2378180	C1orf107	⇩	1.23	8.47E-03
3260666	HIF1AN	⇧	1.24	7.75E-03	3846280	TBXA2R	⇧	1.24	7.25E-03	3851150	ZNF433	⇧	1.23	1.40E-03
3668898	ZFP1	⇧	1.24	4.20E-03	3726375	EME1	⇩	1.24	0.040	2879509	YIPF5	⇩	1.23	0.026
2326410	CCDC21	⇩	1.24	5.93E-03	3048869	H2AFV	⇩	1.24	0.027	2735459	HERC3	⇩	1.23	0.022
3726960	NME2	⇧	1.24	0.015	2622359	RBM6	⇩	1.23	0.031	3243078	ZNF33A	⇧	1.23	0.010
2436338	CRTC2	⇩	1.24	1.05E-04	3328214	ALKBH3	⇧	1.23	0.020	2358171	PRPF3	⇩	1.23	1.22E-04
2855443	LOC100132356	⇩	1.24	0.016	2889698	CLK4	⇩	1.23	0.033	2474322	C2orf28	⇩	1.23	6.75E-03

Table B13: C9-LongvShort Gene List (n=628) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3475324	TMEM120B	⇧	1.23	0.037	2817291	JMY	⇩	1.22	0.048	2336963	C1orf83	⇩	1.21	0.039
2878368	APBB3	⇩	1.23	5.72E-03	2711644	ATP13A3	⇩	1.22	0.042	3869339	ZNF350	⇧	1.21	5.58E-03
2731831	USO1	⇩	1.23	0.026	3458911	CTDSP2	⇧	1.22	0.037	3282268	ACBD5	⇧	1.21	0.031
3464912	POC1B	⇧	1.23	0.023	2342576	ACADM	⇩	1.22	0.025	3843399	ZNF134	⇧	1.21	0.031
2417528	DEPDC1	⇩	1.23	0.044	3016692	PRKRIP1	⇩	1.22	0.040	2954527	ZNF318	⇩	1.21	0.025
2433209	PRKAB2	⇩	1.23	0.036	3366519	FANCF	⇧	1.22	0.032	2818454	XRCC4	⇩	1.21	0.042
3903598	GGT7	⇩	1.23	0.014	2862716	GFM2	⇩	1.22	8.03E-03	3409364	KLHDC5	⇧	1.21	9.71E-03
3840944	ZNF525	⇧	1.23	0.044	4021341	ZDHHC9	⇩	1.22	0.047	3730899	DDX42	⇧	1.21	0.021
2899437	BTN2A1	⇩	1.23	0.011	2524743	FASTKD2	⇩	1.22	0.017	3870162	ZNF665	⇧	1.21	5.37E-04
3334847	C11orf2	⇧	1.22	9.22E-03	3989678	XIAP	⇧	1.22	0.018	3602039	PPCDC	⇧	1.21	0.011
3860491	ZNF260	⇧	1.22	9.42E-03	2437307	SCAMP3	⇩	1.22	0.048	2514441	PPIG	⇩	1.21	2.66E-03
3412296	IRAK4	⇧	1.22	0.026	3716337	CCDC55	⇧	1.22	0.015	3664952	PDP2	⇩	1.21	0.041
3209497	FAM108B1	⇧	1.22	5.26E-03	2902348	MICB	⇩	1.22	0.027	3497659	RAP2A	⇧	1.21	0.038
3438027	RAN	⇧	1.22	0.013	3734453	SLC9A3R1	⇧	1.22	0.028	3763270	MMD	⇧	1.21	0.031
2659521	LRRC33	⇩	1.22	0.020	3079005	RARRES2	⇧	1.22	6.94E-03	2759857	ACOX3	⇩	1.21	5.62E-03
3803120	B4GALT6	⇧	1.22	0.034	3361811	STK33	⇧	1.22	0.025	2346863	RPL5	⇩	1.21	0.043
3221633	HDHD3	⇩	1.22	0.032	3439305	ZNF84	⇧	1.22	5.61E-03	2466039	ZNF692	⇩	1.21	9.61E-03
2456849	RAB3GAP2	⇩	1.22	3.79E-03	2349863	NTNG1	⇩	1.22	0.039	3625761	MNS1	⇧	1.21	0.031
3282117	ANKRD26	⇧	1.22	0.018	2542737	LAPTM4A	⇩	1.22	0.018	2560122	MOGS	⇩	1.21	0.046
2553730	MTIF2	⇩	1.22	0.021	3750785	SPAG5	⇩	1.22	0.020	3334501	PRDX5	⇧	1.21	0.036
2451200	UBE2T	⇩	1.22	0.022	4053534	ISG15	⇧	1.22	0.041	3566304	EXOC5	⇧	1.21	3.84E-03
2783316	SEC24D	⇩	1.22	0.048	2814642	MCCC2	⇩	1.22	0.022	2380991	IARS2	⇩	1.21	0.033
3702689	ZDHHC7	⇧	1.22	6.43E-03	2830010	SMAD5	⇩	1.22	9.43E-03	3037142	PMS2	⇩	1.21	8.60E-03
3064361	ACHE	⇧	1.22	0.036	2708610	MAGEF1	⇧	1.22	0.025	2596162	INO80D	⇩	1.21	3.77E-03
2528620	GMPPA	⇩	1.22	0.016	3859915	U2AF1L4	⇩	1.22	0.035	3130211	PPP2CB	⇧	1.21	0.044
2712632	TFRC	⇩	1.22	0.011	3916576	GABPA	⇧	1.22	3.64E-03	2604223	DNAJB3	⇧	1.21	6.39E-03
3140640	STAU2	⇧	1.22	0.022	3352813	TBCEL	⇧	1.22	0.021	3119376	C8orf31	⇩	1.21	0.023
2739242	GAR1	⇧	1.22	0.035	3619595	FAM82A2	⇩	1.21	0.024	3441011	PARP11	⇧	1.21	0.016
3510858	FOXO1	⇧	1.22	0.048	2979056	NUP43	⇩	1.21	0.024	2907018	TAF8	⇩	1.21	0.015
3311715	UROS	⇧	1.22	0.024	3761054	COPZ2	⇧	1.21	2.99E-03	3956290	PITPNB	⇧	1.21	4.35E-03
3595979	CCNB2	⇩	1.22	0.025	3092663	WRN	⇩	1.21	0.029	2363919	ATF6	⇩	1.21	0.029
3453556	PRKAG1	⇧	1.22	0.014	2437753	KIAA0907	⇩	1.21	0.013	2911944	PHF3	⇩	1.21	0.017

Table B13: C9-LongvShort Gene List (n=628) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2694785	MBD4	⇩	1.21	0.023
2577896	MCM6	⇩	1.21	0.040
3860824	ZNF569	⇧	1.21	2.35E-03
3766960	SMURF2	⇧	1.21	0.036
3215701	FANCC	⇧	1.21	0.032
3346548	BIRC3	⇧	1.21	0.026
2369796	TOR1AIP1	⇩	1.21	0.027
3489957	RNASEH2B	⇧	1.21	8.01E-03
3419641	SRGAP1	⇧	1.21	5.66E-03
3602569	C15orf27	⇧	1.20	6.61E-03
2784131	BBS7	⇩	1.20	0.034
2541230	NBAS	⇩	1.20	6.58E-03
3418298	KIF5A	⇧	1.20	3.82E-03
3261886	C10orf26	⇧	1.20	0.048
3611126	MEF2A	⇧	1.20	4.73E-03
2437329	CLK2	⇩	1.20	0.033
3739162	TBCD	⇧	1.20	0.017
3710681	MAP2K4	⇧	1.20	0.016
3835280	ZNF221	⇧	1.20	9.31E-03
2588827	NFE2L2	⇩	1.20	0.040
3428131	SCYL2	⇧	1.20	0.034
3929664	TMEM50B	⇧	1.20	0.031
3737647	CHMP6	⇧	1.20	0.012
2586989	DLX2	⇧	1.20	4.61E-03
2531779	ARMC9	⇩	1.20	0.028
3088983	XPO7	⇩	1.20	8.56E-03
3212728	AGTPBP1	⇧	1.20	0.014
3164601	KIAA1797	⇧	1.20	0.035
2786578	NDUFC1	⇧	1.20	0.041
3210130	C9orf41	⇧	1.20	0.034
2690776	B4GALT4	⇩	1.20	9.35E-03
2893847	SNRNP48	⇩	1.20	0.027
3784509	ZNF271	⇧	1.20	0.048
2801608	MARCH6	⇩	1.20	7.71E-03
3614087	UBE3A	⇧	1.20	0.014
3465409	BTG1	⇧	1.20	2.52E-03
2619344	NKTR	⇩	1.20	8.93E-03
2693937	TPRA1	⇩	1.20	8.58E-03
3814063	MBP	⇧	1.20	0.040
2835848	SLC36A1	⇩	1.20	0.020
3890870	RAB22A	⇧	1.20	0.015
3433538	RNFT2	⇩	1.20	0.028
3737140	GAA	⇩	1.20	0.012
3740171	CRK	⇧	1.20	0.048
2548776	ATL2	⇩	1.20	0.045
3081707	MNX1	⇧	1.20	0.012
3432754	PLBD2	⇩	1.20	0.044
3636956	WDR73	⇧	1.20	0.019
3738205	MRPL12	⇧	1.20	0.038
2714230	PCGF3	⇩	1.20	0.019
2900299	ZNF192	⇩	1.20	0.010
3860596	ZNF461	⇧	1.20	6.97E-03
3704896	CHMP1A	⇧	1.20	3.48E-03
3806913	SMAD2	⇧	1.20	0.012
3131844	LSM1	⇧	1.20	0.033

Table B14: C9-Long Specific Gene List (n=1,007) ALL SAMPLES COMBINED [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value
4048241	HLA-DRB5	⇩	8.28	1.78E-03	2437247	GBA	⇩	1.52	0.014	2408189	PPT1	⇩	1.44	0.043
4048265	HLA-DRB1	⇩	5.58	0.015	3797295	L3MBTL4	⇧	1.51	9.05E-03	2899413	BTN3A3	⇩	1.43	1.71E-04
3841621	LILRB4	⇩	1.91	6.96E-04	3790479	SEC11C	⇩	1.50	8.48E-03	3743734	C17orf61	⇧	1.43	2.38E-03
2821347	ERAP2	⇧	1.89	0.028	3507798	UBL3	⇧	1.50	3.30E-04	2325192	RPL11	⇧	1.43	8.87E-03
3369249	APIP	⇧	1.77	8.99E-03	2505993	POTEKP	⇧	1.50	5.07E-03	3927226	APP	⇩	1.43	5.68E-03
2399743	AKR7A3	⇩	1.75	4.50E-03	3761632	SNF8	⇧	1.50	1.72E-04	3727712	PCTP	⇧	1.43	8.20E-03
2913694	CD109	⇩	1.73	5.45E-03	3550328	C14orf129	⇧	1.50	8.83E-03	3913483	TCFL5	⇧	1.43	0.027
2845274	CCDC127	⇩	1.72	2.22E-05	2436826	KCNN3	⇩	1.50	1.48E-04	2407478	FHL3	⇧	1.43	0.013
2909020	ENPP4	⇩	1.72	3.90E-03	3385175	PICALM	⇧	1.50	0.015	2452691	SLC41A1	⇩	1.43	0.023
2643592	EPHB1	⇩	1.72	0.043	3053691	GUSB	⇩	1.49	3.33E-05	3470964	GLTP	⇧	1.42	2.05E-04
2678298	DNASE1L3	⇩	1.70	0.045	3618736	RASGRP1	⇩	1.49	0.044	3470523	SELPLG	⇩	1.42	0.048
3142217	PAG1	⇩	1.68	5.43E-03	3936442	PEX26	⇧	1.49	1.48E-04	2447824	EDEM3	⇩	1.42	0.014
3892812	SLCO4A1	⇩	1.68	1.87E-05	3864551	PLAUR	⇩	1.48	6.09E-03	3244539	ZNF22	⇧	1.42	1.96E-03
2820865	ARSK	⇩	1.67	1.05E-03	3824212	DDA1	⇧	1.48	1.67E-03	2418929	PIGK	⇩	1.42	0.039
2768981	SGCB	⇩	1.64	0.015	3208355	CBWD3	⇧	1.47	0.019	2514563	KLHL23	⇧	1.42	0.013
3403841	RIMKLB	⇧	1.62	0.029	3407793	PYROXD1	⇧	1.47	2.67E-03	2319225	H6PD	⇩	1.42	0.019
3856646	ZNF208	⇧	1.61	0.014	4002148	EIF1AX	⇧	1.47	2.60E-04	3428268	GAS2L3	⇩	1.42	0.035
2671101	ANO10	⇩	1.61	0.031	2454661	TMEM206	⇩	1.47	2.14E-03	3035892	GNA12	⇧	1.42	4.68E-03
3018866	DNAJB9	⇩	1.60	7.21E-03	3375999	C11orf48	⇧	1.46	6.47E-03	3435490	DENR	⇧	1.42	2.16E-03
3916527	JAM2	⇩	1.59	4.79E-04	2673547	SLC26A6	⇩	1.46	8.96E-06	3434393	DYNLL1	⇧	1.42	2.78E-03
3309602	RGS10	⇧	1.57	3.97E-03	3202316	MOBKL2B	⇧	1.46	8.38E-03	3770290	CD300LB	⇩	1.41	4.57E-03
3166844	CHMP5	⇧	1.57	4.57E-03	3476330	CCDC92	⇧	1.46	2.89E-03	2877639	SIL1	⇩	1.41	9.28E-03
3925639	NRIP1	⇧	1.57	8.74E-03	2877893	MGC29506	⇩	1.46	0.017	3656223	ITGAL	⇩	1.41	0.033
3518086	TBC1D4	⇧	1.55	0.010	2949256	BAT5	⇩	1.46	4.08E-04	2950307	HLA-DOA	⇩	1.41	0.011
3333899	RARRES3	⇧	1.55	5.12E-03	3167383	NUDT2	⇧	1.46	2.20E-03	3130211	PPP2CB	⇧	1.41	2.56E-04
3892452	LSM14B	⇧	1.54	1.11E-03	3462843	NAP1L1	⇧	1.45	3.78E-03	3845352	UQCR11	⇧	1.41	3.05E-03
3023883	CPA4	⇩	1.54	5.61E-03	3782166	IMPACT	⇧	1.45	4.94E-04	3827218	RPSAP58	⇧	1.41	4.79E-03
3263944	PDCD4	⇧	1.53	3.93E-04	3703885	SLC7A5	⇩	1.45	0.014	3917204	C21orf7	⇧	1.41	7.47E-03
3160658	SLC1A1	⇩	1.53	0.015	2899437	BTN2A1	⇩	1.44	9.18E-06	3403077	C12orf57	⇧	1.41	2.09E-04
2626097	ABHD6	⇩	1.52	6.82E-03	3994451	CXorf40A	⇧	1.44	4.06E-04	4006416	FUNDC1	⇧	1.41	4.32E-04
2958325	DST	⇩	1.52	0.025	2766492	C4orf34	⇧	1.44	0.022	3619165	SRP14	⇧	1.40	4.82E-03

Table B14: C9-Long Specific Gene List (n=1,007) ALL SAMPLES COMBINED [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

3820370	P2RY11	⇩	1.40	0.010	3023060	CALU	⇩	1.37	0.013	2836451	MFAP3	⇩	1.35	0.014
3406421	STRAP	⇧	1.40	8.01E-05	3712041	UBB	⇧	1.37	3.51E-03	2794902	AGA	⇩	1.35	0.027
2409104	SLC2A1	⇩	1.40	5.48E-03	3716993	RNF135	⇧	1.37	8.50E-05	3257670	PCGF5	⇧	1.35	1.11E-03
2320727	TNFRSF1B	⇩	1.40	2.61E-03	2336302	ZFYVE9	⇧	1.37	1.68E-04	3341440	RN28S1	⇧	1.35	6.88E-03
3540353	CHURC1	⇧	1.40	2.69E-03	2645764	ATP1B3	⇩	1.37	0.025	3410695	DNM1L	⇧	1.35	0.036
3253438	RPS24	⇧	1.40	0.013	2361342	SEMA4A	⇩	1.37	6.16E-03	3076753	KIAA1147	⇩	1.35	0.012
2865050	RPS23	⇧	1.40	0.014	2714376	TMEM175	⇩	1.37	0.016	2594497	CLK1	⇩	1.35	0.019
2643324	SRPRB	⇩	1.39	0.013	2611848	SLC6A6	⇩	1.36	2.94E-03	2878662	DIAPH1	⇩	1.35	1.37E-03
3537030	RPL13AP3	⇧	1.39	8.58E-03	3055608	TYW1B	⇩	1.36	0.027	3020496	ST7	⇩	1.35	0.022
2975385	AHI1	⇩	1.39	0.022	2990342	TMEM106B	⇩	1.36	0.048	3851267	ZNF625	⇧	1.35	3.90E-04
3473727	WSB2	⇧	1.39	1.17E-03	3557947	CHMP4A	⇧	1.36	4.32E-03	3417457	MYL6	⇧	1.35	7.19E-03
2420467	CTBS	⇩	1.39	0.016	2373842	PTPRC	⇩	1.36	0.010	2413423	TMEM48	⇩	1.35	0.022
3890870	RAB22A	⇧	1.39	1.75E-05	3184218	C9orf6	⇧	1.36	0.040	3634811	CTSH	⇩	1.35	0.022
3114832	SQLE	⇩	1.39	2.50E-03	3747199	CENPV	⇧	1.36	0.019	3878934	NAA20	⇧	1.35	4.71E-04
3950452	CRELD2	⇩	1.39	8.37E-03	3861302	YIF1B	⇩	1.36	0.011	2504883	UGGT1	⇩	1.34	0.046
3432754	PLBD2	⇩	1.39	2.73E-04	3010082	PHTF2	⇩	1.36	1.09E-03	2835021	PCYOX1L	⇩	1.34	3.75E-03
2960955	SLC17A5	⇩	1.39	2.50E-03	3645836	ZNF75A	⇧	1.36	6.51E-03	2949801	AGPAT1	⇩	1.34	8.41E-04
3842301	ZNF581	⇧	1.39	3.74E-03	2830638	KIF20A	⇩	1.36	6.15E-03	3708245	SLC16A13	⇩	1.34	0.019
3494102	UCHL3	⇧	1.39	4.80E-04	2375212	PPP1R12B	⇩	1.36	8.16E-03	2318736	PARK7	⇧	1.34	1.52E-04
4015763	GLA	⇩	1.39	0.037	2409004	LEPRE1	⇩	1.36	9.52E-04	3458911	CTDSP2	⇧	1.34	2.10E-03
2536996	FLJ41327	⇩	1.38	0.032	3453556	PRKAG1	⇧	1.36	1.59E-04	2971801	MAN1A1	⇩	1.34	0.020
3447863	KRAS	⇧	1.38	7.97E-04	2528159	WNT10A	⇩	1.36	0.038	3741528	TAX1BP3	⇧	1.34	0.037
3726960	NME2	⇧	1.38	2.60E-04	3837464	GLTSCR2	⇧	1.36	2.39E-03	3849797	ZNF561	⇧	1.34	1.16E-04
3936550	USP18	⇧	1.38	8.05E-03	3893033	DPH3P1	⇧	1.36	0.047	3198289	C9orf123	⇧	1.34	1.82E-03
2726483	OCIAD1	⇩	1.38	1.52E-03	3475324	TMEM120B	⇧	1.35	1.56E-03	2620538	LARS2	⇩	1.34	6.48E-03
3725083	SNX11	⇧	1.38	8.67E-04	3433843	SUDS3	⇧	1.35	0.018	2668205	GLB1	⇩	1.34	0.025
3969946	ZRSR2	⇧	1.38	0.020	3072435	TMEM209	⇩	1.35	8.96E-03	2442134	TMCO1	⇩	1.34	3.02E-03
2320411	AGTRAP	⇩	1.38	3.68E-03	3868905	CTU1	⇧	1.35	3.07E-03	2690850	TMEM39A	⇩	1.34	0.011
3507962	KATNAL1	⇧	1.38	3.85E-03	3216276	SLC35D2	⇧	1.35	0.025	3197318	AK3	⇧	1.34	7.77E-04
3447694	BCAT1	⇧	1.38	0.032	3490741	SUGT1	⇧	1.35	2.61E-03	2815965	HMGCR	⇩	1.34	2.64E-03
2384562	RAB4A	⇧	1.38	1.72E-03	3420854	DYRK2	⇧	1.35	0.023	3988987	NDUFA1	⇧	1.34	0.028
3555300	CCNB1IP1	⇧	1.38	0.028	3750685	SLC46A1	⇩	1.35	6.28E-04	3210457	RFK	⇧	1.34	4.28E-04

Table B14: C9-Long Specific Gene List (n=1,007) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2450668	TMEM9	⇩	1.34	3.27E-03
3774096	PDE6G	⇧	1.34	3.56E-03
2426791	CLCC1	⇩	1.33	5.96E-03
2608469	ITPR1	⇩	1.33	4.41E-04
3430389	C12orf23	⇧	1.33	7.78E-03
3421523	YEATS4	⇧	1.33	3.90E-03
3078656	ZNF767	⇩	1.33	5.20E-03
3821015	LDLR	⇩	1.33	1.38E-03
3185063	UGCG	⇩	1.33	6.29E-03
3828162	C19orf2	⇧	1.33	1.24E-04
2884647	C5orf54	⇩	1.33	0.022
2899340	BTN2A2	⇩	1.33	2.64E-03
2452977	FAIM3	⇩	1.33	0.019
3460584	LLPH	⇧	1.33	9.39E-03
2816298	IQGAP2	⇩	1.33	0.012
3665116	CBFB	⇧	1.33	1.26E-03
3642815	NME4	⇧	1.33	2.24E-03
2415084	JUN	⇩	1.33	0.041
2529421	SGPP2	⇩	1.33	2.36E-04
2568968	UXS1	⇩	1.33	0.025
3435681	ARL6IP4	⇧	1.33	2.40E-04
2514122	LASS6	⇩	1.33	0.027
3255284	C10orf99	⇩	1.33	0.029
3629103	KIAA0101	⇧	1.33	0.038
3031967	CHPF2	⇩	1.33	5.66E-03
3866302	AP2S1	⇧	1.33	2.92E-05
3277468	USP6NL	⇧	1.33	0.015
3625271	RAB27A	⇧	1.33	0.020
3758148	CCDC56	⇧	1.33	1.23E-03
3806253	ATP5A1	⇧	1.33	3.51E-03
3041260	TOMM7	⇧	1.33	0.032
3630912	ANP32A	⇧	1.33	1.20E-03
2363084	NCSTN	⇩	1.33	0.024
3962448	RRP7A	⇧	1.33	9.47E-03
2780172	CENPE	⇩	1.32	0.020
2705748	NCEH1	⇩	1.32	0.027
3442854	SLC2A3	⇩	1.32	0.015
3075136	CREB3L2	⇩	1.32	0.029
4005627	CXorf38	⇧	1.32	0.024
3388914	DCUN1D5	⇧	1.32	0.028
2704267	GOLIM4	⇩	1.32	2.48E-03
3444252	CSDA	⇧	1.32	2.04E-03
2892277	NQO2	⇩	1.32	4.29E-03
3989678	XIAP	⇧	1.32	7.05E-04
2708610	MAGEF1	⇧	1.32	1.04E-03
3674146	RPL13	⇧	1.32	0.049
2876257	SAR1B	⇩	1.32	0.019
3836432	QPCTL	⇩	1.32	1.09E-03
3470689	ALKBH2	⇧	1.32	1.46E-03
2324634	CDC42	⇩	1.32	0.029
3303300	CHUK	⇧	1.32	5.82E-03
3868963	ETFB	⇧	1.32	1.39E-04
3996381	ATP6AP1	⇩	1.32	3.64E-03
3427014	SNRPF	⇧	1.32	0.027
3822805	TECR	⇩	1.32	2.30E-03
3426215	MRPL42	⇧	1.32	6.81E-03
3066751	SYPL1	⇩	1.32	7.06E-03
3434760	P2RX4	⇩	1.32	8.92E-03
3129121	CCDC25	⇧	1.32	8.52E-04
3942161	UQCR10	⇧	1.32	3.31E-05
3969422	RAB9A	⇧	1.32	0.013
2997376	ANLN	⇩	1.32	0.012
2370317	MR1	⇩	1.32	0.015
3869379	ZNF614	⇧	1.32	4.24E-03
2639225	PDIA5	⇩	1.32	0.023
3486728	SLC25A15	⇧	1.32	2.61E-03
3406493	DERA	⇧	1.32	9.17E-03
2413907	DHCR24	⇩	1.32	0.022
3722338	IFI35	⇧	1.32	0.020
2502424	INSIG2	⇩	1.32	0.047
3633699	NRG4	⇧	1.32	0.015
3191338	GPR107	⇩	1.32	3.05E-03
2955061	SLC35B2	⇩	1.32	0.021
3173479	FOXD4L3	⇧	1.31	0.020
3260423	CUTC	⇧	1.31	7.72E-03
3394488	PVRL1	⇩	1.31	2.57E-03
2379280	FLVCR1	⇩	1.31	0.018
2518272	ITGA4	⇩	1.31	0.024
3129731	DUSP4	⇩	1.31	0.044
3130850	RNF122	⇩	1.31	0.028
2560122	MOGS	⇩	1.31	3.95E-03
3758775	PYY	⇧	1.31	0.026
3946351	ADSL	⇧	1.31	2.52E-04
3665230	HSF4	⇩	1.31	0.010
3397589	ETS1	⇧	1.31	3.53E-03
3175119	OSTF1	⇧	1.31	0.027
2692411	PTPLB	⇩	1.31	0.022
3969047	PRPS2	⇧	1.31	1.05E-04
2841184	ERGIC1	⇩	1.31	9.53E-04
3358950	CTSD	⇩	1.31	0.015
3099561	T1560	⇧	1.31	7.77E-03
3840224	ZNF528	⇧	1.31	0.015
3466284	NDUFA12	⇧	1.31	1.68E-03
2878368	APBB3	⇩	1.31	2.76E-04
2599955	ATG9A	⇩	1.31	5.87E-04
3663055	C16orf57	⇧	1.31	0.014

Table B14: C9-Long Specific Gene List (n=1,007) ALL SAMPLES COMBINED [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

2930863	PCMT1	⇩	1.31	6.75E-03
3665857	NUTF2	⇧	1.31	3.99E-04
2902574	LY6G5B	⇩	1.31	0.026
3413787	TUBA1C	⇧	1.31	7.96E-03
2853388	C5orf33	⇧	1.31	2.10E-05
2412668	TXNDC12	⇩	1.31	0.029
2628682	ARL6IP5	⇩	1.31	0.032
3916576	GABPA	⇧	1.31	6.26E-05
3996467	PLXNA3	⇩	1.31	9.08E-04
3451318	ZCRB1	⇧	1.30	5.33E-04
3480681	MRP63	⇧	1.30	2.47E-03
3566304	EXOC5	⇧	1.30	5.52E-05
3426257	SOCS2	⇧	1.30	6.07E-03
3976670	EBP	⇩	1.30	0.020
2889698	CLK4	⇩	1.30	5.43E-03
3886512	TTPAL	⇧	1.30	0.024
3349918	RBM7	⇧	1.30	0.016
3790704	PMAIP1	⇧	1.30	0.011
3943207	YWHAH	⇧	1.30	0.015
3438027	RAN	⇧	1.30	8.25E-04
3240095	RAB18	⇧	1.30	8.62E-03
3719362	AATF	⇧	1.30	4.50E-04
2330773	CDCA8	⇩	1.30	0.030
3339167	FAM86C	⇧	1.30	0.016
3263624	MXI1	⇧	1.30	0.037
2520138	MFSD6	⇩	1.30	7.99E-03
2363919	ATF6	⇩	1.30	1.85E-03
3870135	ZNF347	⇧	1.30	0.018
3630099	TIPIN	⇧	1.30	0.011
2325290	LYPLA2	⇧	1.30	3.77E-03
3886179	IFT52	⇧	1.30	8.32E-04
3589972	CHST14	⇩	1.30	1.40E-03
3723348	HEXIM1	⇧	1.30	6.64E-04
3584728	SNRPN	⇧	1.30	0.014
3103523	LY96	⇩	1.30	0.048
3682135	C16orf63	⇧	1.30	6.34E-03
3344861	C11orf54	⇧	1.30	0.012
2977621	PLAGL1	⇩	1.30	0.036
3934669	SUMO3	⇧	1.30	0.018
3954525	ZNF280B	⇧	1.30	2.63E-03
2541230	NBAS	⇩	1.30	1.16E-04
3528895	LRP10	⇩	1.30	0.022
3850576	YIPF2	⇩	1.30	0.018
2964327	LYRM2	⇧	1.30	4.92E-05
3865568	SNRPD2	⇧	1.29	0.039
3956984	ZMAT5	⇧	1.29	4.34E-04
3617412	LPCAT4	⇩	1.29	9.00E-04
2968144	OSTM1	⇩	1.29	3.37E-03
3882949	DYNLRB1	⇧	1.29	2.67E-03
3726406	ACSF2	⇩	1.29	0.019
3338424	FADD	⇧	1.29	1.92E-03
3441011	PARP11	⇧	1.29	9.82E-04
3380697	DHCR7	⇩	1.29	0.019
2614142	NR1D2	⇧	1.29	0.037
3130113	GTF2E2	⇧	1.29	4.10E-03
2930243	SASH1	⇩	1.29	0.019
3137875	GGH	⇩	1.29	0.025
3833443	PLD3	⇩	1.29	7.58E-03
3982423	ATP7A	⇩	1.29	0.047
3060117	ABCB4	⇩	1.29	0.019
2656569	DNAJB11	⇩	1.29	0.023
4004819	DYNLT3	⇧	1.29	0.028
2970897	FRK	⇧	1.29	0.027
3707127	MED11	⇧	1.29	0.017
2948522	KIAA1949	⇩	1.29	1.97E-03
2829562	TXNDC15	⇩	1.29	0.013
3293537	PCBD1	⇧	1.29	0.039
3579205	SETD3	⇧	1.29	1.17E-03
3195344	MRPL41	⇧	1.29	0.027
2542737	LAPTM4A	⇩	1.29	2.31E-03
2604254	HJURP	⇩	1.29	0.015
3311715	UROS	⇧	1.29	3.02E-03
3463522	PAWR	⇧	1.29	0.022
3726325	XYLT2	⇩	1.29	4.04E-03
3518169	COMMD6	⇧	1.29	9.44E-03
2443335	SLC19A2	⇩	1.29	0.047
3555340	TEP1	⇩	1.29	4.58E-04
3513995	DLEU2	⇧	1.29	0.043
3242425	CCNY	⇧	1.29	9.11E-03
3625234	RSL24D1	⇧	1.29	0.011
3377826	RNASEH2C	⇧	1.29	5.80E-05
2758298	LRPAP1	⇩	1.29	0.023
3877776	SNRPB2	⇧	1.29	0.045
2601414	SERPINE2	⇩	1.28	0.032
2815331	BTF3	⇧	1.28	3.13E-04
2721777	PI4K2B	⇧	1.28	3.48E-03
3697563	FTSJD1	⇧	1.28	3.36E-03
3362795	RNF141	⇧	1.28	4.53E-03
2908179	VEGFA	⇩	1.28	0.028
4021341	ZDHHC9	⇩	1.28	9.22E-03
3451264	YAF2	⇧	1.28	6.37E-03
3404436	CLEC2D	⇩	1.28	0.028
3432333	PTPN11	⇧	1.28	5.73E-03
3318844	DNHD1	⇩	1.28	7.32E-04
2866590	LYSMD3	⇩	1.28	0.037
2379863	CENPF	⇩	1.28	0.029

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3559794	C14orf126	⇧	1.28	0.012
3361041	TPP1	⇩	1.28	7.74E-03
3864921	ZNF180	⇧	1.28	2.44E-03
3988740	PGRMC1	⇩	1.28	0.026
3409127	ARNTL2	⇧	1.28	0.017
2874686	HINT1	⇧	1.28	0.025
3722739	G6PC3	⇩	1.28	0.024
3843399	ZNF134	⇧	1.28	4.29E-03
3775157	WDR45L	⇧	1.28	0.045
3269328	ZRANB1	⇧	1.28	2.65E-03
2902736	C6orf48	⇧	1.28	4.73E-03
3352813	TBCEL	⇧	1.28	2.88E-03
3336378	RBM14	⇩	1.28	0.023
2750594	SC4MOL	⇩	1.28	0.017
3976519	RBM3	⇧	1.28	3.13E-04
3707990	TXNDC17	⇧	1.28	0.016
2611779	TMEM43	⇩	1.28	6.30E-03
3991698	HPRT1	⇧	1.28	4.98E-03
3369762	COMMD9	⇧	1.28	0.022
3830216	FXYD5	⇩	1.28	0.034
3759305	CCDC43	⇧	1.28	3.64E-03
3708826	EIF4A1	⇧	1.28	0.025
3824395	PGLS	⇧	1.28	7.68E-05
3784509	ZNF271	⇧	1.27	7.02E-03
3224197	NDUFA8	⇧	1.27	0.019
2413578	TMEM59	⇩	1.27	0.030
3770632	SUMO2	⇧	1.27	0.024
3043165	HIBADH	⇧	1.27	0.011
2663551	NUP210	⇩	1.27	5.47E-03
3412296	IRAK4	⇧	1.27	6.37E-03
2364155	UHMK1	⇧	1.27	1.59E-04
2822215	PAM	⇩	1.27	5.43E-03
3315549	PSMD13	⇧	1.27	9.06E-05
2724671	RHOH	⇧	1.27	3.42E-03
3739108	FN3KRP	⇧	1.27	2.49E-03
3996815	VBP1	⇧	1.27	0.028
3347549	CUL5	⇧	1.27	2.04E-04
3131844	LSM1	⇧	1.27	4.36E-03
2330253	ADPRHL2	⇧	1.27	0.036
3866276	SLC1A5	⇩	1.27	0.020
3727962	DGKE	⇩	1.27	0.030
3734479	TMEM104	⇩	1.27	0.021
3378790	PPP1CA	⇧	1.27	5.25E-03
3142519	ZFAND1	⇧	1.27	0.025
3303392	BLOC1S2	⇧	1.27	0.015
3941010	SRRD	⇧	1.27	0.041
4000132	TRAPPC2	⇧	1.27	7.25E-03
3328214	ALKBH3	⇧	1.27	5.63E-03
3190420	CERCAM	⇩	1.27	0.027
3619595	FAM82A2	⇩	1.27	3.07E-03
3681674	NTAN1	⇧	1.27	7.24E-03
3849865	FBXL12	⇧	1.27	9.86E-03
3703112	GINS2	⇧	1.27	0.033
2370123	XPR1	⇩	1.27	0.014
3280902	DNAJC1	⇩	1.27	0.010
3333622	POLR2G	⇧	1.27	2.41E-03
3394123	HYOU1	⇩	1.27	0.035
3890109	C20orf108	⇧	1.27	1.51E-03
4022106	MBNL3	⇧	1.27	0.034
2916345	SLC35A1	⇩	1.27	0.031
3922793	PDE9A	⇧	1.27	0.023
3421630	CCT2	⇧	1.27	1.72E-03
3822347	C19orf53	⇧	1.27	0.049
2717014	MAN2B2	⇩	1.27	0.018
3379390	SUV420H1	⇧	1.27	5.76E-03
3368707	CD59	⇩	1.27	0.020
3064638	RABL5	⇧	1.27	5.98E-04
3441955	MRPL51	⇧	1.27	1.19E-04
2390976	NCRNA00115	⇩	1.27	0.032
3464967	GALNT4	⇧	1.27	1.60E-03
3728509	DYNLL2	⇧	1.27	1.57E-03
3130161	GSR	⇧	1.27	0.035
2781693	CASP6	⇧	1.27	6.76E-03
3666649	VPS4A	⇧	1.27	5.18E-03
2599371	TMBIM1	⇩	1.27	4.19E-03
2562233	RETSAT	⇩	1.27	0.024
2835792	GM2A	⇩	1.27	0.020
2924492	HEY2	⇧	1.26	0.019
4011768	SNX12	⇧	1.26	1.51E-03
2712632	TFRC	⇩	1.26	1.96E-03
3730899	DDX42	⇧	1.26	3.70E-03
2363202	SLAMF7	⇩	1.26	0.028
2320762	VPS13D	⇩	1.26	6.85E-04
3642358	TM2D3	⇩	1.26	0.036
3738205	MRPL12	⇧	1.26	5.94E-03
3064541	PLOD3	⇩	1.26	1.44E-03
3929931	ATP5O	⇧	1.26	8.41E-03
3487432	DNAJC15	⇩	1.26	0.043
2515933	ZAK	⇧	1.26	0.024
3303255	ERLIN1	⇩	1.26	0.040
2612401	BTD	⇩	1.26	0.042
3422703	ATXN7L3B	⇧	1.26	4.76E-03
3840164	ZNF610	⇧	1.26	0.014
2428501	SLC16A1	⇩	1.26	0.021
3862167	FBL	⇧	1.26	1.52E-05
2377427	CD46	⇩	1.26	4.83E-04

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3878025	DSTN	⇧	1.26	0.030	2640579	PLXNA1	⇩	1.26	0.016	3325680	EIF3M	⇧	1.25	2.26E-03
3387483	MTMR2	⇧	1.26	2.04E-03	3821727	ZNF136	⇧	1.26	7.98E-04	3704896	CHMP1A	⇧	1.25	1.67E-04
3945056	EIF3L	⇧	1.26	3.06E-03	3708074	XAF1	⇧	1.26	5.36E-03	3432678	TPCN1	⇩	1.25	2.62E-03
3770944	H3F3B	⇧	1.26	0.049	3770606	HN1	⇧	1.26	0.016	3142932	C8orf59	⇧	1.25	8.39E-03
3577246	MOAP1	⇧	1.26	0.041	3522225	STK24	⇧	1.26	0.013	3391255	IL18	⇧	1.25	0.041
3860491	ZNF260	⇧	1.26	1.94E-03	3009229	POR	⇩	1.26	0.036	3855506	TMEM161A	⇩	1.25	9.60E-03
2924604	HINT3	⇧	1.26	0.036	3617920	ATPBD4	⇧	1.26	6.28E-03	3947123	SREBF2	⇩	1.25	8.65E-05
3629350	SPG21	⇧	1.26	2.02E-03	3678147	NMRAL1	⇧	1.26	0.012	3719515	DUSP14	⇧	1.25	4.06E-03
3221633	HDHD3	⇩	1.26	9.84E-03	3507710	SLC7A1	⇩	1.26	0.028	3843058	ZNF264	⇧	1.25	0.015
2440664	B4GALT3	⇩	1.26	0.034	2572601	CCDC93	⇩	1.26	8.33E-05	3536663	MAPK1IP1L	⇧	1.25	6.79E-04
3690084	DNAJA2	⇧	1.26	8.25E-03	2331679	MFSD2A	⇩	1.26	0.019	3705412	C17orf97	⇧	1.25	2.27E-03
2395890	CLSTN1	⇩	1.26	0.013	3468925	NFYB	⇧	1.26	2.39E-05	3706651	OR3A3	⇩	1.25	0.024
2777447	NAP1L5	⇧	1.26	2.40E-03	2908052	POLR1C	⇧	1.26	6.36E-04	3829857	ZNF302	⇧	1.25	1.06E-03
4017519	PSMD10	⇧	1.26	2.26E-03	3860596	ZNF461	⇧	1.26	4.12E-04	3668898	ZFP1	⇧	1.25	2.70E-03
3376023	UBXN1	⇧	1.26	0.028	3345107	ANKRD49	⇧	1.26	7.13E-03	3563814	L2HGDH	⇧	1.25	5.00E-04
2766192	TLR10	⇩	1.26	0.039	3020192	TES	⇩	1.26	5.62E-03	3788270	ELAC1	⇧	1.25	6.22E-03
2621122	NBEAL2	⇩	1.26	7.93E-03	3719150	PIGW	⇧	1.26	0.021	2583254	LY75	⇩	1.25	0.022
2523213	BMPR2	⇩	1.26	0.020	3421706	RAB3IP	⇧	1.26	3.81E-03	3994795	MTM1	⇧	1.25	0.049
3304004	NPM3	⇧	1.26	0.029	3019401	ZNF277	⇧	1.26	0.011	2690776	B4GALT4	⇩	1.25	9.39E-04
3838665	RCN3	⇩	1.26	2.77E-03	3403140	EMG1	⇧	1.26	0.031	3869714	ZNF611	⇧	1.25	9.29E-03
2594435	KCTD18	⇧	1.26	2.23E-03	2514516	KLHL23	⇧	1.26	0.032	3471374	PPP1CC	⇧	1.25	1.22E-04
2369796	TOR1AIP1	⇩	1.26	5.45E-03	3812385	CD226	⇩	1.26	0.044	3685306	NDUFAB1	⇧	1.25	0.023
3845175	GAMT	⇧	1.26	0.049	3048778	TMED4	⇩	1.25	4.89E-03	3190659	SET	⇧	1.25	6.53E-04
2655168	YEATS2	⇩	1.26	4.08E-03	3962000	PMM1	⇧	1.25	5.55E-04	3890218	C20orf43	⇧	1.25	0.014
3250019	DDX50	⇧	1.26	0.023	2815791	HEXB	⇩	1.25	7.68E-03	3806913	SMAD2	⇧	1.25	1.56E-03
3354764	STT3A	⇩	1.26	0.027	2599993	ABCB6	⇩	1.25	3.40E-03	3434413	RNF10	⇧	1.25	5.42E-03
3887117	CTSA	⇩	1.26	0.018	2439975	IGSF8	⇩	1.25	3.89E-03	3114600	TRMT12	⇧	1.25	5.08E-04
2694397	RPN1	⇩	1.26	0.010	2888243	KIAA1191	⇧	1.25	0.017	4015693	TIMM8A	⇧	1.25	2.65E-03
3822657	CD97	⇩	1.26	1.70E-03	3557898	TM9SF1	⇩	1.25	0.042	2482230	ERLEC1	⇩	1.25	0.043
3831260	ZNF146	⇧	1.26	4.64E-03	3360364	OR52A4	⇧	1.25	0.031	3195296	SSNA1	⇧	1.25	0.031
3624448	GNB5	⇧	1.26	1.68E-03	3340449	SLCO2B1	⇩	1.25	0.033	3357785	SIRT3	⇧	1.25	3.04E-03
2647458	RNF13	⇩	1.26	0.047	2731542	AREG	⇩	1.25	0.027	2622859	HEMK1	⇩	1.25	2.47E-03

Table B14: C9-Long Specific Gene List (n=1,007) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3325052	EIF2AK2	⇧	1.25	0.031
3014411	TRRAP	⇩	1.25	1.66E-03
3884100	RPN2	⇩	1.25	0.015
2868131	ERAP1	⇩	1.25	0.025
2634494	ALCAM	⇩	1.25	0.015
2404521	PEF1	⇧	1.25	0.014
3917851	SOD1	⇧	1.25	0.043
3415273	C12orf44	⇧	1.25	0.013
2903782	ITPR3	⇩	1.25	4.47E-03
3998632	PNPLA4	⇧	1.25	4.24E-04
3850040	EIF3G	⇧	1.25	1.11E-04
3221543	CDC26	⇧	1.25	0.016
2437307	SCAMP3	⇩	1.25	0.021
3033397	RBM33	⇩	1.25	1.53E-03
3636956	WDR73	⇧	1.25	3.55E-03
3340066	PAAF1	⇧	1.25	6.48E-03
3535922	STYX	⇧	1.25	0.019
2334374	AKR1A1	⇧	1.24	0.014
3893760	TPD52L2	⇧	1.24	6.78E-03
3380980	C11orf59	⇧	1.24	0.013
3482977	POLR1D	⇧	1.24	2.02E-03
3138414	ARMC1	⇧	1.24	6.46E-03
2960010	LMBRD1	⇩	1.24	0.033
2360989	MSTO1	⇩	1.24	0.028
2472914	UBXN2A	⇧	1.24	0.019
3633460	PTPN9	⇧	1.24	0.023
3007438	POM121	⇩	1.24	0.031
3713575	PRPSAP2	⇧	1.24	0.033
2759303	MRFAP1L1	⇧	1.24	0.032
2944491	MBOAT1	⇩	1.24	0.015
2706791	ZMAT3	⇧	1.24	0.017
2902935	STK19	⇧	1.24	0.015
2406139	KIAA0319L	⇩	1.24	5.53E-03
3426917	METAP2	⇧	1.24	8.04E-03
3779756	SEH1L	⇧	1.24	9.16E-03
2466039	ZNF692	⇩	1.24	2.42E-03
3376867	TRMT112	⇧	1.24	7.98E-03
3832777	MRPS12	⇧	1.24	2.20E-03
3104698	ZBTB10	⇧	1.24	0.015
3934591	KRTAP10-5	⇧	1.24	0.026
3553607	EIF5	⇧	1.24	3.26E-03
2681157	TMF1	⇩	1.24	3.82E-03
3387259	SESN3	⇧	1.24	0.018
3608466	MAN2A2	⇩	1.24	7.02E-03
3474104	CIT	⇩	1.24	0.011
3821301	ZNF627	⇧	1.24	0.038
3742727	DHX33	⇧	1.24	2.95E-04
3025740	TMEM140	⇩	1.24	0.049
3590422	RTF1	⇧	1.24	8.92E-03
2474322	C2orf28	⇩	1.24	2.76E-03
3031345	LRRC61	⇧	1.24	1.34E-03
2363902	DUSP12	⇧	1.24	2.64E-03
2565246	TMEM127	⇩	1.24	3.85E-03
3534923	KLHDC2	⇧	1.24	4.02E-03
3823613	FAM32A	⇧	1.24	0.030
2654855	ATP11B	⇩	1.24	0.016
2437401	FDPS	⇩	1.24	7.71E-03
2408681	HIVEP3	⇩	1.24	0.028
2359817	INTS3	⇩	1.24	1.19E-04
3743906	TP53	⇧	1.24	0.042
2320472	CLCN6	⇩	1.24	0.019
2358171	PRPF3	⇩	1.24	3.66E-05
2571457	CKAP2L	⇩	1.24	0.013
3005956	C7orf42	⇩	1.24	6.48E-03
2773655	RCHY1	⇧	1.24	0.018
3744039	TRAPPC1	⇧	1.24	3.17E-04
3851603	DHPS	⇧	1.24	0.026
2398736	ATP13A2	⇩	1.24	0.042
3233547	RBM17	⇧	1.24	2.19E-03
2666904	SLC4A7	⇩	1.24	0.021
2365958	MPZL1	⇩	1.24	5.49E-03
3820906	C19orf52	⇧	1.24	1.39E-04
3775147	FOXK2	⇩	1.24	0.013
2828146	CDC42SE2	⇧	1.24	1.88E-03
3212728	AGTPBP1	⇧	1.24	2.95E-03
2527672	PNKD	⇩	1.24	0.028
3457523	RNF41	⇧	1.24	2.72E-03
2327259	PPP1R8	⇧	1.24	2.23E-04
2404819	PTP4A2	⇧	1.24	0.022
3781124	MIB1	⇧	1.24	1.90E-03
2321849	DNAJC16	⇩	1.23	0.033
3191589	FUBP3	⇧	1.23	9.27E-03
3223605	FBXW2	⇧	1.23	4.09E-05
4015838	ARMCX6	⇩	1.23	7.14E-03
3593261	EID1	⇧	1.23	0.012
2336271	BTF3L4	⇧	1.23	4.03E-03
3633550	IMP3	⇧	1.23	0.013
2413203	LRP8	⇩	1.23	2.67E-03
2977949	EPM2A	⇧	1.23	5.27E-04
3737140	GAA	⇩	1.23	3.10E-03
3985644	TCEAL3	⇩	1.23	0.045
2954280	PEX6	⇩	1.23	8.98E-04
2620315	TMEM42	⇧	1.23	8.94E-04
3235255	ECHDC3	⇧	1.23	1.67E-03
2906591	APOBEC2	⇧	1.23	0.020
2877257	BRD8	⇩	1.23	0.020

Table B14: C9-Long Specific Gene List (n=1,007) ALL SAMPLES COMBINED [Partek® unadjusted $p<0.05$, FC $\geq \pm 1.20$]

3323443	PRMT3	⇧	1.23	2.11E-03	2877141	HNRNPA0	⇧	1.23	3.99E-04	2999544	BLVRA	⇧	1.23	0.042
3569200	ATP6V1D	⇧	1.23	0.022	3750625	POLDIP2	⇧	1.23	4.56E-03	3969396	TCEANC	⇧	1.23	2.63E-03
3886050	SRSF6	⇧	1.23	5.56E-05	3119339	LY6E	⇩	1.23	0.021	3565361	GMFB	⇧	1.23	0.014
2872471	DTWD2	⇧	1.23	0.022	2437645	GON4L	⇩	1.23	1.16E-03	2349848	PRMT6	⇧	1.23	0.019
2324743	ZBTB40	⇩	1.23	2.91E-03	2940987	SLC35B3	⇩	1.23	0.021	3563317	RPS29	⇧	1.23	0.023
3806905	SMAD2	⇧	1.23	0.016	3339880	RELT	⇩	1.23	1.00E-03	3459956	C12orf66	⇧	1.22	1.01E-03
3428131	SCYL2	⇧	1.23	0.013	2608801	EDEM1	⇩	1.23	0.011	2828115	LYRM7	⇧	1.22	1.64E-03
2722377	STIM2	⇩	1.23	0.047	3504791	EFHA1	⇧	1.23	9.86E-03	3829751	PDCD2L	⇧	1.22	0.010
2335986	RNF11	⇧	1.23	5.14E-03	2963313	SNX14	⇩	1.23	0.022	3591909	CTDSPL2	⇧	1.22	7.09E-04
3778823	NAPG	⇧	1.23	0.012	3879467	XRN2	⇧	1.23	3.40E-03	3301512	ALDH18A1	⇩	1.22	0.041
3364119	CYP2R1	⇧	1.23	0.016	2961317	TMEM30A	⇩	1.23	0.032	3581132	AKT1	⇧	1.22	2.94E-03
3659966	ADCY7	⇩	1.23	8.62E-03	2334404	NASP	⇧	1.23	0.041	3260666	HIF1AN	⇧	1.22	0.010
3819104	TRAPPC5	⇧	1.23	5.77E-04	2690900	CD80	⇩	1.23	0.036	2500615	TMEM87B	⇩	1.22	9.41E-03
3815538	GPX4	⇧	1.23	0.023	2427074	PSMA5	⇧	1.23	0.044	2968054	SEC63	⇩	1.22	0.025
3223551	MEGF9	⇩	1.23	0.039	3326400	CAT	⇧	1.23	0.013	2331213	MACF1	⇩	1.22	0.012
3576889	ATXN3	⇧	1.23	0.020	3707352	RNF167	⇩	1.23	2.49E-03	3168841	GRHPR	⇧	1.22	0.017
3977299	CLCN5	⇩	1.23	5.64E-03	3338552	CTTN	⇧	1.23	9.18E-03	3851826	DNASE2	⇩	1.22	0.043
3433538	RNFT2	⇩	1.23	0.012	3728097	AKAP1	⇩	1.23	0.024	3210130	C9orf41	⇧	1.22	0.014
3548346	CALM1	⇧	1.23	0.020	3996667	DKC1	⇧	1.23	0.015	2376799	IKBKE	⇩	1.22	0.017
3440017	FBXL14	⇩	1.23	3.15E-03	3844897	C19orf6	⇩	1.23	9.92E-03	2716655	MSX1	⇧	1.22	0.048
2732611	MRPL1	⇧	1.23	0.018	3375147	VPS37C	⇧	1.23	4.12E-03	3454680	TFCP2	⇧	1.22	4.68E-03
3639007	HDDC3	⇧	1.23	3.12E-03	3458614	DCTN2	⇧	1.23	8.20E-03	3224259	RBM18	⇧	1.22	8.53E-03
3472225	DDX54	⇧	1.23	7.55E-04	3334501	PRDX5	⇧	1.23	0.021	3320251	LOC100129827	⇧	1.22	0.045
3517793	KLF12	⇧	1.23	0.038	2484752	COMMD1	⇧	1.23	0.029	2369843	CEP350	⇩	1.22	3.16E-04
3127334	REEP4	⇩	1.23	0.035	2353881	MAN1A2	⇩	1.23	0.041	3825141	C19orf50	⇧	1.22	7.76E-04
2352106	CTTNBP2NL	⇩	1.23	0.029	2429842	CD58	⇩	1.23	5.02E-03	3506431	RNF6	⇧	1.22	0.025
3864286	PSG9	⇧	1.23	0.010	3168938	POLR1E	⇧	1.23	0.047	3719161	GGNBP2	⇧	1.22	0.012
3375545	FADS1	⇩	1.23	0.026	3135184	RB1CC1	⇧	1.23	1.67E-03	3821908	RNASEH2A	⇧	1.22	6.44E-03
3686080	NSMCE1	⇧	1.23	0.038	2724472	UBE2K	⇧	1.23	3.91E-03	3687698	CD2BP2	⇧	1.22	0.035
2540157	ODC1	⇧	1.23	0.027	3535780	PTGER2	⇧	1.23	0.031	2383479	BTF3P9	⇧	1.22	0.011
3580947	C14orf2	⇧	1.23	6.97E-03	3401099	FKBP4	⇧	1.23	3.15E-03	3088213	SH2D4A	⇧	1.22	0.046
3436236	ZNF664	⇧	1.23	6.57E-04	3468103	GNPTAB	⇩	1.23	0.031	3209497	FAM108B1	⇧	1.22	4.00E-03

Table B14: C9-Long Specific Gene List (n=1,007) ALL SAMPLES COMBINED [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

2411799	BEND5	⇧	1.22	0.020
3464912	POC1B	⇧	1.22	0.023
2610241	FANCD2	⇩	1.22	0.043
3729123	DHX40	⇧	1.22	3.98E-03
3636470	BTBD1	⇧	1.22	1.61E-03
3804143	RPRD1A	⇧	1.22	2.06E-03
2427688	C1orf103	⇩	1.22	0.017
3527684	RNASE3	⇧	1.22	0.038
3486807	WBP4	⇧	1.22	7.92E-03
3820443	ICAM1	⇩	1.22	0.026
3227645	UCK1	⇧	1.22	1.10E-03
3014714	ARPC1B	⇧	1.22	0.013
3838795	BCL2L12	⇧	1.22	1.72E-03
3474228	RAB35	⇧	1.22	3.88E-03
3250055	DDX21	⇧	1.22	0.028
3282268	ACBD5	⇧	1.22	0.020
3883941	TGIF2	⇧	1.22	8.33E-03
3902609	PDRG1	⇧	1.22	0.018
2691718	GOLGB1	⇩	1.22	2.51E-03
3510858	FOXO1	⇧	1.22	0.041
3108901	VPS13B	⇩	1.22	0.022
3821847	ASNA1	⇧	1.22	0.012
3740171	CRK	⇧	1.22	0.028
3402039	KCNA5	⇧	1.22	9.11E-03
3652424	EEF2K	⇩	1.22	2.04E-03
3056131	TBL2	⇩	1.22	0.012
3035049	C7orf50	⇧	1.22	0.012
3381817	UCP2	⇧	1.22	5.27E-03
3726375	EME1	⇩	1.22	0.046
3911795	ATP5E	⇧	1.22	0.028
3656760	STX4	⇧	1.22	0.012
3952703	C22orf39	⇧	1.22	0.020
3960875	DNAL4	⇧	1.22	3.41E-04
3849549	ZNF562	⇧	1.22	0.035
3860793	ZNF585B	⇧	1.22	0.039
3712098	SNORD49A	⇧	1.22	5.23E-03
2589255	FKBP7	⇩	1.22	0.017
3409330	MRPS35	⇧	1.22	0.017
3608113	IQGAP1	⇩	1.22	0.013
2539765	ITGB1BP1	⇧	1.22	0.029
3923537	C21orf33	⇧	1.22	4.96E-03
3560617	SNX6	⇧	1.22	9.66E-03
2837479	THG1L	⇧	1.22	0.031
3417345	RPL41	⇧	1.22	0.025
3012381	AKAP9	⇩	1.22	8.89E-03
2675304	TMEM115	⇩	1.22	9.71E-03
2949471	NEU1	⇩	1.22	0.032
2639054	PARP14	⇩	1.22	0.015
3439063	ZNF26	⇧	1.22	8.56E-03
3854892	LSM4	⇧	1.22	0.049
3203855	DCAF12	⇧	1.22	3.92E-03
3136129	RPS20	⇧	1.22	0.017
2324571	CELA3B	⇩	1.22	6.77E-03
3560575	EAPP	⇧	1.22	8.27E-03
3317309	CD81	⇩	1.22	8.40E-04
2786578	NDUFC1	⇧	1.22	0.022
2842570	FAF2	⇩	1.22	0.046
2619344	NKTR	⇩	1.22	3.10E-03
3914346	NPBWR2	⇧	1.22	4.21E-03
3147591	AZIN1	⇧	1.22	2.89E-03
3643813	GNPTG	⇩	1.22	0.024
2415728	TM2D1	⇩	1.22	0.036
3758157	BECN1	⇧	1.22	0.017
2925724	AKAP7	⇧	1.22	0.045
3883787	C20orf4	⇧	1.22	7.02E-04
3944922	TRIOBP	⇧	1.22	7.25E-03
3248897	NRBF2	⇧	1.22	4.43E-03
3632940	UBL7	⇧	1.21	1.68E-03
3430552	PWP1	⇧	1.21	2.90E-03
2550122	COX7A2L	⇧	1.21	6.58E-03
3680130	DEXI	⇧	1.21	0.041
2339139	INADL	⇩	1.21	0.032
2438504	MRPL24	⇧	1.21	0.029
3334783	SNX15	⇧	1.21	2.79E-03
3446868	LDHB	⇧	1.21	0.019
2438282	IQGAP3	⇩	1.21	0.014
3820177	PIN1	⇧	1.21	0.025
3716579	LRRC37BP1	⇧	1.21	0.042
4027813	F8A1	⇧	1.21	0.034
3954238	MAPK1	⇧	1.21	5.82E-03
3752002	CRLF3	⇧	1.21	0.020
3600212	LRRC49	⇧	1.21	0.020
2437753	KIAA0907	⇩	1.21	8.73E-03
3742384	SLC25A11	⇧	1.21	5.28E-03
3376529	PLA2G16	⇧	1.21	8.47E-03
2909499	GPR115	⇧	1.21	0.023
3816834	NCLN	⇩	1.21	0.017
3348189	FDX1	⇧	1.21	1.10E-03
3893072	C20orf11	⇧	1.21	0.043
2639309	SEC22A	⇩	1.21	0.034
3895795	RNF24	⇩	1.21	0.030
2916825	ANKRD6	⇧	1.21	9.13E-04
2899022	TRIM38	⇩	1.21	5.29E-03
2950590	RGL2	⇩	1.21	0.021
3734575	ICT1	⇧	1.21	0.024
3837836	CYTH2	⇧	1.21	4.70E-03

Table B14: C9-Long Specific Gene List (n=1,007) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3829768	UBA2	⇧	1.21	0.019	2813364	SLC30A5	⇩	1.21	0.026	3919124	FAM165B	⇧	1.20	1.19E-03
3956290	PITPNB	⇧	1.21	3.09E-03	2674748	CDHR4	⇧	1.21	0.012	3762416	ANKRD40	⇧	1.20	0.020
3434525	MLEC	⇩	1.21	0.017	3428573	SPIC	⇧	1.21	0.020	3311775	DHX32	⇧	1.20	0.027
2367537	C1orf9	⇩	1.21	0.043	2331158	AKIRIN1	⇧	1.21	0.019	2694617	ISY1	⇧	1.20	0.028
3851441	ZNF442	⇧	1.21	0.034	2436938	PBXIP1	⇩	1.21	0.019	3261971	CNNM2	⇩	1.20	0.020
2706938	GNB4	⇧	1.21	0.038	3000010	ZMIZ2	⇩	1.21	0.018	3474344	RPLP0	⇧	1.20	1.40E-03
3710681	MAP2K4	⇧	1.21	7.74E-03	3558226	RIPK3	⇩	1.20	6.14E-03	4011844	IL2RG	⇩	1.20	0.013
3407926	CMAS	⇧	1.21	0.044	3335070	CDC42EP2	⇧	1.20	0.027	3429365	TDG	⇧	1.20	0.040
2758043	MFSD10	⇩	1.21	8.90E-03	2479640	PPM1B	⇧	1.20	7.67E-03	3845782	PLEKHJ1	⇧	1.20	9.86E-03
3951732	CECR5	⇧	1.21	0.042	2403557	SNORA44	⇩	1.20	0.041	3725035	NFE2L1	⇩	1.20	0.034
3184940	DNAJC25	⇩	1.21	0.039	3394068	RPS25	⇧	1.20	0.013	3375951	GANAB	⇩	1.20	0.025
2446198	TOR1AIP2	⇩	1.21	9.74E-03	3708798	SENP3	⇧	1.20	8.95E-03	2916716	PNRC1	⇧	1.20	0.015
2448232	TPR	⇩	1.21	1.89E-03	2999948	OGDH	⇩	1.20	0.032	2423264	TMED5	⇩	1.20	0.045
3676649	DCI	⇧	1.21	2.96E-03	2829416	SEC24A	⇩	1.20	0.033	2974188	MED23	⇩	1.20	8.85E-03
3934245	CSTB	⇧	1.21	3.99E-03	2642562	NUDT16	⇧	1.20	6.72E-03	3575567	FOXN3	⇧	1.20	0.025
3971923	ZFX	⇧	1.21	0.025	3977646	GSPT2	⇧	1.20	0.020	2380991	IARS2	⇩	1.20	0.031
3333433	SCGB2A2	⇧	1.21	0.036	2503618	TSN	⇧	1.20	0.017	3903598	GGT7	⇩	1.20	0.022
3504691	ZDHHC20	⇩	1.21	0.035	2698738	XRN1	⇩	1.20	2.29E-03	3860824	ZNF569	⇧	1.20	1.78E-03
3821701	ZNF788	⇧	1.21	5.07E-03	2345196	HS2ST1	⇩	1.20	0.042	3768103	PSMD12	⇧	1.20	0.012
3939545	MIF	⇧	1.21	0.030	3740998	TSR1	⇧	1.20	8.90E-03	3454740	PHB	⇧	1.20	0.045
3824153	C19orf62	⇧	1.21	7.05E-03	3893910	TCEA2	⇧	1.20	0.040	3872441	ZNF552	⇧	1.20	0.038
2327418	MED18	⇧	1.21	2.83E-03	2618702	ZNF620	⇧	1.20	7.04E-04	3496916	GPR180	⇩	1.20	0.028
3959631	EIF3D	⇧	1.21	2.65E-03	3144235	TMEM55A	⇧	1.20	0.019	3065015	POLR2J	⇧	1.20	0.027
3633148	SCAMP2	⇩	1.21	0.025	3688424	C16orf58	⇩	1.20	0.011	3466740	LTA4H	⇧	1.20	0.035
4027532	GAB3	⇧	1.21	0.037	3160735	CDC37L1	⇧	1.20	0.012	3823390	OR10H3	⇧	1.20	0.038
3856594	ZNF43	⇧	1.21	0.013	3864597	C19orf61	⇩	1.20	0.015	3413950	SPATS2	⇧	1.20	0.022
2671652	ZDHHC3	⇩	1.21	0.020	3005332	CRCP	⇧	1.20	0.016	2328633	TMEM39B	⇩	1.20	0.012
2723391	MGC42157	⇧	1.21	0.018	3893086	SLC17A9	⇩	1.20	7.29E-03	2468138	LOC400940	⇧	1.20	2.09E-03
3617230	C15orf24	⇩	1.21	0.040	3203482	BAG1	⇧	1.20	0.013	2330002	EIF2C4	⇧	1.20	0.011
3894228	CSNK2A1	⇧	1.21	8.59E-03	2390298	OR2L2	⇧	1.20	0.040	2588319	KIAA1715	⇩	1.20	0.026
3903836	EIF6	⇧	1.21	2.72E-03	3980560	KIF4A	⇩	1.20	0.045	3845620	BTBD2	⇧	1.20	0.033
2545645	UCN	⇧	1.21	0.034	3576441	CCDC88C	⇩	1.20	9.88E-03	3040073	SNX13	⇩	1.20	0.032

Table B14: C9-Long Specific Gene List (n=1,007) ALL SAMPLES COMBINED [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

3978819	RRAGB	⇧	1.20	0.027	2801608	MARCH6	⇩	1.20	5.37E-03	3326842	TRIM44	⇧	1.20	0.014
2437417	ASH1L	⇩	1.20	9.06E-03	2465324	AHCTF1	⇧	1.20	0.015	3974838	DDX3X	⇧	1.20	9.16E-03
2482505	SPTBN1	⇩	1.20	4.48E-03	2514658	UBR3	⇩	1.20	8.17E-03	2460325	C1orf198	⇧	1.20	8.21E-03
3200689	RPS6	⇧	1.20	6.01E-03	3476265	EIF2B1	⇧	1.20	2.71E-03	3202171	PLAA	⇧	1.20	0.030
3819880	ZNF317	⇧	1.20	2.62E-03	3797015	ZFP161	⇧	1.20	0.023	3734797	KIAA0195	⇩	1.20	4.37E-03
2599433	USP37	⇩	1.20	0.023	3961981	POLR3H	⇧	1.20	0.038	3121023	C8orf33	⇧	1.20	4.32E-03
3872542	ZNF418	⇧	1.20	0.026	3515009	VPS36	⇧	1.20	9.91E-03	2746164	MMAA	⇩	1.20	0.028
2982319	SOD2	⇧	1.20	0.042	2903189	HLA-DRA	⇩	1.20	9.92E-03	3816919	NFIC	⇧	1.20	0.013
3462949	OSBPL8	⇧	1.20	0.034	2672712	SCAP	⇩	1.20	0.037	3657286	KIAA0664L3	⇩	1.20	0.046
3488942	NUDT15	⇧	1.20	0.026	3740304	PITPNA	⇧	1.20	0.039	2359444	LCE1B	⇧	1.20	0.030
3149754	EIF3H	⇧	1.20	1.63E-03	3829020	PDCD5	⇧	1.20	0.021	3765299	APPBP2	⇧	1.20	6.07E-03
2397732	AGMAT	⇧	1.20	1.37E-03	3389273	CASP4	⇧	1.20	0.040	4012868	RLIM	⇧	1.20	8.53E-03
3479438	CHFR	⇧	1.20	8.80E-03	3725456	ATP5G1	⇧	1.20	0.024	2486740	PNO1	⇧	1.20	0.031
2414998	MYSM1	⇩	1.20	0.022	3696057	SLC12A4	⇩	1.20	0.031	3837796	GRWD1	⇧	1.20	0.034
3627076	BNIP2	⇧	1.20	0.013	3507003	LNX2	⇧	1.20	8.47E-03	3201999	TUSC1	⇩	1.20	0.031
3307680	DCLRE1A	⇧	1.20	8.67E-03	3091797	EXTL3	⇩	1.20	0.033	3736162	TMC8	⇩	1.20	0.032
3502710	TFDP1	⇧	1.20	9.66E-03	3842264	NAT14	⇧	1.20	6.01E-03					

Table B15: C9-Short Specific Gene List (n=540) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value
2350981	GSTM1	⇧	3.05	0.022	2973376	PTPRK	⇩	1.66	0.011	3944404	APOL1	⇩	1.49	4.16E-03
3566383	C14orf105	⇩	2.09	1.66E-03	2936657	CCR6	⇩	1.65	0.013	2427208	GSTM3	⇧	1.48	5.30E-03
2440385	CD244	⇩	2.01	2.51E-03	2477073	CRIM1	⇩	1.63	0.011	3409605	FAR2	⇩	1.48	0.033
3388673	MMP7	⇩	1.99	0.016	3209384	TMEM2	⇩	1.62	0.013	3662201	MT1H	⇧	1.48	0.043
3507282	FLT1	⇩	1.97	1.84E-04	3791254	TNFRSF11A	⇩	1.62	9.00E-03	3754797	HNF1B	⇩	1.47	0.012
2607568	CHL1	⇩	1.90	9.38E-03	2705445	PLD1	⇩	1.61	8.38E-03	2849992	FAM134B	⇩	1.47	6.84E-03
3456805	GTSF1	⇧	1.90	0.013	2485406	HSPC159	⇧	1.60	6.41E-04	2615360	TGFBR2	⇩	1.47	7.52E-03
3692999	MT1G	⇧	1.89	3.78E-03	3129361	FBXO16	⇧	1.59	0.016	2973232	C6orf174	⇩	1.47	6.06E-03
2915828	NT5E	⇩	1.88	0.013	3599709	GLCE	⇩	1.59	6.10E-03	3201319	IFNA2	⇩	1.46	0.036
3623031	FBN1	⇩	1.88	3.87E-05	3494137	LMO7	⇩	1.58	1.10E-04	2730746	SLC4A4	⇩	1.46	0.016
3791958	SERPINB10	⇧	1.84	0.020	2403446	PTAFR	⇩	1.56	0.021	2732844	ANXA3	⇩	1.46	7.32E-03
3445908	EPS8	⇩	1.84	4.82E-03	3323891	GAS2	⇩	1.56	0.012	2818517	VCAN	⇩	1.46	0.044
2459042	CDC42BPA	⇩	1.84	5.71E-03	3174510	GDA	⇩	1.56	0.018	3420442	IRAK3	⇩	1.45	0.028
3569814	ACTN1	⇩	1.81	2.33E-03	3141755	HEY1	⇩	1.55	0.027	3450775	KIF21A	⇩	1.45	0.021
2853102	PRLR	⇩	1.81	4.53E-03	3138204	CYP7B1	⇩	1.55	3.00E-03	2775735	SCD5	⇩	1.45	6.58E-04
4022370	GPC4	⇩	1.80	8.64E-03	4002081	MAP7D2	⇩	1.55	0.014	3519309	SPRY2	⇩	1.45	0.025
3778504	RAB31	⇧	1.74	0.012	2664209	SH3BP5	⇧	1.55	4.18E-03	3895118	CPXM1	⇩	1.45	0.010
2731636	PARM1	⇩	1.74	1.24E-03	3841357	LILRA2	⇩	1.54	1.34E-03	2325593	CLIC4	⇧	1.45	3.01E-03
3284596	PARD3	⇩	1.73	8.10E-04	3382216	ARRB1	⇩	1.54	0.046	3721989	CNTNAP1	⇩	1.45	0.011
2898746	LRRC16A	⇩	1.72	1.82E-03	3996598	NCRNA00204	⇧	1.52	0.040	2809128	ITGA1	⇩	1.44	0.011
3150579	ENPP2	⇩	1.72	5.00E-03	2760869	HS3ST1	⇩	1.52	0.021	3396593	FEZ1	⇧	1.44	0.015
2699564	PLOD2	⇩	1.71	5.40E-03	2459173	PRO2012	⇩	1.51	3.54E-03	3139580	SLCO5A1	⇩	1.44	4.89E-04
3512948	C13orf18	⇧	1.71	4.37E-03	3941848	EMID1	⇩	1.51	1.37E-03	3852880	EMR2	⇩	1.44	0.038
3393446	FXYD2	⇩	1.70	5.83E-03	2924253	RNF217	⇩	1.51	0.033	2830861	EGR1	⇧	1.43	0.026
3718555	SLFN5	⇩	1.70	0.035	3560403	EGLN3	⇩	1.51	9.31E-03	2362333	MNDA	⇧	1.43	0.040
2571483	IL1A	⇧	1.70	0.013	3461341	CPM	⇩	1.51	0.031	3724545	ITGB3	⇩	1.43	0.033
2635741	CD96	⇩	1.69	0.018	3212848	GOLM1	⇩	1.50	4.65E-03	3091077	DPYSL2	⇧	1.43	7.30E-03
2738664	SGMS2	⇩	1.69	0.010	2422035	GBP5	⇩	1.49	2.48E-03	2879105	SPRY4	⇩	1.43	2.47E-03
3496409	GPC5	⇩	1.68	5.20E-04	2986999	GPR146	⇩	1.49	0.011	3061997	PON2	⇩	1.42	0.047
3944129	HMOX1	⇧	1.67	2.41E-04	2462160	NID1	⇩	1.49	5.43E-03	3344142	NAALAD2	⇩	1.42	0.027
3449068	TMTC1	⇩	1.66	6.83E-03	3450899	SLC2A13	⇩	1.49	5.32E-04	3164825	IFNA1	⇩	1.42	6.58E-03

Table B15: C9-Short Specific Gene List (n=540) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2584018	DPP4	⇩	1.41	0.033
3385752	RAB38	⇩	1.41	0.025
3402757	LAG3	⇩	1.41	2.34E-03
3705151	DBNDD1	⇩	1.41	0.022
3753500	SLFN11	⇩	1.40	4.71E-05
2910868	TINAG	⇩	1.40	4.73E-03
3011838	STEAP1	⇩	1.40	4.89E-03
2533999	CXCR7	⇩	1.40	0.048
3887210	MMP9	⇩	1.40	0.017
2522094	SPATS2L	⇩	1.40	0.016
2748923	GUCY1B3	⇩	1.40	0.045
2446240	TOR1AIP2	⇧	1.39	0.013
2328273	SERINC2	⇩	1.39	0.042
3972929	GK	⇩	1.39	0.011
4005859	CASK	⇩	1.39	4.60E-03
2327677	EPB41	⇧	1.38	1.28E-03
3609592	MCTP2	⇩	1.38	1.17E-04
3054165	SBDS	⇧	1.38	0.013
2842561	HIGD2A	⇧	1.38	1.46E-03
3766533	CD79B	⇩	1.38	7.82E-03
3788049	SKA1	⇧	1.38	1.01E-03
3132940	ANK1	⇩	1.37	0.012
3065244	RASA4	⇧	1.37	0.028
3236538	RPP38	⇧	1.37	0.019
2626167	PXK	⇧	1.37	2.39E-03
2932508	TIAM2	⇧	1.37	7.33E-03
2323559	MRTO4	⇧	1.36	1.15E-03
2956052	TNFRSF21	⇩	1.36	0.023
2933175	ZDHHC14	⇩	1.36	0.024
3847112	PTPRS	⇧	1.36	0.042
2538600	ADI1	⇧	1.36	4.76E-03
2626141	RPP14	⇧	1.36	3.11E-03
3761313	HOXB3	⇩	1.35	3.82E-06
3273667	ADARB2	⇩	1.35	0.016
2425400	EXTL2	⇩	1.35	7.11E-03
3816827	S1PR4	⇩	1.35	8.34E-03
3887302	CD40	⇩	1.35	9.46E-04
3016636	SH2B2	⇧	1.35	2.31E-03
2912649	COL19A1	⇩	1.35	6.12E-03
3067302	LAMB1	⇩	1.35	0.015
3796620	DLGAP1	⇩	1.35	0.028
3136178	PLAG1	⇧	1.34	0.026
3150455	TNFRSF11B	⇩	1.34	0.022
2338625	HOOK1	⇩	1.34	0.014
3734379	CD300A	⇩	1.34	1.50E-04
2848265	CMBL	⇧	1.34	8.85E-03
3220846	SUSD1	⇩	1.34	0.013
3228523	GBGT1	⇩	1.34	0.013
3103818	HNF4G	⇩	1.34	0.020
3302177	ARHGAP19	⇧	1.34	0.022
2879028	GNPDA1	⇧	1.34	4.99E-03
3011492	ADAM22	⇩	1.34	3.92E-03
2848265	CMBL	⇧	1.34	8.85E-03
3220846	SUSD1	⇩	1.34	0.013
3228523	GBGT1	⇩	1.34	0.013
3103818	HNF4G	⇩	1.34	0.020
3302177	ARHGAP19	⇧	1.34	0.022
2879028	GNPDA1	⇧	1.34	4.99E-03
3011492	ADAM22	⇩	1.34	3.92E-03
3005444	TPST1	⇩	1.33	0.017
3057955	FGL2	⇩	1.33	8.85E-03
2351004	GSTM5	⇧	1.33	4.03E-03
3570373	SLC8A3	⇩	1.33	0.029
2777487	FAM13A	⇩	1.33	0.014
3005444	TPST1	⇩	1.33	0.017
3057955	FGL2	⇩	1.33	8.85E-03
2351004	GSTM5	⇧	1.33	4.03E-03
3570373	SLC8A3	⇩	1.33	0.029
2777487	FAM13A	⇩	1.33	0.014
3712062	TRPV2	⇩	1.33	3.02E-04
3447348	SOX5	⇩	1.33	0.010
3082590	LOC286161	⇧	1.33	9.64E-03
3141589	IL7	⇩	1.33	0.038
3443891	CLEC2B	⇩	1.33	0.036
3714068	ALDH3A2	⇧	1.33	3.32E-04
3712062	TRPV2	⇩	1.33	3.02E-04
3447348	SOX5	⇩	1.33	0.010
3082590	LOC286161	⇧	1.33	9.64E-03
3141589	IL7	⇩	1.33	0.038
3443891	CLEC2B	⇩	1.33	0.036
3714068	ALDH3A2	⇧	1.33	3.32E-04
2902178	TCF19	⇧	1.32	3.14E-03
2902178	TCF19	⇧	1.32	3.14E-03
3424442	TMTC2	⇩	1.32	2.36E-04
2929127	STX11	⇧	1.32	0.022
4018080	CHRDL1	⇩	1.32	0.018
3067644	THAP5	⇧	1.32	4.95E-04
2449711	DENND1B	⇧	1.32	0.045
2946219	HIST1H2AB	⇧	1.32	0.047
3825013	SSBP4	⇩	1.32	4.95E-03
3040897	CDCA7L	⇧	1.32	0.018
2601287	AP1S3	⇧	1.32	4.10E-04
2336585	SCP2	⇧	1.32	6.03E-03
3424442	TMTC2	⇩	1.32	2.36E-04
2929127	STX11	⇧	1.32	0.022
4018080	CHRDL1	⇩	1.32	0.018

Table B15: C9-Short Specific Gene List (n=540) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3067644	THAP5	⇧	1.32	4.95E-04
2449711	DENND1B	⇧	1.32	0.045
2946219	HIST1H2AB	⇧	1.32	0.047
3825013	SSBP4	⇩	1.32	4.95E-03
3040897	CDCA7L	⇧	1.32	0.018
2601287	AP1S3	⇧	1.32	4.10E-04
2336585	SCP2	⇧	1.32	6.03E-03
3761291	HOXB2	⇩	1.31	8.05E-03
2712906	RNF168	⇧	1.31	6.94E-04
3663074	MMP15	⇩	1.31	0.019
2350489	KIAA1324	⇩	1.31	0.041
3345222	AMOTL1	⇩	1.31	2.73E-03
2826295	SNX2	⇧	1.31	7.47E-03
2350489	KIAA1324	⇩	1.31	0.041
3345222	AMOTL1	⇩	1.31	2.73E-03
2826295	SNX2	⇧	1.31	7.47E-03
3761291	HOXB2	⇩	1.31	8.05E-03
2712906	RNF168	⇧	1.31	6.94E-04
3663074	MMP15	⇩	1.31	0.019
2925590	TMEM200A	⇩	1.31	0.045
2427791	DENND2D	⇩	1.31	0.012
2744734	MGST2	⇩	1.31	0.046
3687494	MAPK3	⇧	1.31	3.50E-03
2805176	C5orf22	⇧	1.31	2.06E-03
3284188	ITGB1	⇩	1.31	2.01E-03
2829275	UBE2B	⇧	1.30	4.67E-03
2692060	PARP9	⇧	1.30	0.017
3161113	PDCD1LG2	⇩	1.30	0.025
3245881	WDFY4	⇩	1.30	5.72E-03
3004768	ZNF273	⇧	1.30	0.013
2827525	SLC12A2	⇩	1.30	3.39E-03
3061651	BET1	⇧	1.30	2.89E-03
2608419	SETMAR	⇧	1.30	8.10E-04
2514441	PPIG	⇧	1.30	1.24E-06
2715440	RNF4	⇧	1.30	0.011
3009399	HSPB1	⇧	1.30	0.026
3259978	PI4K2A	⇧	1.30	0.017
2385696	C1orf57	⇧	1.29	0.026
3234277	GATA3	⇩	1.29	0.011
3074912	DGKI	⇩	1.29	6.79E-03
2438482	ISG20L2	⇧	1.29	2.27E-04
2604390	ARL4C	⇧	1.29	0.013
2331178	NDUFS5	⇧	1.29	0.018
2471978	RHOB	⇩	1.29	0.045
3450655	CPNE8	⇩	1.29	0.011
3931112	HLCS	⇩	1.29	7.78E-05
3396107	ESAM	⇩	1.29	0.021
2316245	PRKCZ	⇧	1.29	1.37E-03
3845944	GNG7	⇧	1.29	7.26E-03
3803120	B4GALT6	⇩	1.29	9.87E-04
3402506	CD27	⇧	1.29	0.046
2682568	SHQ1	⇧	1.29	3.23E-03
3044753	LSM5	⇧	1.29	4.37E-03
2325479	RCAN3	⇧	1.29	1.54E-03
2676182	NT5DC2	⇧	1.29	3.46E-03
2558483	C2orf42	⇧	1.29	6.99E-03
3674659	GAS8	⇩	1.28	0.038
3590239	DLL4	⇩	1.28	0.044
2478748	EML4	⇧	1.28	4.42E-03
2927722	HEBP2	⇧	1.28	2.87E-03
4003895	CXorf21	⇩	1.28	0.013
2371346	RGL1	⇧	1.28	0.033
2505957	PLEKHB2	⇧	1.28	2.40E-03
2531522	CAB39	⇧	1.28	1.12E-03
2861952	MRPS27	⇧	1.28	1.51E-04
3624145	DMXL2	⇩	1.28	2.87E-03
2582124	NR4A2	⇧	1.28	7.31E-03
3740432	SCARF1	⇩	1.28	4.31E-03
3887107	ZSWIM1	⇧	1.28	4.59E-03
3385769	CTSC	⇩	1.28	0.033
3278813	FAM107B	⇧	1.28	0.030
2403470	DNAJC8	⇧	1.28	0.017
3848243	INSR	⇩	1.28	0.034
3018652	CBLL1	⇧	1.28	4.79E-05
2910680	LRRC1	⇩	1.28	0.036
2723710	PGM2	⇧	1.28	7.12E-04
3245783	WDFY4	⇩	1.28	4.65E-05
2437893	UBQLN4	⇩	1.28	0.012
3635198	BCL2A1	⇧	1.28	0.041
2442424	ILDR2	⇩	1.27	0.032
2728189	PAICS	⇧	1.27	1.41E-03
3747522	TNFRSF13B	⇩	1.27	0.037
2434159	SF3B4	⇧	1.27	7.22E-03
3851493	ZNF443	⇩	1.27	0.014
2900059	HIST1H2BM	⇧	1.27	4.51E-03
2748346	TLR2	⇩	1.27	0.019
2350922	GSTM4	⇧	1.27	0.043
2961300	COX7A2	⇧	1.27	0.024
3332886	TMEM138	⇧	1.27	0.012
3289235	SGMS1	⇩	1.27	3.90E-03
3503119	ZNF828	⇧	1.27	4.65E-03
3538087	DACT1	⇩	1.27	0.019
2655113	KLHL24	⇧	1.27	0.028
2820893	RFESD	⇧	1.27	6.91E-03
2689208	NAA50	⇧	1.27	8.49E-04
2706985	MRPL47	⇧	1.27	0.037

Table B15: C9-Short Specific Gene List (n=540) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2638962	DTX3L	⇧	1.27	0.027
2713111	MFI2	⇩	1.27	0.016
2434139	SV2A	⇩	1.27	0.025
3291601	EGR2	⇧	1.27	0.045
3342426	C11orf82	⇧	1.26	0.015
3508898	STARD13	⇩	1.26	0.032
2659887	FYTTD1	⇧	1.26	7.46E-03
2871241	MCC	⇩	1.26	9.38E-03
2696379	ANAPC13	⇧	1.26	0.012
2626258	KCTD6	⇧	1.26	4.82E-03
3350775	SIDT2	⇩	1.26	9.52E-05
3880827	GINS1	⇧	1.26	0.024
3091699	PNOC	⇧	1.26	0.015
3101385	MTFR1	⇧	1.26	7.72E-03
2979679	ZBTB2	⇧	1.26	2.85E-03
2957462	GSTA4	⇧	1.26	7.23E-03
2334279	UROD	⇧	1.26	4.43E-04
3498837	PCCA	⇩	1.26	8.25E-03
3655574	SPN	⇩	1.26	6.84E-04
3934407	ICOSLG	⇩	1.26	1.01E-04
2443989	VAMP4	⇧	1.26	0.018
2724338	LIAS	⇧	1.26	7.91E-03
2332767	C1orf50	⇧	1.26	3.93E-03
3521484	UGGT2	⇩	1.26	0.037
3005717	RABGEF1	⇧	1.26	1.17E-03
3267382	INPP5F	⇧	1.26	0.018
2633460	C3orf26	⇧	1.26	7.48E-03
2745220	ZNF330	⇧	1.26	3.49E-03
2636272	GTPBP8	⇧	1.26	3.59E-03
4024160	ATP11C	⇩	1.26	3.09E-03
2489172	MTHFD2	⇧	1.26	0.016
3748323	SHMT1	⇧	1.26	0.031
2336913	LRRC42	⇧	1.26	1.48E-04
3279982	PTPLA	⇩	1.26	0.039
2520069	C2orf88	⇩	1.26	0.024
2364189	UAP1	⇧	1.26	6.33E-03
3286975	ANUBL1	⇧	1.26	2.81E-03
2898562	ACOT13	⇧	1.26	0.011
3622386	GATM	⇧	1.25	0.011
3073981	AKR1B1	⇧	1.25	0.027
2469910	LPIN1	⇧	1.25	0.020
2766456	UGDH	⇧	1.25	7.14E-03
3316375	TSPAN4	⇩	1.25	0.047
3670700	BCMO1	⇩	1.25	0.014
2724094	FAM114A1	⇧	1.25	0.040
2538000	RNASEH1	⇧	1.25	5.58E-03
2564599	MRPS5	⇧	1.25	8.70E-03
3311157	OAT	⇧	1.25	0.036
3850660	SPC24	⇧	1.25	0.035
3272205	INPP5A	⇩	1.25	0.012
2624147	ITIH1	⇩	1.25	0.015
3118451	CHRAC1	⇧	1.25	3.16E-03
2814642	MCCC2	⇧	1.25	1.25E-03
2359433	LCE1E	⇧	1.25	7.71E-03
2523354	FAM117B	⇧	1.25	1.76E-03
2317317	TP73	⇧	1.25	0.025
2901660	PRR3	⇧	1.25	1.10E-03
3742067	UBE2G1	⇧	1.25	5.67E-03
3222128	TNFSF15	⇩	1.24	8.11E-03
2479943	SIX3	⇩	1.24	9.88E-03
3596109	FAM81A	⇧	1.24	3.45E-03
3662247	MT1X	⇧	1.24	0.014
3394412	THY1	⇩	1.24	0.040
3851055	ELOF1	⇧	1.24	0.014
2703217	KPNA4	⇧	1.24	2.27E-03
2367963	RABGAP1L	⇧	1.24	0.047
3816264	DOT1L	⇩	1.24	4.29E-03
2905404	PIM1	⇧	1.24	0.024
2758686	LYAR	⇧	1.24	8.94E-04
3927081	NCRNA00158	⇩	1.24	0.027
3344990	PANX1	⇩	1.24	0.014
3288518	C10orf72	⇩	1.24	0.046
2813442	CENPH	⇧	1.24	0.023
2363444	USP21	⇧	1.24	1.85E-04
3037304	C7orf70	⇧	1.24	0.015
2560141	MRPL53	⇧	1.24	1.89E-04
2945645	TDP2	⇧	1.24	8.23E-03
3438617	EP400	⇩	1.24	2.04E-03
3833238	LGALS14	⇧	1.24	0.044
2444790	MRPS14	⇧	1.24	2.68E-04
3758291	VAT1	⇧	1.24	0.047
2931683	C6orf211	⇧	1.24	0.020
3864430	ETHE1	⇧	1.24	0.013
3736087	TNRC6C	⇩	1.24	2.56E-03
2815455	UTP15	⇧	1.24	6.43E-03
3914273	SAMD10	⇩	1.24	0.017
3079803	PRKAG2	⇧	1.24	4.69E-04
3704376	FAM38A	⇩	1.24	4.67E-03
3454576	SLC11A2	⇩	1.24	9.89E-03
2798915	TRIP13	⇧	1.23	0.030
3561110	RALGAPA1	⇩	1.23	0.013
2838042	TTC1	⇧	1.23	0.014
2434862	LYSMD1	⇧	1.23	3.44E-03
3904527	NDRG3	⇧	1.23	0.017
2413943	USP24	⇧	1.23	0.046
3741800	ATP2A3	⇩	1.23	0.022

Table B15: C9-Short Specific Gene List (n=540) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3164601	KIAA1797	⇩	1.23	2.34E-03	3416909	BLOC1S1	⇧	1.23	0.038	3293724	C10orf54	⇩	1.22	0.039
2855443	LOC100132356	⇧	1.23	3.67E-03	3841574	LILRB1	⇩	1.23	0.037	2559494	C2orf7	⇧	1.22	0.027
3106243	RIPK2	⇧	1.23	0.039	2907568	KLHDC3	⇧	1.23	1.77E-04	3094286	PROSC	⇧	1.22	0.017
2636483	SIDT1	⇩	1.23	7.39E-03	3590108	GCHFR	⇧	1.23	0.027	2541699	FAM49A	⇧	1.22	0.048
2885099	NUDCD2	⇧	1.23	2.96E-03	3487095	DGKH	⇩	1.23	0.021	3634458	TBC1D2B	⇩	1.22	1.35E-03
2443518	C1orf156	⇧	1.23	0.013	2934167	MRPL18	⇧	1.23	3.15E-03	3757745	GHDC	⇩	1.22	2.78E-03
3920385	TTC3	⇧	1.23	0.024	2327630	YTHDF2	⇧	1.22	0.048	3448152	ITPR2	⇩	1.21	0.044
3936887	MRPL40	⇧	1.23	0.015	2334350	MMACHC	⇧	1.22	0.033	3648247	C16orf75	⇧	1.21	0.044
3852565	ASF1B	⇧	1.23	0.030	3829313	CEBPG	⇧	1.22	0.029	3651955	METTL9	⇧	1.21	7.92E-03
2877465	ETF1	⇧	1.23	6.98E-03	2342576	ACADM	⇧	1.22	3.80E-03	2911903	PTP4A1	⇧	1.21	7.01E-03
3328389	EXT2	⇩	1.23	9.44E-03	2492496	NCRNA00152	⇧	1.22	0.044	2949210	BAT4	⇧	1.21	3.48E-03
2548617	CDC42EP3	⇧	1.23	0.035	2339414	USP1	⇧	1.22	0.014	3929395	GCFC1	⇧	1.21	0.022
3434490	CABP1	⇩	1.23	0.020	3542689	PCNX	⇩	1.22	1.71E-03	3940992	ASPHD2	⇩	1.21	0.019
3539724	SYNE2	⇩	1.23	0.014	3396179	LOC100130428	⇩	1.22	0.023	3006133	STAG3L4	⇧	1.21	0.044
2694644	CNBP	⇧	1.23	7.62E-03	3489481	PHF11	⇩	1.22	1.15E-03	2881413	RPS14	⇧	1.21	0.031
2889753	ZNF354A	⇧	1.23	9.43E-03	2596955	CRYGC	⇧	1.22	0.011	3836317	VASP	⇩	1.21	4.00E-03
2964200	UBE2J1	⇧	1.23	0.013	2693149	SNX4	⇧	1.22	6.54E-03	2597273	C2orf67	⇩	1.21	4.10E-03
3771675	ST6GALNAC2	⇧	1.23	0.027	3662444	NLRC5	⇩	1.22	1.33E-03	2359780	NPR1	⇩	1.21	0.030
2645579	RASA2	⇧	1.23	7.98E-03	2403215	FGR	⇩	1.22	0.013	2398789	SDHB	⇧	1.21	6.33E-03
2986350	DLL1	⇩	1.23	0.013	3255938	OPN4	⇧	1.22	0.044	3175597	VPS13A	⇩	1.21	7.84E-03
3660175	NOD2	⇩	1.23	1.62E-03	2700500	COMMD2	⇧	1.22	0.013	3005684	KCTD7	⇧	1.21	0.015
2976727	TXLNB	⇧	1.23	0.018	3339812	ARHGEF17	⇩	1.22	0.045	2666566	NGLY1	⇧	1.21	5.76E-03
3721926	TUBG1	⇧	1.23	0.010	3048869	H2AFV	⇧	1.22	9.23E-03	2712858	UBXN7	⇧	1.21	2.43E-03
2356205	PEX11B	⇧	1.23	3.13E-04	3919033	SLC5A3	⇩	1.22	1.67E-03	2595443	WDR12	⇧	1.21	9.71E-03
2351872	RAP1A	⇧	1.23	1.16E-03	2515183	DCAF17	⇧	1.22	4.14E-03	3800070	C18orf19	⇧	1.21	0.041
2396121	DFFA	⇧	1.23	1.18E-03	2544164	C2orf44	⇧	1.22	0.015	3445643	HIST4H4	⇩	1.21	0.035
2435195	MRPL9	⇧	1.23	6.45E-03	3907934	ZNF334	⇩	1.22	0.046	3015178	ZSCAN21	⇧	1.21	1.57E-03
2489806	MRPL19	⇧	1.23	0.010	2654069	NDUFB5	⇧	1.22	8.23E-03	3818897	PNPLA6	⇩	1.21	3.03E-04
2389016	PPPDE1	⇧	1.23	0.028	2723752	TBC1D1	⇧	1.22	3.18E-03	2598099	BARD1	⇧	1.21	8.11E-04
3830993	HCST	⇩	1.23	0.022	2555630	CCT4	⇧	1.22	1.20E-04	3072368	ZC3HC1	⇧	1.21	1.51E-04
2835006	GRPEL2	⇧	1.23	3.99E-03	3665997	DUS2L	⇧	1.22	6.61E-03	3824427	FAM129C	⇧	1.21	0.022
3146103	STK3	⇩	1.23	5.91E-03	2601341	WDFY1	⇧	1.22	0.013	3761348	HOXB4	⇩	1.21	1.83E-03

Table B15: C9-Short Specific Gene List (n=540) ALL SAMPLES COMBINED [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3521174	ABCC4	⇩	1.21	0.027	2385258	C1orf124	⇧	1.21	8.12E-03	2356181	RBM8A	⇧	1.20	7.20E-03
2999816	YKT6	⇧	1.21	5.69E-03	2802398	TRIO	⇩	1.20	1.17E-03	3148963	KCNV1	⇩	1.20	2.02E-03
3860101	NFKBID	⇧	1.21	0.044	3747717	COPS3	⇧	1.20	8.37E-04	2842911	FGFR4	⇩	1.20	0.018
3536905	KTN1	⇩	1.21	1.17E-03	3934695	PTTG1IP	⇩	1.20	9.67E-03	2409220	EBNA1BP2	⇧	1.20	0.046
2319802	PGD	⇧	1.21	0.022	2946268	HIST1H2BC	⇧	1.20	0.019	3018509	DUS4L	⇧	1.20	1.64E-04
3323052	NAV2	⇩	1.21	5.62E-03	3774218	DYSFIP1	⇧	1.20	3.88E-03	3325820	DEPDC7	⇩	1.20	0.010
2662473	PRRT3	⇩	1.21	0.027	3859915	U2AF1L4	⇧	1.20	0.013	2317434	TPRG1L	⇧	1.20	0.013
3337516	LRP5	⇩	1.21	0.024	3275690	IL15RA	⇩	1.20	1.14E-03	2379132	ATF3	⇧	1.20	0.022
2750227	C4orf43	⇧	1.21	2.07E-03	3715874	ERAL1	⇧	1.20	0.012	3282974	SVIL	⇩	1.20	0.011
2979056	N⇧43	⇧	1.21	4.94E-03	2739160	CCDC109B	⇧	1.20	0.020	2807862	C5orf51	⇧	1.20	0.023
2621583	ZNF589	⇧	1.21	0.043	2534564	UBE2F	⇧	1.20	0.046	3563395	POLE2	⇧	1.20	0.049
2519140	ZC3H15	⇧	1.21	1.24E-03	2991103	BZW2	⇧	1.20	0.033	3283920	ARHGAP12	⇩	1.20	4.54E-03
3831475	ZNF382	⇧	1.21	0.038	2831567	PURA	⇧	1.20	3.65E-04	3329904	NDUFS3	⇧	1.20	4.10E-03
2475407	CLIP4	⇧	1.21	0.011	2863535	WDR41	⇧	1.20	1.50E-04	2990464	ARL4A	⇧	1.20	5.10E-03
3537264	C14orf101	⇩	1.21	2.45E-03	3000167	CCM2	⇧	1.20	0.013	2852274	MTMR12	⇧	1.20	1.25E-03
2484970	EHBP1	⇩	1.21	0.032	2952834	KCNK5	⇩	1.20	0.047	2716432	ZBTB49	⇧	1.20	1.39E-03
3302495	AVPI1	⇧	1.21	5.28E-03	2963614	CGA	⇧	1.20	9.74E-03	3556966	HAUS4	⇧	1.20	0.036
3352948	SORL1	⇩	1.21	4.21E-03	3542145	KIAA0247	⇩	1.20	0.031	3048413	POLD2	⇧	1.20	1.61E-03
3944690	CYTH4	⇩	1.21	0.024	3139722	NCOA2	⇩	1.20	8.39E-03	2767378	ATP8A1	⇩	1.20	0.019
2942578	CCDC90A	⇧	1.21	1.69E-03	2685776	MINA	⇧	1.20	9.32E-03	3101802	SGK3	⇧	1.20	1.15E-03
2549260	MAP4K3	⇧	1.21	0.025	2443537	SCYL3	⇧	1.20	5.33E-04	2951221	C6orf106	⇧	1.20	0.010
2847264	MED10	⇧	1.21	0.012	2827388	PRRC1	⇧	1.20	3.03E-03	3662106	MT1A	⇧	1.20	0.049
2825629	TNFAIP8	⇧	1.21	4.27E-03	2950214	TAP1	⇩	1.20	1.47E-03	3191147	TOR1B	⇩	1.20	0.013
3304746	USMG5	⇧	1.21	0.020	3048212	MRPS24	⇧	1.20	4.37E-04	3244622	ALOX5	⇧	1.20	0.025
2901352	PPP1R11	⇧	1.21	6.81E-03	3590086	RAD51	⇧	1.20	0.031	3781429	RBBP8	⇧	1.20	0.010
3610982	SYNM	⇩	1.21	4.97E-03	3015603	AGFG2	⇧	1.20	7.54E-03	3153428	ASAP1	⇧	1.20	5.04E-03
3654956	LAT	⇩	1.21	4.02E-03	3675116	TMEM8A	⇩	1.20	1.23E-03	3901665	C20orf3	⇩	1.20	3.91E-03
3416522	COPZ1	⇧	1.21	0.044	3019981	MDFIC	⇧	1.20	0.023	2519860	ASNSD1	⇧	1.20	0.015
3074260	WDR91	⇩	1.21	4.34E-03	2838688	MAT2B	⇧	1.20	0.013					

Table B16: C9-LongvShort Specific Gene List (n=550) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value
2421995	GBP4	⇧	2.90	4.49E-03	2452691	SLC41A1	⇩	1.80	0.015	2845274	CCDC127	⇩	1.57	0.026
2523801	CD28	⇧	2.68	0.040	3055608	TYW1B	⇩	1.79	3.88E-04	3016636	SH2B2	⇩	1.57	0.010
3174510	GDA	⇧	2.54	0.021	3726498	MYCBPAP	⇩	1.76	1.96E-03	2320727	TNFRSF1B	⇩	1.57	0.016
2497161	IL18RAP	⇧	2.50	0.032	2869438	NUDT12	⇧	1.75	0.011	3645836	ZNF75A	⇧	1.57	0.012
2742109	FGF2	⇧	2.49	4.96E-04	4035833	CD24	⇧	1.74	0.020	2775259	RASGEF1B	⇧	1.56	9.88E-03
2821347	ERAP2	⇧	2.49	0.039	3203382	SMU1	⇧	1.74	0.011	3250093	KIAA1279	⇧	1.56	0.011
3141755	HEY1	⇧	2.41	9.20E-03	3238962	KIAA1217	⇩	1.72	0.016	3066818	NAMPT	⇩	1.56	0.015
2678298	DNASE1L3	⇩	2.37	0.045	3382061	XRRA1	⇧	1.71	9.10E-03	3434393	DYNLL1	⇧	1.56	0.028
2522094	SPATS2L	⇧	2.36	4.11E-05	3916527	JAM2	⇩	1.70	0.024	2502424	INSIG2	⇩	1.55	0.024
3748449	CCDC144B	⇩	2.23	0.030	3175119	OSTF1	⇧	1.70	0.013	2902574	LY6G5B	⇩	1.54	0.014
3433466	NCRNA00173	⇩	2.23	0.012	3840224	ZNF528	⇧	1.69	6.06E-03	3856184	ZNF737	⇧	1.54	7.04E-03
2973376	PTPRK	⇧	2.22	0.015	2422035	GBP5	⇧	1.69	0.042	3375091	SLC15A3	⇩	1.54	0.043
3409605	FAR2	⇧	2.17	0.020	3149528	TRPS1	⇧	1.69	0.030	3857105	ZNF91	⇧	1.53	0.043
3652902	SCNN1B	⇩	2.08	0.030	3100497	CLVS1	⇧	1.68	0.019	4007216	UXT	⇧	1.52	0.030
2760869	HS3ST1	⇧	2.03	0.041	3494137	LMO7	⇧	1.68	0.034	3969422	RAB9A	⇧	1.52	0.021
3840194	ZNF880	⇧	1.97	6.99E-04	3184218	C9orf6	⇧	1.66	9.56E-03	3565524	GCH1	⇧	1.52	0.027
2734047	AGPAT9	⇩	1.96	0.022	2324634	CDC42	⇩	1.66	0.016	3883064	ACSS2	⇩	1.52	8.22E-03
3156307	PTK2	⇧	1.96	5.47E-03	3444086	KLRK1	⇧	1.65	4.97E-03	3876645	BTBD3	⇧	1.51	0.030
2528159	WNT10A	⇩	1.95	1.36E-03	2638728	SLC15A2	⇩	1.65	0.023	2469910	LPIN1	⇩	1.51	0.013
3214451	NFIL3	⇧	1.94	0.027	3216276	SLC35D2	⇧	1.60	0.046	4027585	MPP1	⇧	1.51	0.045
3453036	ASB8	⇧	1.89	8.76E-03	3101153	BHLHE22	⇧	1.60	0.021	2343231	NEXN	⇧	1.51	0.036
3839103	ATF5	⇩	1.88	0.036	3581637	ADAM6	⇩	1.60	0.034	3830216	FXYD5	⇩	1.50	0.023
3519309	SPRY2	⇧	1.88	0.024	2908179	VEGFA	⇩	1.60	0.016	3851441	ZNF442	⇧	1.50	1.54E-03
2777564	FAM13A	⇧	1.87	0.047	2957462	GSTA4	⇩	1.60	9.60E-03	3375735	AHNAK	⇩	1.50	0.028
3703885	SLC7A5	⇩	1.87	5.16E-03	3507798	UBL3	⇧	1.60	0.014	3142485	IMPA1	⇧	1.50	1.62E-03
2877893	MGC29506	⇩	1.86	0.019	3651639	TMEM159	⇧	1.59	0.017	2361342	SEMA4A	⇩	1.50	0.040
3841357	LILRA2	⇧	1.84	3.67E-03	3227816	RAPGEF1	⇩	1.59	8.38E-03	3577246	MOAP1	⇧	1.50	0.027
3450899	SLC2A13	⇧	1.84	6.29E-04	3382698	GUCY2E	⇩	1.59	0.014	3413875	TROAP	⇩	1.49	3.70E-04
3944129	HMOX1	⇩	1.82	0.047	3311715	UROS	⇧	1.58	2.65E-04	2620641	LIMD1	⇩	1.49	0.021
3892812	SLCO4A1	⇩	1.81	4.13E-03	3476330	CCDC92	⇧	1.58	0.017	3846831	PLIN5	⇩	1.49	0.040
3969946	ZRSR2	⇧	1.81	7.88E-03	3390641	ARHGAP20	⇧	1.58	0.013	2740507	UGT8	⇧	1.49	0.025

Table B16: C9-LongvShort Specific Gene List (n=550) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2691575	POLQ	⇩	1.49	0.035	3088213	SH2D4A	⇧	1.45	0.031	3590108	GCHFR	⇩	1.41	0.022
3726375	EME1	⇩	1.49	0.020	3090697	CDCA2	⇩	1.45	0.045	3716664	SUZ12P	⇩	1.41	0.030
3325052	EIF2AK2	⇧	1.49	0.029	3904508	SLA2	⇧	1.45	0.033	3320169	AMPD3	⇩	1.41	5.18E-03
3727712	PCTP	⇧	1.48	0.043	3366519	FANCF	⇧	1.45	0.011	2603897	TIGD1	⇩	1.41	0.014
3137875	GGH	⇩	1.48	0.030	3286393	ZNF32	⇧	1.45	0.011	2866045	TMEM161B	⇩	1.41	0.045
3167383	NUDT2	⇧	1.48	0.011	2579572	ZEB2	⇧	1.45	0.027	2330393	C1orf113	⇩	1.41	4.42E-03
2327677	EPB41	⇩	1.48	0.023	2949801	AGPAT1	⇩	1.45	0.014	3860491	ZNF260	⇧	1.40	3.03E-05
3531479	ARHGAP5	⇧	1.48	3.18E-03	3860824	ZNF569	⇧	1.45	9.59E-05	3845352	UQCR11	⇧	1.40	0.037
2878622	TAF7	⇧	1.48	0.046	3075932	PARP12	⇧	1.44	0.035	3890218	C20orf43	⇧	1.40	0.021
2914777	TTK	⇩	1.48	0.038	3670668	ATMIN	⇧	1.44	9.86E-03	2332711	PPIH	⇩	1.40	0.040
2735362	HERC6	⇧	1.48	0.040	4014191	POF1B	⇩	1.44	0.038	3633460	PTPN9	⇧	1.40	0.015
2673547	SLC26A6	⇩	1.47	3.57E-03	2813414	CCNB1	⇩	1.44	0.038	3986230	CXorf57	⇩	1.40	2.49E-03
3351895	C2CD2L	⇩	1.47	0.012	2432851	NBPF11	⇩	1.44	0.026	3375935	B3GAT3	⇩	1.40	0.016
3517793	KLF12	⇧	1.47	0.022	3724989	CDK5RAP3	⇩	1.44	6.35E-03	3251353	ANAPC16	⇧	1.40	0.019
2782292	C4orf21	⇩	1.47	0.030	3881874	ASXL1	⇩	1.43	5.08E-03	3976670	EBP	⇩	1.40	0.032
3697563	FTSJD1	⇧	1.47	2.02E-03	3380996	C11orf51	⇧	1.43	0.016	3494706	SLAIN1	⇧	1.40	0.037
3665230	HSF4	⇩	1.47	0.012	3882949	DYNLRB1	⇧	1.43	4.54E-03	3376556	ATL3	⇧	1.39	0.045
3120358	HSF1	⇩	1.47	0.029	3648306	SNN	⇧	1.43	0.021	3854877	JUND	⇩	1.39	4.23E-03
2360989	MSTO1	⇩	1.46	0.027	3409127	ARNTL2	⇧	1.43	0.041	3140640	STAU2	⇧	1.39	0.013
2908261	C6orf223	⇩	1.46	0.026	3894098	C20orf96	⇩	1.43	2.46E-03	2878368	APBB3	⇩	1.39	6.54E-03
3511698	EPSTI1	⇧	1.46	0.012	3439356	ZNF140	⇧	1.43	0.048	2391425	DVL1	⇩	1.39	0.013
3518169	COMMD6	⇧	1.46	0.017	2396009	LZIC	⇧	1.42	0.019	4010768	ZC4H2	⇧	1.39	0.015
2475678	LBH	⇧	1.46	0.016	3968664	HCCS	⇧	1.42	0.036	3911814	SLMO2	⇧	1.39	5.18E-03
3145240	C8orf37	⇧	1.46	0.040	3242425	CCNY	⇧	1.42	0.038	3139950	LACTB2	⇧	1.39	0.023
3177111	NTRK2	⇧	1.46	0.011	3909395	DPM1	⇧	1.42	6.12E-03	3440192	DCP1B	⇧	1.38	0.047
2604254	HJURP	⇩	1.45	0.030	2925724	AKAP7	⇧	1.42	0.025	2957499	ICK	⇧	1.38	0.020
3426215	MRPL42	⇧	1.45	6.73E-03	2336302	ZFYVE9	⇧	1.42	8.46E-03	3841474	LENG8	⇩	1.38	4.22E-03
3403244	CLSTN3	⇩	1.45	0.014	3351359	ATP5L	⇧	1.42	0.042	2411799	BEND5	⇧	1.38	0.028
3686080	NSMCE1	⇧	1.45	0.017	2941784	NEDD9	⇧	1.42	0.018	2458742	LIN9	⇩	1.38	0.021
2485784	ACTR2	⇧	1.45	0.023	3793760	CNDP2	⇧	1.41	6.82E-03	3507710	SLC7A1	⇩	1.38	0.018
3512050	CCDC122	⇧	1.45	0.014	3514849	NEK3	⇧	1.41	0.027	2924492	HEY2	⇧	1.37	0.037
2826295	SNX2	⇧	1.45	0.035	2413153	CPT2	⇧	1.41	0.016	3621140	LCMT2	⇧	1.37	9.30E-03

Table B16: C9-LongvShort Specific Gene List (n=550) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3397589	ETS1	⇧	1.37	0.037	3464967	GALNT4	⇧	1.35	5.57E-03	2349848	PRMT6	⇧	1.33	0.037
3318443	TRIM22	⇧	1.37	0.015	3996467	PLXNA3	⇩	1.35	4.69E-03	3788270	ELAC1	⇧	1.33	0.036
3931112	HLCS	⇧	1.37	4.56E-03	3680213	SOCS1	⇩	1.35	0.027	3462949	OSBPL8	⇧	1.33	0.041
3364119	CYP2R1	⇧	1.37	0.026	3253683	ZMIZ1	⇩	1.35	0.030	2437753	KIAA0907	⇩	1.33	0.025
3750785	SPAG5	⇩	1.37	0.017	2949118	LTB	⇧	1.35	0.036	2758043	MFSD10	⇩	1.33	0.019
3643938	TMEM204	⇧	1.37	0.031	2571457	CKAP2L	⇩	1.35	0.019	3541137	EIF2S1	⇧	1.33	0.020
3608095	ZNF774	⇧	1.37	8.89E-03	4052881	FAM72D	⇩	1.35	0.042	3929395	GCFC1	⇩	1.33	0.030
3344897	MED17	⇧	1.37	1.36E-03	3079005	RARRES2	⇧	1.35	9.57E-03	2673312	PFKFB4	⇩	1.33	0.012
2706791	ZMAT3	⇧	1.37	0.026	3432754	PLBD2	⇩	1.35	0.027	3893086	SLC17A9	⇩	1.33	4.66E-03
2426791	CLCC1	⇩	1.37	0.042	3553607	EIF5	⇧	1.35	0.024	3198289	C9orf123	⇧	1.33	0.047
3294438	ANXA7	⇧	1.37	7.52E-03	3197318	AK3	⇧	1.35	0.012	3839305	POLD1	⇩	1.33	5.90E-03
2621122	NBEAL2	⇩	1.36	0.028	2528275	FAM134A	⇩	1.34	0.017	2777639	GPRIN3	⇧	1.32	0.033
3706659	ASPA	⇧	1.36	0.017	3656760	STX4	⇧	1.34	7.97E-03	3942384	MTFP1	⇩	1.32	0.029
2899437	BTN2A1	⇩	1.36	7.34E-03	3644057	MAPK8IP3	⇩	1.34	9.73E-05	2888879	DOK3	⇩	1.32	0.045
3521174	ABCC4	⇧	1.36	0.047	2642543	NUDT16P1	⇧	1.34	0.037	2335922	CDKN2C	⇧	1.32	4.96E-03
3127334	REEP4	⇩	1.36	0.040	3677612	ZNF597	⇧	1.34	0.026	3256689	PTEN	⇧	1.32	3.32E-04
3470964	GLTP	⇧	1.36	0.039	3441011	PARP11	⇧	1.34	0.013	3864921	ZNF180	⇧	1.32	0.035
2422885	GLMN	⇩	1.36	0.039	3903598	GGT7	⇩	1.34	0.033	3367036	CCDC34	⇩	1.32	1.01E-03
3474104	CIT	⇩	1.36	0.020	3374856	MRPL16	⇧	1.34	0.039	3114600	TRMT12	⇧	1.32	6.32E-04
2560122	MOGS	⇩	1.36	0.036	3381241	ARAP1	⇩	1.34	2.41E-03	2974469	STX7	⇧	1.32	6.38E-03
3611744	LRRK1	⇩	1.36	0.020	3447863	KRAS	⇧	1.34	0.040	3007438	POM121	⇩	1.32	0.033
3494102	UCHL3	⇧	1.36	0.031	3257268	IFIT5	⇧	1.34	0.030	2356142	LIX1L	⇧	1.32	0.030
2739242	GAR1	⇧	1.36	0.027	2902427	LST1	⇧	1.34	0.035	3836432	QPCTL	⇩	1.32	0.017
3885537	PLCG1	⇩	1.35	0.019	3771602	RHBDF2	⇩	1.34	0.016	3970130	SYAP1	⇧	1.32	0.044
2422227	GEMIN8P4	⇩	1.35	0.032	3704980	FANCA	⇩	1.34	0.024	3310413	ATE1	⇧	1.32	0.030
2741901	KIAA1109	⇩	1.35	7.49E-03	2528620	GMPPA	⇩	1.34	0.042	3282268	ACBD5	⇧	1.32	0.023
3226181	ST6GALNAC4	⇩	1.35	0.012	3742783	NLRP1	⇩	1.34	0.030	3569200	ATP6V1D	⇧	1.32	0.031
2629782	EBLN2	⇩	1.35	0.018	3865586	FBXO46	⇩	1.33	0.016	3630668	CALML4	⇩	1.32	6.85E-03
3767465	AXIN2	⇩	1.35	0.030	3387483	MTMR2	⇧	1.33	5.04E-03	3603408	PSMA4	⇧	1.31	0.032
3644764	CCNF	⇩	1.35	0.037	3954238	MAPK1	⇧	1.33	9.97E-03	3303478	SEC31B	⇩	1.31	6.08E-03
3019401	ZNF277	⇧	1.35	0.019	3696035	LCAT	⇩	1.33	0.012	3945376	TOMM22	⇧	1.31	0.039
2345196	HS2ST1	⇩	1.35	0.040	3659966	ADCY7	⇩	1.33	0.014	3971923	ZFX	⇧	1.31	0.027

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3253880	PPIF	⇩	1.31	0.019	2327259	PPP1R8	⇧	1.30	1.38E-03	3333622	POLR2G	⇧	1.28	0.046
3945863	MGAT3	⇩	1.31	0.033	3536663	MAPK1IP1L	⇧	1.30	9.78E-03	3025500	BPGM	⇧	1.28	0.017
3256590	PAPSS2	⇧	1.31	9.40E-03	3480508	IL17D	⇧	1.30	0.028	3620054	RPAP1	⇩	1.28	0.030
2619344	NKTR	⇩	1.31	7.86E-03	3302328	EXOSC1	⇧	1.30	0.023	2365958	MPZL1	⇩	1.28	0.024
3716893	ATAD5	⇩	1.31	0.035	7385611	HPCAL1	⇩	1.30	0.028	2694617	ISY1	⇧	1.28	0.038
3000010	ZMIZ2	⇩	1.31	0.035	2891092	TRIM52	⇩	1.30	0.015	3475545	VPS33A	⇧	1.28	0.039
3657286	KIAA0664L3	⇩	1.31	0.023	3319613	RPL27A	⇩	1.30	0.017	3405531	DDX47	⇧	1.28	0.046
2944021	NHLRC1	⇧	1.31	0.048	3051753	FKBP9	⇧	1.30	0.039	3707352	RNF167	⇩	1.28	0.022
3928040	RWDD2B	⇧	1.31	0.027	3005332	CRCP	⇧	1.29	0.039	3751164	DHRS13	⇩	1.28	0.031
3303392	BLOC1S2	⇧	1.31	0.033	3969396	TCEANC	⇧	1.29	0.034	3649052	MKL2	⇧	1.28	0.022
2744674	RAB33B	⇧	1.31	0.046	3452970	SENP1	⇧	1.29	0.031	2982319	SOD2	⇧	1.28	0.048
3996755	BRCC3	⇧	1.31	0.023	3209497	FAM108B1	⇧	1.29	0.017	3960388	PLA2G6	⇩	1.28	0.011
2681157	TMF1	⇩	1.31	0.037	3947123	SREBF2	⇩	1.29	3.00E-03	3826601	ZNF493	⇧	1.28	0.030
2386828	EDARADD	⇧	1.31	6.83E-03	3719362	AATF	⇧	1.29	0.022	3843346	ZNF549	⇧	1.28	7.51E-03
3027503	ADCK2	⇩	1.31	0.013	2439975	IGSF8	⇩	1.29	0.027	3594066	TMOD3	⇧	1.28	6.23E-04
3578089	C14orf49	⇩	1.31	0.035	3591674	C15orf63	⇩	1.29	0.037	3965393	ALG12	⇩	1.28	0.037
2786567	C4orf49	⇧	1.31	0.013	3333358	INCENP	⇩	1.29	6.72E-03	3756344	SMARCE1	⇧	1.28	0.011
2954355	CUL7	⇩	1.31	0.019	3339880	RELT	⇩	1.29	0.014	3891643	C20orf177	⇧	1.28	0.043
3310479	NSMCE4A	⇧	1.31	6.16E-03	3378895	PITPNM1	⇩	1.29	0.015	3882533	CBFA2T2	⇩	1.28	0.040
3835280	ZNF221	⇧	1.30	0.013	3260586	SCD	⇩	1.29	9.20E-04	3031383	REPIN1	⇩	1.28	0.035
3399623	THYN1	⇩	1.30	0.049	4027387	FAM3A	⇩	1.29	4.91E-03	2913594	MTO1	⇩	1.28	0.046
2771654	CENPC1	⇩	1.30	0.039	3414512	LARP4	⇧	1.29	0.049	2622859	HEMK1	⇩	1.27	0.013
3325680	EIF3M	⇧	1.30	0.022	3580876	PPP1R13B	⇧	1.29	0.020	3317309	CD81	⇩	1.27	8.99E-04
3765299	APPBP2	⇧	1.30	0.019	3948590	RIBC2	⇧	1.29	0.019	2955025	MRPL14	⇩	1.27	0.046
2715580	SH3BP2	⇩	1.30	0.032	2559619	NAT8	⇧	1.29	0.047	3192653	GTF3C5	⇩	1.27	0.016
3695916	CENPT	⇩	1.30	2.56E-03	3428573	SPIC	⇧	1.29	0.039	3439305	ZNF84	⇧	1.27	0.011
3899551	RBBP9	⇧	1.30	0.027	3347549	CUL5	⇧	1.29	0.016	2544012	ATAD2B	⇩	1.27	0.046
2674963	MON1A	⇧	1.30	0.035	3931329	DSCR3	⇧	1.29	0.027	3617412	LPCAT4	⇩	1.27	0.035
2404521	PEF1	⇧	1.30	0.043	2436283	DENND4B	⇩	1.29	0.010	3823625	AP1M1	⇧	1.27	0.021
3204721	TPM2	⇧	1.30	0.038	3623683	GABPB1	⇧	1.29	0.025	2333168	C1orf84	⇩	1.27	0.039
3099566	FAM110B	⇧	1.30	7.69E-03	3499585	BIVM	⇧	1.29	0.016	3576441	CCDC88C	⇩	1.27	9.55E-03
2939814	RPP40	⇧	1.30	4.71E-03	3982811	SH3BGRL	⇧	1.28	0.047	3722770	C17orf53	⇩	1.27	0.039

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3600212	LRRC49	⇧	1.27	0.035	3887049	UBE2C	⇩	1.26	0.031	3689922	VPS35	⇧	1.25	0.013
3841545	LILRA1	⇧	1.27	5.12E-03	3848871	CD320	⇩	1.26	0.024	3985218	ARMCX5	⇧	1.24	0.016
2890859	MGAT1	⇩	1.27	0.043	3157138	LYPD2	⇧	1.26	0.026	3327906	API5	⇧	1.24	2.81E-03
2950474	RXRB	⇩	1.27	0.022	3692895	NUDT21	⇧	1.26	0.022	2900299	ZNF192	⇩	1.24	0.048
3672661	FOXL1	⇩	1.27	0.027	3226709	C9orf114	⇧	1.26	0.040	2407729	RRAGC	⇧	1.24	0.030
3611049	LRRC28	⇧	1.27	0.037	3504392	N6AMT2	⇧	1.26	0.020	2904528	ZNF76	⇩	1.24	0.028
3688424	C16orf58	⇩	1.27	0.030	3860208	ALKBH6	⇩	1.26	0.042	3244061	ZNF487P	⇧	1.24	0.039
3201277	KLHL9	⇧	1.27	0.022	2852742	AMACR	⇧	1.26	0.029	3602526	FBXO22	⇧	1.24	0.023
3918696	SON	⇧	1.27	0.015	2609608	SETD5	⇩	1.25	0.015	2375011	ELF3	⇧	1.24	0.025
2954423	MRPL2	⇩	1.27	0.048	2806376	SPEF2	⇧	1.25	0.015	2711225	ATP13A4	⇩	1.24	9.82E-03
2888674	MXD3	⇩	1.27	0.021	3229797	QSOX2	⇩	1.25	0.037	2607020	MTERFD2	⇩	1.24	0.044
3843399	ZNF134	⇧	1.26	0.045	3657367	ZNF267	⇧	1.25	0.027	3275611	ANKRD16	⇧	1.24	0.020
3184940	DNAJC25	⇩	1.26	0.048	2493813	ZNF2	⇧	1.25	6.67E-03	3892561	FLJ44790	⇧	1.24	0.037
3636470	BTBD1	⇧	1.26	0.014	2451155	PTPN7	⇩	1.25	6.46E-03	2903782	ITPR3	⇩	1.24	0.036
3212277	C9orf64	⇧	1.26	0.024	3774635	FASN	⇩	1.25	0.040	3294242	ECD	⇧	1.24	0.028
2395626	GPR157	⇩	1.26	0.042	3709327	CNTROB	⇩	1.25	0.014	3224259	RBM18	⇧	1.24	0.041
3487600	C13orf31	⇧	1.26	5.34E-03	3739827	GLOD4	⇧	1.25	0.011	3334749	PPP2R5B	⇩	1.24	0.049
4051226	SEMA4D	⇩	1.26	4.91E-03	3391029	PPP2R1B	⇧	1.25	1.91E-03	2907018	TAF8	⇩	1.23	0.047
3599432	FEM1B	⇧	1.26	0.020	2440018	DCAF8	⇩	1.25	4.58E-03	3377358	BATF2	⇧	1.23	0.041
3482977	POLR1D	⇧	1.26	7.06E-03	3677315	PKMYT1	⇩	1.25	0.036	2715076	WHSC1	⇩	1.23	0.032
3555340	TEP1	⇩	1.26	0.037	3340410	NEU3	⇧	1.25	0.023	3204692	C9orf100	⇩	1.23	0.035
2620985	TMIE	⇧	1.26	0.047	3895297	DDRGK1	⇩	1.25	0.011	2633166	OR5K2	⇩	1.23	0.027
3363979	PSMA1	⇧	1.26	0.016	4011768	SNX12	⇧	1.25	0.012	2348792	CCDC76	⇩	1.23	0.014
3645253	SRRM2	⇩	1.26	2.65E-04	3590422	RTF1	⇧	1.25	0.036	3820921	SMARCA4	⇩	1.23	0.041
3168309	RECK	⇧	1.26	0.022	3334325	VEGFB	⇩	1.25	0.031	2621917	WDR6	⇩	1.23	9.49E-03
2488114	ZNF638	⇩	1.26	0.043	3874438	CDC25B	⇩	1.25	0.010	3677356	HCFC1R1	⇩	1.23	0.018
3195363	ARRDC1	⇧	1.26	0.013	3294476	ZMYND17	⇩	1.25	0.034	2325358	GRHL3	⇧	1.23	0.049
3908631	PREX1	⇩	1.26	3.91E-03	3865776	IRF2BP1	⇩	1.25	1.17E-03	2333678	B4GALT2	⇩	1.23	0.036
3221646	POLE3	⇧	1.26	0.045	2892738	PRPF4B	⇩	1.25	0.049	2949588	DOM3Z	⇩	1.23	0.034
3228373	TSC1	⇩	1.26	0.021	3181600	GALNT12	⇩	1.25	0.049	3751323	MYO18A	⇩	1.23	0.013
3719150	PIGW	⇧	1.26	0.041	3695631	TPPP3	⇧	1.25	0.048	3863021	TGFB1	⇩	1.23	0.014
2502300	DDX18	⇧	1.26	0.049	3299578	CH25H	⇧	1.25	1.71E-03	3601675	ARID3B	⇩	1.23	0.023

Table B16: C9-LongvShort Specific Gene List (n=550) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3418513	MARCH9	⇩	1.23	0.037
2500875	CHCHD5	⇩	1.23	0.026
2829463	CAMLG	⇩	1.23	0.039
3139722	NCOA2	⇧	1.23	0.034
3653619	LCMT1	⇧	1.23	0.015
3853063	ILVBL	⇩	1.23	0.036
2410574	LRRC41	⇩	1.23	0.032
3855410	SUGP2	⇩	1.22	4.99E-03
2402601	UBXN11	⇩	1.22	6.18E-03
2834093	TCERG1	⇩	1.22	0.030
3645881	ZNF174	⇧	1.22	0.028
3475350	LOC338799	⇩	1.22	0.039
3834674	CIC	⇩	1.22	3.13E-03
3826542	ZNF738	⇧	1.22	0.012
3264004	SHOC2	⇧	1.22	0.040
2643095	BFSP2	⇧	1.22	0.034
3334604	LOC439914	⇩	1.22	0.044
3754227	MYO19	⇩	1.22	0.024
3807370	DYM	⇧	1.22	0.045
3549708	SERPINA4	⇧	1.22	0.040
3135452	ATP6V1H	⇧	1.22	0.015
3436236	ZNF664	⇧	1.22	0.017
2436338	CRTC2	⇩	1.22	0.036
2949148	BAT3	⇩	1.22	0.012
2662956	VGLL4	⇩	1.22	0.025
3325307	ELP4	⇧	1.22	0.036
3077766	TPK1	⇧	1.22	0.048
2358520	SETDB1	⇩	1.22	0.039
2756673	GAK	⇩	1.21	0.039
3432438	OAS1	⇧	1.21	0.012
2977471	ADAT2	⇩	1.21	0.048
3064230	GIGYF1	⇩	1.21	0.012
3645402	FLYWCH1	⇩	1.21	0.030
2335048	CYP4A22	⇧	1.21	8.26E-03
2964052	SRSF12	⇧	1.21	0.016
3742384	SLC25A11	⇧	1.21	0.024
3373962	UBE2L6	⇧	1.21	6.52E-03
2641532	COPG	⇩	1.21	0.049
3228097	TTF1	⇩	1.21	6.66E-03
3742212	ALOX15	⇧	1.21	0.022
3845365	TCF3	⇩	1.21	0.042
2582562	ACVR1	⇧	1.21	0.026
3483348	POMP	⇧	1.20	0.046
3652424	EEF2K	⇩	1.20	0.021
3513883	KPNA3	⇧	1.20	0.036
3830712	MLL4	⇩	1.20	0.027
3016098	TRIM56	⇩	1.20	0.036
2655438	DVL3	⇩	1.20	1.84E-03
3195174	MAN1B1	⇩	1.20	7.53E-03
3863435	POU2F2	⇩	1.20	0.030
2560149	CCDC142	⇩	1.20	4.94E-03
3642060	CHSY1	⇩	1.20	0.045
3224087	TTLL11	⇧	1.20	0.034
2358171	PRPF3	⇩	1.20	0.016
3742236	PELP1	⇩	1.20	8.47E-03
3963754	SMC1B	⇧	1.20	0.039
3223605	FBXW2	⇧	1.20	0.017
2713016	C3orf34	⇧	1.20	0.041
2536625	BOK	⇧	1.20	0.033
2867145	FAM172A	⇧	1.20	0.049
3748909	SLC47A2	⇧	1.20	0.033
3707258	MINK1	⇩	1.20	4.83E-03
3595096	TCF12	⇧	1.20	7.03E-03
2894711	TMEM14B	⇧	1.20	9.40E-03

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value
4048241	HLA-DRB5	⇩	11.7	0.018	2766492	C4orf34	⇧	1.77	0.015	3257204	IFIT3	⇧	1.65	0.044
3718555	SLFN5	⇧	2.97	0.023	2768981	SGCB	⇩	1.77	0.046	3351841	HMBS	⇧	1.65	0.019
2821347	ERAP2	⇧	2.44	0.026	3507798	UBL3	⇧	1.76	1.62E-03	2899437	BTN2A1	⇩	1.65	2.24E-05
2678298	DNASE1L3	⇩	2.40	0.026	2528159	WNT10A	⇩	1.76	2.51E-03	3453036	ASB8	⇧	1.65	0.021
3175971	PSAT1	⇩	2.26	0.019	2820865	ARSK	⇩	1.76	0.013	3061805	SGCE	⇩	1.64	0.014
3456805	GTSF1	⇧	2.05	0.052	3945314	KDELR3	⇩	1.76	0.031	3782166	IMPACT	⇧	1.64	4.75E-03
3841621	LILRB4	⇩	2.04	0.020	3840194	ZNF880	⇧	1.76	1.55E-03	3380996	C11orf51	⇧	1.63	6.78E-04
3856646	ZNF208	⇧	1.97	0.046	4007216	UXT	⇧	1.75	2.47E-03	3916527	JAM2	⇩	1.63	0.022
3892812	SLCO4A1	⇩	1.93	7.09E-04	3354443	SLC37A2	⇩	1.75	0.030	3761714	GNGT2	⇧	1.63	1.46E-03
2887490	STC2	⇩	1.91	9.30E-03	3458587	DDIT3	⇩	1.74	0.018	3849752	ZNF426	⇧	1.63	1.15E-03
3023883	CPA4	⇩	1.90	0.024	3433466	NCRNA00173	⇩	1.74	0.049	3911814	SLMO2	⇧	1.63	3.50E-05
2734047	AGPAT9	⇩	1.90	0.017	3309602	RGS10	⇧	1.74	4.03E-03	3137875	GGH	⇩	1.63	4.24E-03
3439178	PXMP2	⇧	1.89	5.99E-03	2475678	LBH	⇧	1.73	3.47E-04	3707199	PSMB6	⇧	1.62	8.93E-03
2400518	ECE1	⇩	1.88	0.028	3741528	TAX1BP3	⇧	1.73	0.011	3311715	UROS	⇧	1.62	4.57E-05
3764738	SKA2	⇧	1.86	0.015	3216276	SLC35D2	⇧	1.72	0.014	3175119	OSTF1	⇧	1.62	0.013
3913483	TCFL5	⇧	1.85	0.022	3236538	RPP38	⇧	1.72	2.73E-03	2638728	SLC15A2	⇩	1.62	0.016
3925639	NRIP1	⇧	1.85	0.039	2786322	SLC7A11	⇩	1.72	0.024	3969422	RAB9A	⇧	1.62	4.70E-03
3333899	RARRES3	⇧	1.85	0.010	2909020	ENPP4	⇩	1.71	0.021	4035833	CD24	⇧	1.62	0.025
3127745	TNFRSF10D	⇩	1.84	7.50E-03	3727712	PCTP	⇧	1.71	3.78E-03	3651639	TMEM159	⇧	1.62	7.43E-03
2877893	MGC29506	⇩	1.84	0.012	3721989	CNTNAP1	⇩	1.71	0.029	3840142	ZNF480	⇧	1.62	0.031
3043936	FKBP14	⇩	1.81	0.036	3839103	ATF5	⇩	1.70	0.050	3403244	CLSTN3	⇩	1.61	9.55E-04
3703885	SLC7A5	⇩	1.81	3.73E-03	3402315	CD9	⇩	1.70	0.039	2756029	FRG1	⇩	1.61	0.021
3476330	CCDC92	⇧	1.80	1.27E-03	3132016	FGFR1	⇩	1.69	0.019	2594497	CLK1	⇩	1.61	0.021
3550328	C14orf129	⇧	1.80	0.010	3618736	RASGRP1	⇩	1.69	0.041	3670668	ATMIN	⇧	1.61	5.26E-04
3676262	SEPX1	⇧	1.79	8.12E-03	2908179	VEGFA	⇩	1.69	4.18E-03	2949256	BAT5	⇩	1.61	1.28E-03
3577940	CLMN	⇧	1.79	0.053	2601414	SERPINE2	⇩	1.68	4.75E-03	3202316	MOBKL2B	⇧	1.60	0.027
3969946	ZRSR2	⇧	1.78	4.52E-03	3382061	XRRA1	⇧	1.68	5.68E-03	2725013	UCHL1	⇩	1.60	0.052
3018866	DNAJB9	⇩	1.78	0.024	3936550	USP18	⇧	1.68	9.55E-03	2877639	SIL1	⇩	1.60	0.019
3453405	FKBP11	⇩	1.78	7.39E-03	2845274	CCDC127	⇩	1.66	7.47E-03	3987446	ALG13	⇧	1.59	0.025
3203382	SMU1	⇧	1.78	4.19E-03	2742109	FGF2	⇧	1.66	0.021	3057755	POMZP3	⇧	1.59	5.94E-03
2354634	PHGDH	⇩	1.77	0.037	3980455	IGBP1	⇧	1.65	3.13E-03	3432754	PLBD2	⇩	1.59	4.66E-04

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3543673	ACOT2	⇧	1.59	0.021
3251353	ANAPC16	⇧	1.59	8.06E-04
3994451	CXorf40A	⇧	1.59	7.19E-04
2356115	TXNIP	⇧	1.59	0.051
3663055	C16orf57	⇧	1.58	1.83E-03
3355021	FAM118B	⇧	1.58	0.015
3840224	ZNF528	⇧	1.58	8.10E-03
3936442	PEX26	⇧	1.58	3.63E-03
2407478	FHL3	⇧	1.58	0.038
2438892	FCRL5	⇩	1.58	0.052
3375999	C11orf48	⇧	1.58	0.035
3747199	CENPV	⇧	1.58	0.023
3156307	PTK2	⇧	1.58	0.031
2643324	SRPRB	⇩	1.57	0.016
3263944	PDCD4	⇧	1.57	0.013
3645338	PRSS21	⇩	1.57	0.034
3734355	GPRC5C	⇩	1.56	0.047
3893033	DPH3P1	⇧	1.56	0.048
2837810	UBLCP1	⇧	1.56	0.033
2826295	SNX2	⇧	1.56	6.84E-03
2379280	FLVCR1	⇩	1.56	0.015
2324634	CDC42	⇩	1.56	0.018
2562821	VPS24	⇧	1.56	2.44E-03
3002873	LANCL2	⇧	1.56	0.026
3387537	MAML2	⇧	1.55	0.043
2375212	PPP1R12B	⇩	1.55	5.78E-03
3434726	P2RX7	⇩	1.55	0.026
3697563	FTSJD1	⇧	1.55	2.21E-04
3605268	TM6SF1	⇩	1.55	0.047
4013434	TAF9B	⇧	1.55	0.011
3414695	ATF1	⇧	1.55	0.029
3019401	ZNF277	⇧	1.55	5.09E-04
3866276	SLC1A5	⇩	1.54	5.21E-03
2502424	INSIG2	⇩	1.54	0.015
3184218	C9orf6	⇧	1.54	0.015
2452691	SLC41A1	⇩	1.54	0.046
2892277	NQO2	⇩	1.53	7.22E-03
4010768	ZC4H2	⇧	1.53	8.94E-04
3666686	NIP7	⇧	1.53	0.012
4022106	MBNL3	⇧	1.53	0.012
3996467	PLXNA3	⇩	1.52	6.71E-05
3416909	BLOC1S1	⇧	1.52	7.43E-03
3992408	FHL1	⇧	1.52	0.045
3988538	IL13RA1	⇩	1.52	0.047
3976670	EBP	⇩	1.52	4.64E-03
3055608	TYW1B	⇩	1.52	3.33E-03
2384562	RAB4A	⇧	1.52	4.18E-03
2349848	PRMT6	⇧	1.52	1.68E-03
3023060	CALU	⇩	1.52	0.024
2821981	FAM174A	⇩	1.52	0.018
3238962	KIAA1217	⇩	1.52	0.038
2443335	SLC19A2	⇩	1.51	0.026
2690850	TMEM39A	⇩	1.51	0.034
2673547	SLC26A6	⇩	1.51	9.18E-04
3100497	CLVS1	⇧	1.51	0.039
3407793	PYROXD1	⇧	1.51	0.032
2954324	MEA1	⇧	1.51	4.40E-03
2560122	MOGS	⇩	1.51	3.16E-03
3053691	GUSB	⇩	1.50	6.74E-03
3945376	TOMM22	⇧	1.50	1.49E-03
3633460	PTPN9	⇧	1.50	2.06E-03
3198289	C9orf123	⇧	1.49	3.05E-03
3950452	CRELD2	⇩	1.49	0.026
3645836	ZNF75A	⇧	1.49	0.014
3224197	NDUFA8	⇧	1.49	0.011
3719362	AATF	⇧	1.49	3.16E-04
3114832	SQLE	⇩	1.49	7.36E-03
3557947	CHMP4A	⇧	1.49	0.014
3716411	CPD	⇩	1.49	0.034
3890218	C20orf43	⇧	1.49	4.00E-03
2320727	TNFRSF1B	⇩	1.49	0.020
2640579	PLXNA1	⇩	1.49	0.011
3507710	SLC7A1	⇩	1.48	1.93E-03
3333711	SLC3A2	⇩	1.48	2.90E-03
3244539	ZNF22	⇧	1.48	0.011
3101153	BHLHE22	⇧	1.48	0.033
3857105	ZNF91	⇧	1.48	0.040
3665230	HSF4	⇩	1.48	5.56E-03
3190420	CERCAM	⇩	1.48	6.54E-03
3907111	TOMM34	⇧	1.48	0.012
3866094	PTGIR	⇩	1.48	0.013
2409104	SLC2A1	⇩	1.48	0.027
2794902	AGA	⇩	1.48	0.040
3543619	C14orf169	⇧	1.48	0.044
3256560	MINPP1	⇩	1.47	0.019
3242425	CCNY	⇧	1.47	0.014
2951567	FKBP5	⇧	1.47	2.59E-03
3821015	LDLR	⇩	1.47	1.21E-03
3440192	DCP1B	⇧	1.47	0.011
3404436	CLEC2D	⇩	1.47	0.024
3397589	ETS1	⇧	1.47	6.66E-03
3659966	ADCY7	⇩	1.47	6.84E-04
3826803	ZNF492	⇧	1.47	0.047
2320581	PLOD1	⇩	1.47	0.016
3254488	C10orf58	⇩	1.47	0.050
3101622	RRS1	⇧	1.47	0.034

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2318736	PARK7	⇧	1.47	2.98E-03
2899216	HIST1H4E	⇧	1.47	0.030
3434393	DYNLL1	⇧	1.46	0.037
3230141	NOTCH1	⇩	1.46	5.98E-03
3726325	XYLT2	⇩	1.46	4.69E-03
3243908	CSGALNACT2	⇩	1.46	0.019
2899413	BTN3A3	⇩	1.46	6.13E-03
2439508	OR6N2	⇧	1.46	0.019
3595846	FAM63B	⇩	1.46	8.19E-03
3888949	MOCS3	⇧	1.46	4.65E-03
3928040	RWDD2B	⇧	1.46	1.31E-03
4004819	DYNLT3	⇧	1.45	0.035
3892918	C20orf20	⇧	1.45	0.013
2495806	MRPL30	⇧	1.45	0.013
3793760	CNDP2	⇧	1.45	1.73E-03
3771602	RHBDF2	⇩	1.45	1.12E-03
3886512	TTPAL	⇧	1.45	0.013
3564872	GNPNAT1	⇧	1.45	0.029
2620538	LARS2	⇩	1.45	0.012
2941784	NEDD9	⇧	1.45	6.68E-03
2426791	CLCC1	⇩	1.45	9.54E-03
3167383	NUDT2	⇧	1.45	8.25E-03
3738629	SLC16A3	⇩	1.45	3.41E-03
3883064	ACSS2	⇩	1.44	0.010
2539765	ITGB1BP1	⇧	1.44	0.011
3031967	CHPF2	⇩	1.44	0.024
3489538	ARL11	⇧	1.44	9.86E-03
3406421	STRAP	⇧	1.44	6.13E-03
3648306	SNN	⇧	1.44	0.010
3722338	IFI35	⇧	1.44	0.021
3486728	SLC25A15	⇧	1.44	0.015
3470964	GLTP	⇧	1.44	8.84E-03
3130211	PPP2CB	⇧	1.44	0.011
3177111	NTRK2	⇧	1.44	7.62E-03
3617920	ATPBD4	⇧	1.44	2.84E-03
4027585	MPP1	⇧	1.43	0.053
3790704	PMAIP1	⇧	1.43	0.015
3986933	NXT2	⇧	1.43	4.54E-03
3380980	C11orf59	⇧	1.43	4.69E-03
2888243	KIAA1191	⇧	1.43	7.89E-03
3277468	USP6NL	⇧	1.43	0.049
3725083	SNX11	⇧	1.43	0.023
3708826	EIF4A1	⇧	1.43	0.041
3931329	DSCR3	⇧	1.43	1.18E-03
3860491	ZNF260	⇧	1.43	3.97E-06
2912889	SMAP1	⇧	1.43	8.85E-03
3010082	PHTF2	⇩	1.43	0.014
3954525	ZNF280B	⇧	1.43	4.68E-03
3369762	COMMD9	⇧	1.43	0.027
3840164	ZNF610	⇧	1.43	0.028
3899551	RBBP9	⇧	1.43	1.96E-03
3625326	CCPG1	⇩	1.43	0.029
3375935	B3GAT3	⇩	1.43	6.17E-03
3747522	TNFRSF13B	⇩	1.42	0.023
3881282	HM13	⇩	1.42	0.015
3227816	RAPGEF1	⇩	1.42	0.024
3954238	MAPK1	⇧	1.42	8.90E-04
3340589	SERPINH1	⇩	1.42	0.038
2356142	LIX1L	⇧	1.42	3.62E-03
3607927	SEMA4B	⇩	1.42	0.017
3531479	ARHGAP5	⇧	1.42	3.31E-03
3494102	UCHL3	⇧	1.42	7.34E-03
3629378	MTFMT	⇧	1.42	2.95E-03
2515933	ZAK	⇧	1.42	0.039
2395890	CLSTN1	⇩	1.42	0.017
3225398	HSPA5	⇩	1.42	0.052
3628923	FAM96A	⇧	1.42	0.035
2436826	KCNN3	⇩	1.42	0.040
3590422	RTF1	⇧	1.42	7.71E-04
2829171	TCF7	⇧	1.42	0.038
4000132	TRAPPC2	⇧	1.42	0.021
2562233	RETSAT	⇩	1.42	0.014
3904527	NDRG3	⇧	1.42	0.011
3076753	KIAA1147	⇩	1.42	0.039
2639225	PDIA5	⇩	1.42	0.048
3184940	DNAJC25	⇩	1.42	2.29E-03
3590341	CHP	⇧	1.42	6.68E-03
3856184	ZNF737	⇧	1.42	0.016
3557898	TM9SF1	⇩	1.42	0.019
3387483	MTMR2	⇧	1.41	4.16E-04
2529546	ACSL3	⇩	1.41	0.029
2706791	ZMAT3	⇧	1.41	7.57E-03
3565524	GCH1	⇧	1.41	0.042
3836432	QPCTL	⇩	1.41	1.71E-03
2878368	APBB3	⇩	1.41	2.04E-03
3201437	CDKN2A	⇧	1.41	0.029
3850576	YIPF2	⇩	1.41	0.025
2957499	ICK	⇧	1.41	7.36E-03
3453556	PRKAG1	⇧	1.41	2.11E-03
3325680	EIF3M	⇧	1.41	1.89E-03
3394123	HYOU1	⇩	1.41	0.042
3351895	C2CD2L	⇩	1.41	0.013
2611848	SLC6A6	⇩	1.41	0.016
3474104	CIT	⇩	1.41	5.09E-03
3303300	CHUK	⇧	1.41	0.035
3344861	C11orf54	⇧	1.41	0.014

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

3073981	AKR1B1	⇧	1.41	0.027	2565579	ANKRD39	⇧	1.40	8.68E-05	3434760	P2RX4	⇩	1.38	0.031
2450668	TMEM9	⇩	1.41	0.029	3687789	DCTPP1	⇧	1.40	0.026	3742067	UBE2G1	⇧	1.38	4.47E-03
3815014	BSG	⇩	1.41	7.98E-03	2599955	ATG9A	⇩	1.40	0.011	2704267	GOLIM4	⇩	1.38	0.014
3558145	CIDEB	⇧	1.41	0.018	3406493	DERA	⇧	1.40	0.019	3078656	ZNF767	⇩	1.38	0.016
3849797	ZNF561	⇧	1.41	3.39E-03	2464484	FAM36A	⇩	1.39	0.017	2360989	MSTO1	⇩	1.38	0.038
3946351	ADSL	⇧	1.41	1.21E-03	2835576	SYNPO	⇧	1.39	0.015	3328214	ALKBH3	⇧	1.38	8.33E-03
3588658	C15orf41	⇧	1.41	0.016	3317309	CD81	⇩	1.39	6.95E-06	3597977	TRIP4	⇧	1.38	5.27E-03
3861302	YIF1B	⇩	1.41	0.047	2815965	HMGCR	⇩	1.39	0.019	2899333	BTN3A2	⇩	1.38	0.031
3197318	AK3	⇧	1.40	2.07E-03	3881874	ASXL1	⇩	1.39	4.56E-03	3712363	MPRIP	⇩	1.38	0.021
2396461	SRM	⇧	1.40	9.65E-03	2758043	MFSD10	⇩	1.39	3.58E-03	2621122	NBEAL2	⇩	1.38	0.014
3442854	SLC2A3	⇩	1.40	0.022	3708074	XAF1	⇧	1.39	9.97E-03	3824197	MRPL34	⇧	1.38	0.015
3517793	KLF12	⇧	1.40	0.026	3065638	DNAJC2	⇩	1.39	0.024	2741901	KIAA1109	⇩	1.38	2.33E-03
2567583	RNF149	⇩	1.40	0.011	3607183	MRPS11	⇧	1.39	2.60E-03	3677612	ZNF597	⇧	1.38	8.47E-03
2579572	ZEB2	⇧	1.40	0.025	3257670	PCGF5	⇧	1.39	0.018	2730531	UTP3	⇧	1.38	0.029
2739242	GAR1	⇧	1.40	8.12E-03	3748432	FAM106A	⇩	1.39	2.10E-03	3145240	C8orf37	⇧	1.38	0.053
3579205	SETD3	⇧	1.40	2.97E-03	2617563	MYD88	⇧	1.39	0.017	3148582	EIF3E	⇧	1.38	0.027
3750685	SLC46A1	⇩	1.40	0.020	3023384	AHCYL2	⇧	1.39	0.018	3617412	LPCAT4	⇩	1.38	3.27E-03
3962219	NAGA	⇩	1.40	0.019	3986514	PRPS1	⇧	1.39	0.040	3698055	TXNL4B	⇧	1.37	0.026
2813414	CCNB1	⇩	1.40	0.035	3127334	REEP4	⇩	1.39	0.017	2574798	MAP3K2	⇧	1.37	5.40E-03
3589972	CHST14	⇩	1.40	7.09E-03	2407729	RRAGC	⇧	1.39	7.77E-04	3704376	FAM38A	⇩	1.37	7.78E-03
3820370	P2RY11	⇩	1.40	0.028	3317915	STIM1	⇩	1.39	9.63E-03	3686080	NSMCE1	⇧	1.37	0.023
2503200	RALB	⇧	1.40	0.027	2409004	LEPRE1	⇩	1.39	0.020	3872560	ZNF256	⇧	1.37	4.99E-03
2620641	LIMD1	⇩	1.40	0.031	2439975	IGSF8	⇩	1.39	2.91E-03	3260586	SCD	⇩	1.37	2.49E-05
2889698	CLK4	⇩	1.40	0.028	3285552	ZNF248	⇩	1.39	0.045	2696379	ANAPC13	⇧	1.37	0.029
3806253	ATP5A1	⇧	1.40	0.022	3590164	SPINT1	⇩	1.39	0.037	3774096	PDE6G	⇧	1.37	0.027
2594435	KCTD18	⇧	1.40	1.45E-03	3823625	AP1M1	⇧	1.39	1.12E-03	3982811	SH3BGRL	⇧	1.37	7.51E-03
4027813	F8A1	⇧	1.40	7.34E-03	3453120	ZNF641	⇧	1.39	0.030	3064541	PLOD3	⇩	1.37	6.08E-03
2668035	DYNC1LI1	⇧	1.40	0.016	2721777	PI4K2B	⇧	1.39	0.027	2642543	NUDT16P1	⇧	1.37	0.014
3657286	KIAA0664L3	⇩	1.40	2.92E-03	3535628	GNG2	⇧	1.38	0.027	3452970	SENP1	⇧	1.37	5.06E-03
2331158	AKIRIN1	⇧	1.40	6.05E-03	3848871	CD320	⇩	1.38	9.95E-04	3559794	C14orf126	⇧	1.37	0.017
2929036	LTV1	⇧	1.40	0.028	3441011	PARP11	⇧	1.38	3.18E-03	3893086	SLC17A9	⇩	1.37	7.84E-04
3947123	SREBF2	⇩	1.40	8.10E-05	3566652	TIMM9	⇧	1.38	0.031	3428131	SCYL2	⇧	1.37	5.18E-03

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3575567	FOXN3	⇧	1.37	4.13E-03	2934308	IGF2R	⇩	1.36	7.87E-03	4002148	EIF1AX	⇧	1.35	0.050
3692895	NUDT21	⇧	1.37	1.15E-03	3699707	ADAT1	⇧	1.36	0.029	3380697	DHCR7	⇩	1.35	0.052
2402111	C1orf63	⇩	1.37	0.016	2473149	NCOA1	⇧	1.36	0.023	3294438	ANXA7	⇧	1.35	4.88E-03
3833443	PLD3	⇩	1.37	0.016	3823583	HSH2D	⇧	1.36	0.035	2437753	KIAA0907	⇩	1.35	0.010
3075932	PARP12	⇧	1.37	0.046	2902633	MSH5	⇩	1.36	0.011	2694617	ISY1	⇧	1.35	7.40E-03
3841474	LENG8	⇩	1.37	2.48E-03	2599993	ABCB6	⇩	1.36	4.94E-03	3852565	ASF1B	⇧	1.35	0.024
3974904	NYX	⇧	1.37	0.032	2494749	CNNM3	⇩	1.36	0.016	3717737	PSMD11	⇧	1.35	0.012
2815455	UTP15	⇧	1.37	0.037	3354764	STT3A	⇩	1.36	0.026	3592484	PLDN	⇧	1.35	0.025
3114600	TRMT12	⇧	1.37	6.13E-05	3823613	FAM32A	⇧	1.36	0.028	2901333	ZNRD1	⇧	1.35	0.017
2713789	ZNF595	⇧	1.37	0.039	3480681	MRP63	⇧	1.36	0.036	2404521	PEF1	⇧	1.35	0.013
3743906	TP53	⇧	1.37	0.043	2903782	ITPR3	⇩	1.36	1.92E-03	3031345	LRRC61	⇧	1.35	3.26E-03
3375545	FADS1	⇩	1.37	0.014	3996381	ATP6AP1	⇩	1.36	0.019	2403557	SNORA44	⇩	1.35	0.012
2782292	C4orf21	⇩	1.37	0.052	3886639	YWHAB	⇧	1.36	0.015	3412296	IRAK4	⇧	1.35	0.011
3600212	LRRC49	⇧	1.36	3.72E-03	3824471	GLT25D1	⇩	1.36	0.034	2674748	CDHR4	⇧	1.35	6.32E-03
2656569	DNAJB11	⇩	1.36	0.041	4017519	PSMD10	⇧	1.36	4.72E-03	2982319	SOD2	⇧	1.35	0.011
2320472	CLCN6	⇩	1.36	0.026	3886179	IFT52	⇧	1.35	2.93E-03	3724989	CDK5RAP3	⇩	1.34	0.013
3845352	UQCR11	⇧	1.36	0.036	3619595	FAM82A2	⇩	1.35	8.86E-03	3678147	NMRAL1	⇧	1.34	0.028
3318731	DNHD1	⇩	1.36	0.032	2872471	DTWD2	⇧	1.35	0.026	3417371	ESYT1	⇩	1.34	0.034
3980035	YIPF6	⇩	1.36	3.78E-03	3042012	C7orf31	⇧	1.35	0.027	3976120	INE1	⇩	1.34	4.45E-03
3816834	NCLN	⇩	1.36	2.46E-03	2949471	NEU1	⇩	1.35	0.019	3685610	ARHGAP17	⇧	1.34	0.027
2898499	ALDH5A1	⇧	1.36	8.02E-03	3209497	FAM108B1	⇧	1.35	2.77E-03	2968144	OSTM1	⇩	1.34	0.011
3728097	AKAP1	⇩	1.36	1.28E-03	2726483	OCIAD1	⇩	1.35	0.043	3991698	HPRT1	⇧	1.34	0.031
3389273	CASP4	⇧	1.36	0.023	2336706	CPT2	⇧	1.35	4.40E-03	3373893	SLC43A1	⇩	1.34	0.025
3687452	YPEL3	⇧	1.36	0.039	3304746	USMG5	⇧	1.35	0.038	3554282	INF2	⇩	1.34	0.026
4011768	SNX12	⇧	1.36	3.76E-04	2365958	MPZL1	⇩	1.35	3.53E-03	4006416	FUNDC1	⇧	1.34	0.041
2485784	ACTR2	⇧	1.36	0.036	3303478	SEC31B	⇩	1.35	1.23E-03	3290785	CCDC6	⇧	1.34	9.95E-03
3962054	NHP2L1	⇧	1.36	9.55E-03	3319685	C11orf17	⇧	1.35	0.026	2899506	HMGN4	⇧	1.34	0.012
3832616	EIF3K	⇧	1.36	9.32E-03	2564634	ZNF514	⇩	1.35	0.011	3476097	CDK2AP1	⇧	1.34	0.048
3318844	DNHD1	⇩	1.36	3.96E-03	3970130	SYAP1	⇧	1.35	0.018	3653619	LCMT1	⇧	1.34	3.37E-04
3943207	YWHAH	⇧	1.36	0.053	2392584	TNFRSF14	⇩	1.35	0.023	2824286	SRP19	⇧	1.34	0.031
3831260	ZNF146	⇧	1.36	6.04E-03	3255402	FAM190B	⇧	1.35	8.76E-03	3286921	MARCH8	⇧	1.34	9.38E-03
3724969	PNPO	⇧	1.36	2.77E-03	3225456	MAPKAP1	⇧	1.35	1.15E-03	3856594	ZNF43	⇧	1.34	0.018

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3210457	RFK	⇧	1.34	7.65E-03	3280902	DNAJC1	⇩	1.33	0.037	3129121	CCDC25	⇧	1.32	0.016
3846900	C19orf10	⇩	1.34	0.015	3850832	TMEM205	⇩	1.33	0.017	3578089	C14orf49	⇩	1.32	0.016
2642562	NUDT16	⇧	1.34	3.89E-03	3413875	TROAP	⇩	1.33	3.31E-03	3879467	XRN2	⇧	1.32	7.14E-03
3555340	TEP1	⇩	1.34	5.43E-03	2726323	SLAIN2	⇧	1.33	6.02E-04	4017281	N⇧62CL	⇩	1.32	0.042
3927226	APP	⇩	1.34	0.051	3873629	SIRPA	⇩	1.33	0.039	3806913	SMAD2	⇧	1.32	9.08E-03
3591044	HAUS2	⇧	1.34	0.011	2489035	DGUOK	⇧	1.33	0.020	3758148	CCDC56	⇧	1.32	0.030
3682135	C16orf63	⇧	1.34	0.024	3843399	ZNF134	⇧	1.33	9.33E-03	3644057	MAPK8IP3	⇩	1.32	4.93E-05
3496916	GPR180	⇩	1.34	0.015	3643813	GNPTG	⇩	1.33	0.037	3775147	FOXK2	⇩	1.32	0.012
3260666	HIF1AN	⇧	1.34	7.48E-03	3560575	EAPP	⇧	1.33	1.93E-03	2690776	B4GALT4	⇩	1.32	0.018
3227121	C9orf78	⇧	1.34	0.017	3173831	FXN	⇧	1.33	0.029	3757745	GHDC	⇩	1.32	5.30E-03
3565361	GMFB	⇧	1.34	0.032	3226138	AK1	⇩	1.33	0.038	3378895	PITPNM1	⇩	1.32	4.06E-03
2414998	MYSM1	⇩	1.34	0.014	2815791	HEXB	⇩	1.33	0.020	4053534	ISG15	⇧	1.32	0.037
3896034	RASSF2	⇧	1.34	9.45E-03	2986825	SUN1	⇩	1.33	9.93E-03	3142554	SNX16	⇩	1.32	0.040
3914307	RGS19	⇧	1.34	0.031	2878662	DIAPH1	⇩	1.33	0.028	3007438	POM121	⇩	1.32	0.019
3104260	PKIA	⇧	1.34	4.52E-03	3416522	COPZ1	⇧	1.33	0.047	2694397	RPN1	⇩	1.32	0.042
2734992	NUDT9	⇩	1.33	0.036	3909395	DPM1	⇧	1.33	0.014	3629350	SPG21	⇧	1.32	0.011
2824872	AP3S1	⇧	1.33	0.036	3340066	PAAF1	⇧	1.33	0.024	3226709	C9orf114	⇧	1.32	8.82E-03
3127878	ENTPD4	⇩	1.33	0.024	2505957	PLEKHB2	⇧	1.33	0.026	3969396	TCEANC	⇧	1.32	0.013
3855910	ATP13A1	⇩	1.33	0.038	3339880	RELT	⇩	1.33	3.47E-03	3719150	PIGW	⇧	1.32	8.16E-03
3952543	SLC25A1	⇧	1.33	0.047	2899340	BTN2A2	⇩	1.33	0.030	2672712	SCAP	⇩	1.32	0.027
3687475	GDPD3	⇩	1.33	0.013	3851826	DNASE2	⇩	1.33	0.037	3714068	ALDH3A2	⇧	1.32	0.027
3056414	RFC2	⇧	1.33	0.047	3980560	KIF4A	⇩	1.33	0.035	2703217	KPNA4	⇧	1.32	0.021
3667766	KIAA0174	⇧	1.33	0.026	2848464	DAP	⇧	1.33	0.033	3996755	BRCC3	⇧	1.32	0.010
2676041	WDR82	⇧	1.33	0.036	3869379	ZNF614	⇧	1.33	0.035	3632940	UBL7	⇧	1.32	3.88E-05
3444180	KLRAP1	⇩	1.33	0.053	3318443	TRIM22	⇧	1.33	0.016	3362795	RNF141	⇧	1.32	0.022
2398789	SDHB	⇧	1.33	0.031	3783749	RNF138	⇧	1.33	0.013	2729884	UGT2B10	⇩	1.32	0.012
3893910	TCEA2	⇧	1.33	4.16E-03	3240095	RAB18	⇧	1.33	0.049	3934867	POFUT2	⇩	1.32	0.025
3742783	NLRP1	⇩	1.33	0.019	3611049	LRRC28	⇧	1.32	8.09E-03	3759305	CCDC43	⇧	1.32	0.016
2538000	RNASEH1	⇧	1.33	0.018	3625271	RAB27A	⇧	1.32	0.043	2722377	STIM2	⇩	1.32	0.044
2484752	COMMD1	⇧	1.33	0.053	3765299	APPBP2	⇧	1.32	7.09E-03	2428501	SLC16A1	⇩	1.32	0.022
3806689	HDHD2	⇧	1.33	7.71E-03	3064638	RABL5	⇧	1.32	2.51E-03	3014714	ARPC1B	⇧	1.32	0.016
2813364	SLC30A5	⇩	1.33	0.018	3029129	ZYX	⇧	1.32	0.044	3504791	EFHA1	⇧	1.32	0.022

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3726960	NME2	⇧	1.32	0.035
3569200	ATP6V1D	⇧	1.32	0.018
3567984	PPP2R5E	⇧	1.32	0.017
2454378	SLC30A1	⇩	1.32	0.029
3891643	C20orf177	⇧	1.32	0.013
3202171	PLAA	⇧	1.32	0.029
2327259	PPP1R8	⇧	1.32	3.11E-04
2761941	TAPT1	⇩	1.32	0.042
3458614	DCTN2	⇧	1.32	7.00E-03
2954280	PEX6	⇩	1.32	3.88E-03
3969047	PRPS2	⇧	1.32	5.00E-03
2434633	ARNT	⇧	1.32	5.74E-03
3945863	MGAT3	⇩	1.32	0.019
3629206	OAZ2	⇧	1.32	9.51E-03
3882949	DYNLRB1	⇧	1.32	0.014
2330393	C1orf113	⇩	1.32	0.010
3377933	EFEMP2	⇩	1.32	0.022
3580876	PPP1R13B	⇧	1.32	6.69E-03
3662041	OGFOD1	⇧	1.32	0.013
3005332	CRCP	⇧	1.32	0.017
3665116	CBFB	⇧	1.31	0.026
3205162	RNF38	⇧	1.31	4.12E-04
2902427	LST1	⇧	1.31	0.033
3048778	TMED4	⇩	1.31	0.027
2924492	HEY2	⇧	1.31	0.053
3421523	YEATS4	⇧	1.31	0.052
3168841	GRHPR	⇧	1.31	6.66E-03
2610317	C3orf10	⇧	1.31	4.24E-03
3742384	SLC25A11	⇧	1.31	8.78E-04
3513883	KPNA3	⇧	1.31	1.51E-03
3740304	PITPNA	⇧	1.31	0.026
2663551	N⇧210	⇩	1.31	0.027
3986230	CXorf57	⇩	1.31	6.15E-03
3866605	NAPA	⇧	1.31	0.012
2374422	C1orf106	⇩	1.31	0.013
2542737	LAPTM4A	⇩	1.31	0.016
3446868	LDHB	⇧	1.31	0.024
3302328	EXOSC1	⇧	1.31	0.010
3191338	GPR107	⇩	1.31	0.031
3348852	DLAT	⇧	1.31	2.78E-03
2711644	ATP13A3	⇩	1.31	0.029
3990512	SASH3	⇧	1.31	0.050
3432678	TPCN1	⇩	1.31	0.019
3734453	SLC9A3R1	⇧	1.31	0.024
3945056	EIF3L	⇧	1.31	6.88E-03
3888850	BCAS4	⇧	1.31	0.042
3608095	ZNF774	⇧	1.31	0.013
3426215	MRPL42	⇧	1.31	0.027
3774635	FASN	⇩	1.31	8.79E-03
2712632	TFRC	⇩	1.31	0.013
3825141	C19orf50	⇧	1.31	6.42E-04
3364119	CYP2R1	⇧	1.31	0.036
4003954	TAB3	⇧	1.31	4.64E-03
3127579	FLJ14107	⇩	1.31	0.051
3864921	ZNF180	⇧	1.31	0.027
2695648	ACAD11	⇩	1.31	0.016
2367537	C1orf9	⇩	1.31	0.045
3687870	ZNF688	⇧	1.31	7.27E-03
3644764	CCNF	⇩	1.31	0.041
3666649	VPS4A	⇧	1.31	0.037
3566304	EXOC5	⇧	1.31	7.39E-03
3380769	KRTAP5-11	⇧	1.30	0.031
2901620	HLA-E	⇩	1.30	0.013
2523540	NBEAL1	⇩	1.30	0.037
3893760	TPD52L2	⇧	1.30	0.015
3936256	BCL2L13	⇧	1.30	9.74E-03
3844897	C19orf6	⇩	1.30	0.015
2707359	DNAJC19	⇩	1.30	0.014
2359329	LCE3B	⇧	1.30	0.016
3822805	TECR	⇩	1.30	0.032
3752002	CRLF3	⇧	1.30	0.022
2572601	CCDC93	⇩	1.30	1.39E-03
3134922	PCMTD1	⇧	1.30	0.037
3436236	ZNF664	⇧	1.30	1.03E-03
3828032	POP4	⇧	1.30	0.018
2327630	YTHDF2	⇧	1.30	0.038
2528275	FAM134A	⇩	1.30	0.021
3368707	CD59	⇩	1.30	0.023
3603199	IDH3A	⇧	1.30	0.010
3743486	GABARAP	⇧	1.30	6.13E-04
2916246	C6orf162	⇧	1.30	0.033
3256689	PTEN	⇧	1.30	2.66E-04
2377427	CD46	⇩	1.30	3.09E-03
3464983	ATP2B1	⇩	1.30	0.030
2358171	PRPF3	⇩	1.30	4.99E-04
3310413	ATE1	⇧	1.30	0.026
3841231	PRPF31	⇧	1.30	0.014
2406597	TRAPPC3	⇧	1.30	0.023
2822215	PAM	⇩	1.30	0.016
3828162	C19orf2	⇧	1.30	0.019
3563734	SOS2	⇧	1.30	1.15E-03
3636470	BTBD1	⇧	1.30	2.86E-03
2708610	MAGEF1	⇧	1.30	0.015
3451318	ZCRB1	⇧	1.30	5.80E-03
3965393	ALG12	⇩	1.30	0.014
3645402	FLYWCH1	⇩	1.30	1.76E-03

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3883787	C20orf4	⇧	1.30	2.96E-03
3818897	PNPLA6	⇩	1.30	1.14E-03
2484552	AHSA2	⇩	1.30	0.023
3513096	ESD	⇧	1.30	0.023
2903285	PSMB9	⇧	1.30	0.019
3988874	UBE2A	⇧	1.30	0.021
3775842	TYMS	⇧	1.30	0.029
3680610	GSPT1	⇧	1.30	9.36E-03
3375582	FADS3	⇩	1.30	0.023
3831168	CAPNS1	⇧	1.30	3.58E-03
3352813	TBCEL	⇧	1.30	0.050
3772090	TMC6	⇩	1.30	9.35E-03
3333622	POLR2G	⇧	1.30	0.022
3933331	C2CD2	⇩	1.30	0.014
3447863	KRAS	⇧	1.30	0.040
3633794	ETFA	⇧	1.30	0.014
3434142	PRKAB1	⇧	1.30	0.010
2571457	CKAP2L	⇩	1.30	0.022
3750625	POLDIP2	⇧	1.30	7.60E-03
3681674	NTAN1	⇧	1.30	0.034
3454662	CSRNP2	⇧	1.30	0.049
2950590	RGL2	⇩	1.29	0.050
3536663	MAPK1IP1L	⇧	1.29	5.48E-03
3505937	CENPJ	⇩	1.29	0.020
3405531	DDX47	⇧	1.29	0.024
3887107	ZSWIM1	⇧	1.29	0.022
3721548	CNP	⇧	1.29	0.053
2921022	GPR6	⇧	1.29	0.017
3855506	TMEM161A	⇩	1.29	0.025
3591674	C15orf63	⇩	1.29	0.023
2536298	SEPT2	⇧	1.29	3.97E-03
4027387	FAM3A	⇩	1.29	2.20E-03
3690084	DNAJA2	⇧	1.29	0.053
3757630	KAT2A	⇩	1.29	0.032
2622859	HEMK1	⇩	1.29	4.99E-03
3885537	PLCG1	⇩	1.29	0.028
3191589	FUBP3	⇧	1.29	0.039
2364155	UHMK1	⇧	1.29	6.03E-03
2771654	CENPC1	⇩	1.29	0.031
3696454	CHTF8	⇧	1.29	0.022
3418436	OS9	⇩	1.29	0.053
3190737	TBC1D13	⇧	1.29	8.39E-03
3869954	ZNF321	⇧	1.29	0.047
3788270	ELAC1	⇧	1.29	0.041
3860824	ZNF569	⇧	1.29	1.67E-03
3774701	CCDC57	⇩	1.29	0.035
2776998	KLHL8	⇧	1.29	5.52E-03
3315549	PSMD13	⇧	1.29	9.36E-03
2336302	ZFYVE9	⇧	1.29	0.032
3035049	C7orf50	⇧	1.29	0.018
2622359	RBM6	⇩	1.29	0.044
3706659	ASPA	⇧	1.29	0.031
3751164	DHRS13	⇩	1.29	0.016
3822657	CD97	⇩	1.29	9.23E-03
3688424	C16orf58	⇩	1.29	0.012
3375951	GANAB	⇩	1.29	0.021
3269065	LHPP	⇧	1.29	5.33E-03
3056108	BCL7B	⇧	1.29	0.030
3851603	DHPS	⇧	1.29	3.39E-03
2320762	VPS13D	⇩	1.29	0.012
2877257	BRD8	⇩	1.29	0.027
3462949	OSBPL8	⇧	1.29	0.042
3475545	VPS33A	⇧	1.29	0.020
3257938	BTAF1	⇩	1.29	0.036
2901660	PRR3	⇧	1.28	0.044
3699044	RFWD3	⇧	1.28	0.037
3878934	NAA20	⇧	1.28	0.048
3347549	CUL5	⇧	1.28	9.37E-03
3944922	TRIOBP	⇧	1.28	1.13E-03
3435681	ARL6IP4	⇧	1.28	0.020
3779684	PSMG2	⇧	1.28	0.019
3252170	ADK	⇧	1.28	8.02E-03
2603897	TIGD1	⇩	1.28	0.043
3139950	LACTB2	⇧	1.28	0.051
3817072	GIPC3	⇧	1.28	0.011
3872542	ZNF418	⇧	1.28	0.020
3063337	ZNF394	⇧	1.28	0.018
3707352	RNF167	⇩	1.28	0.012
3217123	TRIM14	⇧	1.28	0.031
3710681	MAP2K4	⇧	1.28	0.028
3645881	ZNF174	⇧	1.28	3.83E-03
2681157	TMF1	⇩	1.28	0.033
3329904	NDUFS3	⇧	1.28	0.023
3849865	FBXL12	⇧	1.28	0.031
2553576	RTN4	⇩	1.28	0.021
3945877	SMCR7L	⇧	1.28	1.29E-03
3859026	PEPD	⇧	1.28	0.029
3653123	PRKCB	⇧	1.28	0.021
2404999	MARCKSL1	⇧	1.28	0.023
3764384	S⇧T4H1	⇧	1.28	7.35E-03
3140640	STAU2	⇧	1.28	0.035
2589255	FKBP7	⇩	1.28	0.051
3758157	BECN1	⇧	1.28	0.036
3415273	C12orf44	⇧	1.28	0.036
3971367	YY2	⇩	1.28	0.043
3337918	TPCN2	⇩	1.28	8.89E-03

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2939814	RPP40	⇧	1.28	3.79E-03	3580319	CINP	⇧	1.27	0.028	3015216	COPS6	⇧	1.26	0.031
2458513	TMEM63A	⇩	1.28	0.041	2427342	ALX3	⇧	1.27	0.011	3005280	VKORC1L1	⇧	1.26	0.020
2384956	COG2	⇧	1.28	0.032	3706651	OR3A3	⇩	1.27	0.041	3722152	PSME3	⇧	1.26	0.050
2892738	PRPF4B	⇩	1.28	0.019	3553607	EIF5	⇧	1.27	0.042	3757664	RAB5C	⇧	1.26	4.95E-03
3809324	TXNL1	⇧	1.28	0.010	2486811	PLEK	⇧	1.27	0.042	3381241	ARAP1	⇩	1.26	6.16E-03
3035682	FTSJ2	⇧	1.28	0.039	2827156	PHAX	⇧	1.27	0.025	3471374	PPP1CC	⇧	1.26	2.72E-03
3581132	AKT1	⇧	1.28	8.65E-03	3195174	MAN1B1	⇩	1.27	3.78E-04	3057650	YWHAG	⇧	1.26	0.027
3807370	DYM	⇧	1.28	8.12E-03	2336497	ZYG11B	⇧	1.27	0.034	3506648	GPR12	⇧	1.26	2.50E-03
3894228	CSNK2A1	⇧	1.28	2.46E-03	3896524	TRMT6	⇧	1.27	0.039	3843346	ZNF549	⇧	1.26	6.15E-03
2893847	SNRNP48	⇩	1.28	0.030	3301218	PDLIM1	⇧	1.27	0.030	2866576	MBLAC2	⇧	1.26	0.027
2924619	TRMT11	⇩	1.28	0.040	3541137	EIF2S1	⇧	1.27	0.029	3961981	POLR3H	⇧	1.26	0.044
3923218	RRP1B	⇧	1.28	9.75E-03	3578152	TCL1A	⇧	1.27	0.039	2899519	ABT1	⇧	1.26	0.029
3929821	CRYZL1	⇩	1.28	0.035	2545092	HADHA	⇧	1.27	0.014	3816424	SPPL2B	⇩	1.26	0.032
3624697	ARPP19	⇧	1.27	0.013	3264004	SHOC2	⇧	1.27	8.61E-03	3698919	GLG1	⇩	1.26	0.015
2610136	CRELD1	⇩	1.27	0.042	3435853	TMED2	⇩	1.27	7.10E-03	3502632	TMCO3	⇩	1.26	0.021
3391029	PPP2R1B	⇧	1.27	3.57E-04	3909064	TMEM189	⇧	1.27	0.017	2817386	PAPD4	⇧	1.26	0.011
3976519	RBM3	⇧	1.27	4.65E-03	2619344	NKTR	⇩	1.27	0.010	3880706	ENTPD6	⇩	1.26	0.025
3866302	AP2S1	⇧	1.27	5.59E-03	2890292	C5orf45	⇩	1.27	0.032	2361697	C1orf66	⇩	1.26	0.031
3645204	KCTD5	⇧	1.27	8.44E-03	3723572	MGC57346	⇩	1.27	0.037	2924898	RNF146	⇧	1.26	0.035
2877141	HNRNPA0	⇧	1.27	0.011	3695433	TRADD	⇧	1.27	0.016	3868283	VRK3	⇧	1.26	9.86E-03
3238491	BMI1	⇧	1.27	0.043	3235255	ECHDC3	⇧	1.27	0.025	2519140	ZC3H15	⇧	1.26	0.033
3099561	T1560	⇧	1.27	0.046	2547386	DPY30	⇧	1.27	0.048	2833024	RNF14	⇧	1.26	0.029
2391647	SSU72	⇧	1.27	0.046	2989537	GLCCI1	⇧	1.27	0.042	3256669	CFLP1	⇧	1.26	3.13E-03
3338424	FADD	⇧	1.27	0.026	3850040	EIF3G	⇧	1.27	1.30E-03	3456700	ZNF385A	⇧	1.26	0.022
3282268	ACBD5	⇧	1.27	0.030	2922521	NT5DC1	⇧	1.26	0.017	3656760	STX4	⇧	1.26	0.020
3466740	LTA4H	⇧	1.27	0.036	2816506	S100Z	⇧	1.26	0.017	3025500	BPGM	⇧	1.26	0.015
3972025	PDK3	⇧	1.27	0.050	3666732	CYB5B	⇧	1.26	7.64E-03	3560617	SNX6	⇧	1.26	0.046
2436132	ILF2	⇧	1.27	0.053	3954331	TOP3B	⇩	1.26	0.028	3560864	PPP2R3C	⇧	1.26	0.035
2899393	BTN2A3	⇩	1.27	0.025	3426917	METAP2	⇧	1.26	0.035	3377964	FIBP	⇧	1.26	0.011
3878533	DTD1	⇧	1.27	0.043	2777639	GPRIN3	⇧	1.26	0.048	3590709	PLA2G4B	⇩	1.26	4.13E-03
3750842	SGK494	⇩	1.27	1.78E-03	3837731	EMP3	⇩	1.26	7.49E-03	3164914	MTAP	⇧	1.26	0.022
3943414	FBXO7	⇧	1.27	0.014	3773742	SLC38A10	⇩	1.26	0.024	3630668	CALML4	⇩	1.26	0.011

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2440625	DEDD	⇧	1.26	6.35E-03	3051753	FKBP9	⇧	1.25	0.046	3147591	AZIN1	⇧	1.25	0.018
2352501	LRIG2	⇩	1.26	0.018	3964154	CERK	⇧	1.25	0.036	2768273	NFXL1	⇩	1.25	0.038
3846280	TBXA2R	⇧	1.26	0.025	3589141	SPRED1	⇩	1.25	0.049	4041923	CCNL2	⇩	1.25	0.036
3830246	LSR	⇩	1.26	0.034	3077766	TPK1	⇧	1.25	0.016	3535922	STYX	⇧	1.25	0.044
3220977	ROD1	⇧	1.26	2.02E-03	3434193	CCDC64	⇩	1.25	3.20E-03	3221135	C9orf80	⇧	1.25	0.031
3129948	TMEM66	⇩	1.26	2.56E-03	2317434	TPRG1L	⇧	1.25	0.034	3294242	ECD	⇧	1.25	0.012
3815210	AZU1	⇧	1.26	4.86E-03	3378007	C11orf68	⇧	1.25	0.017	2443537	SCYL3	⇧	1.25	0.035
3830712	MLL4	⇩	1.26	3.52E-03	4007086	ZNF41	⇧	1.25	2.70E-03	3633048	EDC3	⇧	1.25	0.025
3666282	ZFP90	⇧	1.26	0.050	3684782	RRN3P3	⇧	1.25	0.038	3225003	PSMB7	⇧	1.25	0.033
3705135	CENPBD1	⇧	1.26	5.21E-03	3482977	POLR1D	⇧	1.25	5.21E-03	3405032	ETV6	⇧	1.25	1.04E-03
2801608	MARCH6	⇩	1.26	0.016	2359817	INTS3	⇩	1.25	0.016	3226181	ST6GALNAC4	⇩	1.25	0.037
3820443	ICAM1	⇩	1.26	0.044	3725481	UBE2Z	⇧	1.25	0.012	3971923	ZFX	⇧	1.25	0.044
4051226	SEMA4D	⇩	1.26	2.44E-03	3283378	MTPAP	⇧	1.25	0.026	3985218	ARMCX5	⇧	1.25	7.80E-03
2536625	BOK	⇧	1.26	4.16E-03	3418513	MARCH9	⇩	1.25	0.015	3739827	GLOD4	⇧	1.24	7.64E-03
3005069	ZNF92	⇧	1.26	0.035	3405207	BCL2L14	⇧	1.25	0.030	3864597	C19orf61	⇩	1.24	0.037
3363979	PSMA1	⇧	1.26	8.91E-03	2858793	C5orf43	⇧	1.25	7.80E-03	3337390	TCIRG1	⇩	1.24	0.041
3712582	MED9	⇧	1.26	0.022	3014159	LMTK2	⇩	1.25	0.053	2525182	CCNYL1	⇧	1.24	9.96E-03
3644220	NDUFB10	⇧	1.26	0.051	2724472	UBE2K	⇧	1.25	0.041	2759404	GRPEL1	⇧	1.24	0.032
2608469	ITPR1	⇩	1.26	0.025	3723264	NMT1	⇧	1.25	0.010	3643703	UBE2I	⇧	1.24	0.014
3959631	EIF3D	⇧	1.26	0.013	2575980	CCDC115	⇧	1.25	0.040	2545869	IFT172	⇩	1.24	8.93E-03
3722417	NBR1	⇧	1.26	0.032	2488959	STAMBP	⇧	1.25	0.013	2620315	TMEM42	⇧	1.24	0.012
3168245	LOC92973	⇩	1.26	0.040	2666904	SLC4A7	⇩	1.25	0.050	3841545	LILRA1	⇧	1.24	5.20E-03
4026669	BCAP31	⇩	1.25	0.045	3453774	LMBR1L	⇩	1.25	0.036	3329793	SLC39A13	⇩	1.24	0.043
3737140	GAA	⇩	1.25	0.033	2698565	TFDP2	⇧	1.25	0.043	2548274	STRN	⇧	1.24	0.020
3638048	MRPL46	⇧	1.25	0.052	2890859	MGAT1	⇩	1.25	0.035	3662265	N⇧93	⇧	1.24	0.050
3135452	ATP6V1H	⇧	1.25	3.35E-03	2964327	LYRM2	⇧	1.25	0.011	2429842	CD58	⇩	1.24	0.042
3713195	SMCR8	⇧	1.25	7.36E-03	3275611	ANKRD16	⇧	1.25	8.20E-03	3223605	FBXW2	⇧	1.24	2.77E-03
3902609	PDRG1	⇧	1.25	0.042	3185558	PRPF4	⇧	1.25	0.035	4014251	CHM	⇧	1.24	0.047
3677592	ZNF434	⇧	1.25	0.011	4043943	INPP5B	⇧	1.25	0.028	3421706	RAB3IP	⇧	1.24	0.046
3549708	SERPINA4	⇧	1.25	0.013	3195363	ARRDC1	⇧	1.25	8.28E-03	3322048	C11orf58	⇧	1.24	0.051
3497790	IPO5	⇧	1.25	2.43E-03	3382319	GDPD5	⇩	1.25	0.047	3851441	ZNF442	⇧	1.24	0.048
3729014	GDPD1	⇩	1.25	0.016	2867145	FAM172A	⇧	1.25	9.32E-03	4019486	SEPT6	⇧	1.24	5.93E-03

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3470793	KCTD10	⇧	1.24	0.049	3623683	GABPB1	⇧	1.24	0.035	3386638	SLC36A4	⇩	1.23	0.029
3479181	POLE	⇩	1.24	0.049	3821727	ZNF136	⇧	1.24	0.013	3453370	ARF3	⇧	1.23	7.96E-03
3074640	LUZP6	⇧	1.24	0.024	3962734	TTLL1	⇧	1.24	0.044	2831209	PAIP2	⇧	1.23	0.050
3620276	EHD4	⇧	1.24	0.045	3433538	RNFT2	⇩	1.24	0.038	3268588	ACADSB	⇧	1.23	0.044
3942998	SFI1	⇩	1.24	0.022	2333168	C1orf84	⇩	1.24	0.044	3642060	CHSY1	⇩	1.23	0.015
2405893	C1orf212	⇧	1.24	0.042	3394092	SLC37A4	⇩	1.24	0.044	3696035	LCAT	⇩	1.23	0.042
3311775	DHX32	⇧	1.24	0.053	4026722	IDH3G	⇧	1.24	0.042	2336099	OSBPL9	⇧	1.23	0.044
2643095	BFSP2	⇧	1.24	0.013	3515009	VPS36	⇧	1.24	0.041	3602873	HMG20A	⇧	1.23	0.016
3702293	MBTPS1	⇩	1.24	0.049	3819880	ZNF317	⇧	1.24	0.027	3865464	OPA3	⇧	1.23	4.69E-03
3310675	CUZD1	⇩	1.24	0.031	2474527	NRBP1	⇧	1.24	0.034	3887017	DNTTIP1	⇧	1.23	0.024
3377886	CFL1	⇧	1.24	0.050	3867195	FAM83E	⇧	1.24	0.048	2400220	DDOST	⇩	1.23	0.023
2446198	TOR1AIP2	⇩	1.24	0.048	3027503	ADCK2	⇩	1.24	0.029	3371673	ARHGAP1	⇧	1.23	0.022
3421630	CCT2	⇧	1.24	0.035	3231389	ZMYND11	⇧	1.23	0.051	3986672	ATG4A	⇧	1.23	0.051
3903836	EIF6	⇧	1.24	0.011	3551303	CCNK	⇧	1.23	2.03E-03	3705641	TIMM22	⇧	1.23	0.011
2428405	RHOC	⇧	1.24	3.77E-03	3619650	DNAJC17	⇧	1.23	0.030	3476265	EIF2B1	⇧	1.23	9.20E-03
3603687	TMED3	⇩	1.24	0.027	3847989	CD70	⇩	1.23	0.015	3459604	PPM1H	⇧	1.23	0.036
3719515	DUSP14	⇧	1.24	0.032	3421579	FRS2	⇧	1.23	0.053	3751323	MYO18A	⇩	1.23	7.24E-03
3466284	NDUFA12	⇧	1.24	0.047	3327948	TTC17	⇩	1.23	2.67E-03	3382948	CLNS1A	⇧	1.23	0.028
2413203	LRP8	⇩	1.24	0.050	3432030	ACAD10	⇩	1.23	0.011	2488114	ZNF638	⇩	1.23	0.048
3778823	NAPG	⇧	1.24	0.047	3960388	PLA2G6	⇩	1.23	0.016	3225348	PPP6C	⇧	1.23	0.042
2436283	DENND4B	⇩	1.24	0.014	2320347	FBXO44	⇩	1.23	0.022	2325479	RCAN3	⇧	1.23	0.032
3577078	LGMN	⇩	1.24	0.047	2659577	PAK2	⇧	1.23	0.034	3192525	GTF3C4	⇧	1.23	0.044
3292590	PBLD	⇧	1.24	0.044	2406139	KIAA0319L	⇩	1.23	0.039	2853388	C5orf33	⇧	1.23	0.029
3037344	DAGLB	⇩	1.24	0.041	3340410	NEU3	⇧	1.23	0.019	3430552	PWP1	⇧	1.23	0.023
2336271	BTF3L4	⇧	1.24	0.052	3294816	NDST2	⇩	1.23	0.022	3558012	TINF2	⇧	1.23	4.38E-03
3159167	ZNF252	⇧	1.24	0.022	3795466	RBFA	⇧	1.23	0.052	3639007	HDDC3	⇧	1.23	0.017
3557614	AP1G2	⇩	1.24	0.012	3862167	FBL	⇧	1.23	2.90E-03	3757487	DNAJC7	⇧	1.23	0.016
2828146	CDC42SE2	⇧	1.24	0.023	3689922	VPS35	⇧	1.23	0.011	2899110	HFE	⇩	1.23	0.040
3759356	EFTUD2	⇧	1.24	0.013	3755714	MED1	⇧	1.23	6.41E-03	3952453	DGCR2	⇩	1.23	0.046
3372368	MTCH2	⇧	1.24	0.018	4012204	HDAC8	⇧	1.23	0.041	3860596	ZNF461	⇧	1.23	0.026
3534201	PRPF39	⇩	1.24	0.025	3079005	RARRES2	⇧	1.23	0.040	3479438	CHFR	⇧	1.23	0.046
3797015	ZFP161	⇧	1.24	0.029	3294854	CAMK2G	⇧	1.23	5.86E-03	3315024	ADAM8	⇩	1.23	0.029

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3623424	COPS2	⇧	1.22	0.047
3602526	FBXO22	⇧	1.22	0.021
3299255	ATAD1	⇩	1.22	0.033
2844461	LTC4S	⇧	1.22	5.79E-03
2780999	PAPSS1	⇧	1.22	0.038
3645850	OR2C1	⇧	1.22	0.026
3831143	TBCB	⇧	1.22	0.012
2928392	VTA1	⇧	1.22	0.050
3435946	GTF2H3	⇧	1.22	0.039
3225224	GOLGA1	⇩	1.22	1.22E-03
2392528	PANK4	⇩	1.22	0.016
3818376	CLPP	⇧	1.22	0.017
3691193	SNX20	⇧	1.22	0.039
2902884	SKIV2L	⇩	1.22	0.011
3970833	PDHA1	⇧	1.22	6.50E-03
3853063	ILVBL	⇩	1.22	0.026
2977949	EPM2A	⇧	1.22	0.023
2586989	DLX2	⇧	1.22	0.040
3681377	PARN	⇧	1.22	9.30E-03
3119735	ZNF623	⇧	1.22	0.030
3895297	DDRGK1	⇩	1.22	0.012
3645253	SRRM2	⇩	1.22	5.24E-04
3571542	PNMA1	⇧	1.22	0.053
2436716	UBE2Q1	⇧	1.22	0.037
3688197	VKORC1	⇩	1.22	0.025
2358044	PLEKHO1	⇧	1.22	0.053
3802129	SS18	⇧	1.22	0.030
2560141	MRPL53	⇧	1.22	0.011
3230282	AGPAT2	⇩	1.22	0.048
2642325	ATP2C1	⇩	1.22	0.051
2620222	ZNF501	⇧	1.22	0.048
2335986	RNF11	⇧	1.22	0.024
3865776	IRF2BP1	⇩	1.22	1.23E-03
2786567	C4orf49	⇧	1.22	0.037
2431031	HMGCS2	⇧	1.22	0.040
2363902	DUSP12	⇧	1.22	0.024
3327906	API5	⇧	1.22	2.62E-03
3915087	USP25	⇧	1.22	0.027
3382861	PAK1	⇧	1.22	0.036
3597857	SNX1	⇧	1.22	0.050
2964052	SRSF12	⇧	1.22	6.16E-03
3754227	MYO19	⇩	1.22	0.012
3708798	SENP3	⇧	1.22	0.048
2600068	TUBA4A	⇧	1.22	0.033
2397732	AGMAT	⇧	1.22	0.046
3599432	FEM1B	⇧	1.22	0.025
3417842	LRP1	⇩	1.22	0.047
2460325	C1orf198	⇧	1.22	0.012
2324743	ZBTB40	⇩	1.22	0.043
2834093	TCERG1	⇩	1.22	0.018
2606643	MYEOV2	⇧	1.22	0.031
2675836	ABHD14B	⇧	1.22	0.038
3269328	ZRANB1	⇧	1.22	0.049
3282016	ABI1	⇧	1.22	0.050
2838598	CCNG1	⇧	1.22	0.033
3457696	PAN2	⇩	1.22	0.033
2886977	FBXW11	⇧	1.22	0.024
2571979	SLC35F5	⇩	1.22	0.050
3976848	HDAC6	⇩	1.22	2.53E-03
3947863	PARVB	⇧	1.22	0.011
3755396	CWC25	⇩	1.22	0.027
2495555	UNC50	⇩	1.22	0.013
3837836	CYTH2	⇧	1.22	0.011
3649052	MKL2	⇧	1.22	0.038
3683783	THUMPD1	⇧	1.22	0.028
3439305	ZNF84	⇧	1.22	0.022
3440017	FBXL14	⇩	1.22	0.049
3467315	IKBIP	⇩	1.22	0.041
3981959	SLC16A2	⇧	1.22	0.028
3819104	TRAPPC5	⇧	1.22	0.020
2624110	SPCS1	⇩	1.22	0.017
3074362	CNOT4	⇧	1.21	0.051
2475628	YPEL5	⇧	1.21	0.049
3565303	CNIH	⇩	1.21	0.023
3847005	PLIN3	⇧	1.21	0.016
3333358	INCENP	⇩	1.21	0.022
2538924	FLJ42418	⇧	1.21	0.033
3226005	PTRH1	⇧	1.21	8.37E-03
3576812	TRIP11	⇩	1.21	0.029
3099566	FAM110B	⇧	1.21	0.030
3704717	ANKRD11	⇩	1.21	0.029
3825225	C19orf60	⇧	1.21	0.040
3529547	DCAF11	⇧	1.21	0.029
2365496	POGK	⇧	1.21	0.013
3462693	KRR1	⇧	1.21	0.037
3645377	FLYWCH2	⇧	1.21	0.044
3548152	TDP1	⇧	1.21	2.29E-03
3128362	GNRH1	⇩	1.21	0.017
3882069	MAPRE1	⇧	1.21	0.039
3996339	TAZ	⇩	1.21	0.012
4007376	SSX3	⇧	1.21	0.053
2966253	SFRS18	⇩	1.21	0.036
3845620	BTBD2	⇧	1.21	0.042
2561955	SUCLG1	⇧	1.21	0.027
3865378	ERCC1	⇧	1.21	0.052
3998632	PNPLA4	⇧	1.21	0.043

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3756344	SMARCE1	⇧	1.21	0.029
2391188	SDF4	⇩	1.21	0.026
3345340	KDM4D	⇧	1.21	0.029
3708306	ACADVL	⇩	1.21	3.95E-03
3919124	FAM165B	⇧	1.21	0.017
2614054	UBE2E1	⇧	1.21	0.029
4007643	OTUD5	⇧	1.21	0.034
2950214	TAP1	⇩	1.21	0.052
3832777	MRPS12	⇧	1.21	0.045
3159013	ZNF34	⇧	1.21	0.042
3696571	TERF2	⇧	1.21	7.84E-03
3956854	THOC5	⇧	1.21	0.018
4016045	TCEAL6	⇩	1.21	0.032
3748126	ATPAF2	⇧	1.21	0.021
3301713	BLNK	⇧	1.21	5.12E-03
2351872	RAP1A	⇧	1.21	0.026
3224366	RC3H2	⇧	1.21	5.12E-03
3994846	MTMR1	⇧	1.21	0.020
3878429	POLR3F	⇧	1.21	6.67E-03
3686164	GTF3C1	⇩	1.21	0.012
3948590	RIBC2	⇧	1.21	0.045
2348792	CCDC76	⇩	1.21	0.013
2325274	C1orf128	⇧	1.21	0.026
3591909	CTDSPL2	⇧	1.21	0.010
3504392	N6AMT2	⇧	1.21	0.028
3702382	TAF1C	⇩	1.21	0.024
3538703	MNAT1	⇧	1.21	0.038
2921086	CDC40	⇧	1.21	7.07E-03
2983030	AGPAT4	⇩	1.21	0.035
3709540	PFAS	⇩	1.21	0.021
3645901	NAT15	⇧	1.21	0.037
3843233	ZNF17	⇧	1.21	0.040
3377358	BATF2	⇧	1.21	0.040
3922100	MX1	⇧	1.21	0.047
3624448	GNB5	⇧	1.21	0.011
3742727	DHX33	⇧	1.21	0.019
2904528	ZNF76	⇩	1.20	0.037
3812426	RTTN	⇩	1.20	0.028
3538470	C14orf135	⇩	1.20	0.024
3228373	TSC1	⇩	1.20	0.037
3251926	KIAA0913	⇩	1.20	0.032
2676352	NEK4	⇧	1.20	0.049
3332838	DAK	⇧	1.20	0.042
3571810	ABCD4	⇩	1.20	0.024
3502710	TFDP1	⇧	1.20	0.033
3855410	SUGP2	⇩	1.20	4.59E-03
3934407	ICOSLG	⇩	1.20	0.015
3654227	IL21R	⇩	1.20	0.036
2874794	RAPGEF6	⇩	1.20	0.048
3673921	ZNF778	⇧	1.20	0.022
3696295	SLC7A6OS	⇧	1.20	0.017
3458033	ATP5B	⇧	1.20	2.42E-03
2333195	KIAA0467	⇩	1.20	0.012
3872983	CHMP2A	⇧	1.20	0.022
3483348	POMP	⇧	1.20	0.031
3377149	MEN1	⇩	1.20	0.016
2863535	WDR41	⇧	1.20	0.035
3815610	ATP5D	⇧	1.20	0.011
3831917	ZNF570	⇧	1.20	0.034
3047202	C7orf11	⇧	1.20	0.043
3869339	ZNF350	⇧	1.20	0.052
3509910	FAM48A	⇧	1.20	8.39E-03
3056264	ABHD11	⇧	1.20	0.040
3945084	MICALL1	⇧	1.20	0.039
3445786	ARHGDIB	⇧	1.20	0.016
3675116	TMEM8A	⇩	1.20	0.044
3656800	ZNF646	⇩	1.20	0.037
2386828	EDARADD	⇧	1.20	0.036
3770699	MIF4GD	⇧	1.20	0.038
3755580	CACNB1	⇩	1.20	0.015
3167511	GALT	⇩	1.20	0.032
3159132	COMMD5	⇧	1.20	8.68E-03
3015706	MOSPD3	⇧	1.20	0.046
3628994	PPIB	⇩	1.20	0.021
2530599	AGFG1	⇧	1.20	0.015
2881370	CD74	⇩	1.20	7.51E-03
3774975	C17orf101	⇩	1.20	0.016
3033397	RBM33	⇩	1.20	0.043
3294348	MRPS16	⇧	1.20	0.031
3924674	DIP2A	⇩	1.20	0.018
3824226	GTPBP3	⇩	1.20	0.027
2321942	RSC1A1	⇧	1.20	0.045
3332626	TMEM132A	⇩	1.20	0.046
3429312	HSP90B1	⇩	1.20	0.018
2562198	TGOLN2	⇩	1.20	0.014
3668898	ZFP1	⇧	1.20	0.036
3545403	GSTZ1	⇧	1.20	0.037
3695916	CENPT	⇩	1.20	0.019
4050485	TUBB2C	⇧	1.20	0.032
3334954	CAPN1	⇧	1.20	0.045
3442812	SLC2A14	⇩	1.20	2.73E-03
2894711	TMEM14B	⇧	1.20	6.07E-03
2402942	SLC9A1	⇩	1.20	0.024
3414390	SMARCD1	⇧	1.20	0.020
3541073	MPP5	⇧	1.20	0.019
3542063	SLC39A9	⇩	1.20	0.030

Table B17: C9-Long Specific Gene List (n=1,250) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3435050	PSMD9	⇧	1.20	0.020	3456006	CSAD	⇩	1.20	0.036	3212277	C9orf64	⇧	1.20	0.049
2560254	A⇧1	⇩	1.20	0.045										

Table B18: C9-Short Specific Gene List (n=137) FEMALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value
3662201	MT1H	⇧	2.05	0.023	3847873	SLC25A23	⇧	1.39	7.79E-03	3931112	HLCS	⇩	1.30	8.65E-03
3433796	PEBP1	⇧	1.76	0.033	2986350	DLL1	⇩	1.39	0.040	3901665	C20orf3	⇩	1.30	5.70E-03
2933522	GTF2H5	⇧	1.74	0.046	2356818	BCL9	⇧	1.38	6.15E-03	2362157	CD1D	⇩	1.30	0.016
3507282	FLT1	⇩	1.73	0.033	3788049	SKA1	⇧	1.38	0.033	3839006	PTOV1	⇧	1.30	0.040
3212848	GOLM1	⇩	1.72	0.034	3974556	ATP6AP2	⇩	1.38	0.035	3856075	ZNF682	⇧	1.29	0.030
3948543	FAM118A	⇩	1.67	0.049	2992963	CCDC126	⇧	1.38	0.040	3767465	AXIN2	⇧	1.29	0.042
3318500	OR52N4	⇧	1.66	0.019	3188231	OR1L4	⇧	1.38	2.73E-03	3251648	FAM149B1	⇧	1.29	0.039
3933625	RSPH1	⇧	1.66	0.030	3120358	HSF1	⇧	1.38	0.043	3392871	ZNF259	⇧	1.29	0.025
2775735	SCD5	⇩	1.64	8.04E-03	3016636	SH2B2	⇧	1.37	0.042	3454576	SLC11A2	⇩	1.29	0.045
2676854	CHDH	⇧	1.60	0.035	3730240	TLK2	⇧	1.36	0.025	3275690	IL15RA	⇩	1.28	2.08E-03
2703377	B3GALNT1	⇩	1.60	0.049	3894098	C20orf96	⇧	1.36	4.01E-03	2606574	NDUFA10	⇧	1.28	0.012
3444476	TAS2R20	⇩	1.57	0.047	2803329	BASP1	⇧	1.35	9.34E-03	3458133	PRIM1	⇧	1.28	0.029
2950125	HLA-DQB2	⇩	1.54	0.032	2832081	ZMAT2	⇧	1.35	7.91E-03	2861952	MRPS27	⇧	1.28	0.029
3325503	RCN1	⇩	1.53	0.017	2774971	ANTXR2	⇩	1.35	0.036	3567187	DHRS7	⇩	1.28	0.012
2869438	NUDT12	⇩	1.53	0.031	3498589	CLYBL	⇧	1.35	0.028	3677356	HCFC1R1	⇧	1.27	3.61E-03
3841357	LILRA2	⇩	1.52	0.023	2360939	POU5F1P4	⇩	1.34	0.010	3302495	AVPI1	⇧	1.27	0.042
3917582	KRTAP6-3	⇩	1.51	0.018	3590086	RAD51	⇧	1.34	0.035	2438531	HDGF	⇧	1.27	0.033
2893392	LY86	⇩	1.49	0.043	2422227	GEMIN8P4	⇧	1.34	0.024	3735505	AANAT	⇧	1.27	0.014
3903361	AHCY	⇧	1.46	0.023	2723752	TBC1D1	⇧	1.33	0.015	3334325	VEGFB	⇧	1.27	0.012
3850660	SPC24	⇧	1.46	0.039	3990795	RBMX2	⇩	1.33	0.032	3811459	KDSR	⇩	1.27	9.42E-03
3868659	C19orf48	⇧	1.46	7.85E-03	4019849	LAMP2	⇩	1.33	0.034	3325839	TCP11L1	⇧	1.26	0.018
3830993	HCST	⇩	1.45	0.024	2666566	NGLY1	⇧	1.32	0.028	2383550	ZNF678	⇧	1.26	0.035
3959593	TXN2	⇧	1.45	0.019	3354879	HYLS1	⇧	1.32	0.024	3713093	ALKBH5	⇧	1.26	0.042
3164181	RRAGA	⇩	1.43	0.018	2728189	PAICS	⇧	1.32	0.032	2440476	F11R	⇩	1.26	0.021
3450899	SLC2A13	⇩	1.42	0.020	2673873	IMPDH2	⇧	1.31	0.011	2334279	UROD	⇧	1.26	0.043
2842561	HIGD2A	⇧	1.41	0.038	3328389	EXT2	⇩	1.31	0.032	3203482	BAG1	⇧	1.26	0.026
2610417	C3orf42	⇧	1.41	0.018	3168309	RECK	⇩	1.31	4.94E-03	3816699	ZNF57	⇧	1.26	0.044
2520069	C2orf88	⇩	1.40	0.049	3191147	TOR1B	⇩	1.31	0.046	3918696	SON	⇩	1.26	9.81E-03
3726498	MYCBPAP	⇧	1.40	0.033	2712794	TCTEX1D2	⇧	1.31	0.046	2335922	CDKN2C	⇩	1.25	0.011
3124537	CTSB	⇩	1.40	0.027	2359433	LCE1E	⇧	1.31	0.034	3844855	C19orf22	⇧	1.25	0.036
3377423	CDCA5	⇧	1.39	0.045	3819522	MARCH2	⇩	1.31	0.037	3442282	MLF2	⇧	1.25	2.77E-03

Table B18: C9-Short Specific Gene List (n=137) FEMALE ONLY SAMPLES [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

3261419	HPS6	⇧	1.25	0.049
2444117	PIGC	⇩	1.25	0.029
3142485	IMPA1	⇩	1.25	0.044
3016177	AP1S1	⇧	1.25	0.045
3855071	FKBP8	⇧	1.24	0.017
2399718	AKR7A2	⇧	1.24	0.013
2955025	MRPL14	⇧	1.24	0.048
2390489	ZNF672	⇧	1.24	0.039
3637006	SEC11A	⇩	1.24	0.027
3621140	LCMT2	⇩	1.24	0.049
2363042	PEA15	⇧	1.24	2.72E-03
3029213	TAS2R41	⇩	1.23	0.030
3980745	FOXO4	⇧	1.23	0.017
2363444	USP21	⇧	1.23	0.018
2712906	RNF168	⇧	1.23	0.032
3079756	RHEB	⇧	1.23	9.25E-03
2881554	DCTN4	⇧	1.23	0.038
3157138	LYPD2	⇩	1.23	0.029
2831875	SLC35A4	⇧	1.23	0.040
2878726	HDAC3	⇧	1.22	0.024
3920512	DSCR9	⇩	1.22	7.15E-03
3712517	NT5M	⇧	1.22	3.85E-03
3401197	C12orf32	⇧	1.22	4.28E-03
2832467	PCDHB18	⇩	1.21	0.023
3200689	RPS6	⇧	1.21	3.58E-03
2450865	CSRP1	⇧	1.21	0.048
2619120	TRAK1	⇧	1.21	0.015
2410330	GPBP1L1	⇧	1.21	0.017
3644541	TRAF7	⇧	1.21	7.47E-03
3862564	C19orf47	⇧	1.21	9.43E-03
3724931	SP2	⇧	1.21	0.033
3883941	TGIF2	⇧	1.21	0.048
3216319	ZNF367	⇧	1.21	0.018
2737069	METAP1	⇧	1.21	0.033
3417485	OBFC2B	⇧	1.20	0.013
3822195	NACC1	⇧	1.20	0.019
2943236	DTNBP1	⇧	1.20	0.018
3643552	SSTR5	⇧	1.20	9.87E-03
3673684	CDT1	⇧	1.20	0.033
3240012	MASTL	⇧	1.20	0.040
3620515	TMEM87A	⇩	1.20	0.015
3536396	CGRRF1	⇩	1.20	0.023
3825496	ARMC6	⇧	1.20	0.043

Table B19: C9-LongvShort Gene List (n=1,024) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value
2940145	NRN1	⇧	3.24	0.018	2534324	PRLH	⇩	1.80	7.39E-03	2826295	SNX2	⇩	1.64	2.64E-03
3369249	APIP	⇧	2.54	2.58E-03	2474240	KHK	⇩	1.80	0.043	2902178	TCF19	⇩	1.64	3.85E-03
3560403	EGLN3	⇧	2.51	1.33E-03	2761837	FGFBP2	⇩	1.79	0.023	2773907	SDAD1	⇩	1.64	8.43E-03
2902707	HSPA1A	⇩	2.50	5.88E-04	2477933	GALM	⇩	1.78	0.028	3444436	TAS2R14	⇧	1.63	0.023
3385175	PICALM	⇧	2.39	2.77E-04	3020496	ST7	⇩	1.77	4.54E-03	3151943	TATDN1	⇧	1.63	0.013
3972929	GK	⇧	2.38	6.17E-04	2371346	RGL1	⇩	1.76	7.66E-03	3009399	HSPB1	⇩	1.62	0.031
2662581	C3orf10	⇩	2.38	3.78E-03	3635198	BCL2A1	⇩	1.75	4.18E-03	2638962	DTX3L	⇩	1.62	0.010
3449068	TMTC1	⇧	2.29	0.018	3444493	TAS2R19	⇧	1.75	0.030	3147020	ZNF706	⇧	1.62	0.014
3403841	RIMKLB	⇧	2.29	0.016	2454661	TMEM206	⇩	1.74	3.82E-03	3466284	NDUFA12	⇧	1.61	4.88E-04
4022370	GPC4	⇧	2.23	0.048	2638988	PARP15	⇩	1.74	0.037	2893392	LY86	⇩	1.61	5.63E-03
2944025	TPMT	⇩	2.21	2.86E-03	2638789	CD86	⇩	1.74	0.012	3818395	ALKBH7	⇧	1.61	0.026
2950125	HLA-DQB2	⇩	2.21	0.040	2895841	CD83	⇩	1.73	0.012	2351004	GSTM5	⇩	1.61	0.016
4002081	MAP7D2	⇧	2.19	6.23E-03	3447863	KRAS	⇧	1.72	3.61E-04	2841491	C5orf41	⇩	1.60	0.013
3945545	APOBEC3B	⇩	2.14	4.01E-03	2708855	LIPH	⇩	1.72	0.036	2626097	ABHD6	⇩	1.60	0.032
2399743	AKR7A3	⇩	2.12	7.82E-03	3324713	METT5D1	⇧	1.72	0.041	2350922	GSTM4	⇩	1.60	0.026
2633191	GPR15	⇩	2.05	0.021	3893849	PRPF6	⇧	1.72	1.58E-03	3887107	ZSWIM1	⇩	1.60	4.51E-03
3617458	GOLGA8A	⇧	2.01	0.025	3513995	DLEU2	⇧	1.71	8.52E-03	2443518	C1orf156	⇩	1.59	1.18E-03
2878246	PFDN1	⇩	1.96	0.022	2638017	C3orf1	⇩	1.71	0.037	2587618	OLA1	⇧	1.59	2.30E-03
3577443	ASB2	⇩	1.96	0.040	3851072	ACP5	⇩	1.70	0.013	2447414	NCF2	⇩	1.59	0.043
2902725	HSPA1B	⇩	1.95	1.14E-03	2950307	HLA-DOA	⇩	1.69	0.014	2334350	MMACHC	⇩	1.58	0.010
2362333	MNDA	⇩	1.94	0.030	2946364	HIST1H3F	⇧	1.68	0.041	3742627	C17orf87	⇩	1.58	0.034
2677723	ARHGEF3	⇩	1.93	0.011	3288013	BMS1P1	⇧	1.68	1.53E-03	2515050	GORASP2	⇩	1.58	6.37E-03
2950145	HLA-DOB	⇩	1.92	0.012	2976113	IFNGR1	⇩	1.67	0.025	2608419	SETMAR	⇩	1.57	8.38E-04
2991233	AHR	⇩	1.87	3.80E-03	3103523	LY96	⇩	1.66	9.76E-03	2367843	DARS2	⇩	1.57	1.10E-03
3797295	L3MBTL4	⇧	1.86	0.014	2378068	G0S2	⇩	1.66	0.039	3427014	SNRPF	⇧	1.57	0.028
3273667	ADARB2	⇧	1.84	6.04E-03	3263944	PDCD4	⇧	1.66	2.81E-03	3074039	SLC35B4	⇩	1.57	0.024
2408189	PPT1	⇩	1.84	0.026	3518086	TBC1D4	⇧	1.66	0.040	2711818	LSG1	⇩	1.56	0.025
3434490	CABP1	⇧	1.82	2.15E-04	2970897	FRK	⇧	1.66	8.35E-03	2837810	UBLCP1	⇩	1.56	0.025
2664209	SH3BP5	⇩	1.82	0.019	3812385	CD226	⇩	1.65	5.67E-03	3981735	NCRNA00183	⇧	1.56	0.021
4037708	ND6	⇧	1.81	0.023	3281621	ARHGAP21	⇩	1.65	0.029	2950277	HLA-DMA	⇩	1.56	0.030
2418929	PIGK	⇩	1.81	0.026	2582124	NR4A2	⇩	1.65	5.68E-03	3067592	PNPLA8	⇩	1.56	0.011

Table B19: C9-LongvShort Gene List (n=1,024) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3848243	INSR	⇧	1.56	0.021
3304970	SH3PXD2A	⇧	1.55	0.038
3761632	SNF8	⇧	1.54	2.80E-03
3743734	C17orf61	⇧	1.54	5.69E-03
3420497	HELB	⇧	1.54	2.29E-03
3462843	NAP1L1	⇧	1.54	0.026
3373487	OR5M1	⇧	1.54	8.66E-04
2499158	RANBP2	⇩	1.54	1.79E-04
3624145	DMXL2	⇧	1.54	2.18E-03
3471264	VPS29	⇧	1.54	4.08E-03
3458400	NDUFA4L2	⇧	1.54	0.013
2420467	CTBS	⇩	1.54	0.040
3513856	EBPL	⇧	1.54	7.49E-03
3564919	FERMT2	⇧	1.54	7.84E-03
2500919	SLC20A1	⇩	1.53	0.042
3413950	SPATS2	⇧	1.53	1.37E-03
2836451	MFAP3	⇩	1.53	0.019
2716655	MSX1	⇧	1.53	5.88E-03
3951732	CECR5	⇧	1.53	3.16E-03
3332886	TMEM138	⇩	1.53	0.026
3714068	ALDH3A2	⇩	1.53	1.89E-03
3683018	RPS15A	⇧	1.52	0.043
2946845	ZNF204P	⇩	1.52	1.35E-03
2385095	ARV1	⇩	1.52	0.049
2879739	PRELID2	⇧	1.52	0.019
2330773	CDCA8	⇩	1.52	0.018
2752725	NEIL3	⇩	1.51	0.036
3865223	TRAPPC6A	⇧	1.51	0.038
3864551	PLAUR	⇩	1.51	0.035
3633699	NRG4	⇧	1.51	0.017
3485292	NBEA	⇧	1.51	0.018
3072435	TMEM209	⇩	1.50	0.023
2403470	DNAJC8	⇩	1.50	0.020
2501317	LOC654433	⇧	1.50	0.042
3210179	C9orf95	⇧	1.50	1.82E-03
2612401	BTD	⇩	1.50	0.024
2835792	GM2A	⇩	1.50	0.012
3334847	C11orf2	⇧	1.50	8.79E-04
2375212	PPP1R12B	⇩	1.49	0.023
2790570	PLRG1	⇩	1.49	5.77E-03
3250019	DDX50	⇧	1.49	7.54E-03
3362468	SBF2	⇧	1.49	0.030
2668205	GLB1	⇩	1.49	0.046
3712041	UBB	⇧	1.49	0.011
3058156	TMEM60	⇩	1.49	6.09E-03
2628682	ARL6IP5	⇩	1.49	0.036
3403077	C12orf57	⇧	1.48	4.02E-03
2604390	ARL4C	⇩	1.48	0.026
2939034	SERPINB9	⇩	1.48	0.017
3405515	APOLD1	⇧	1.48	0.019
3460584	LLPH	⇧	1.48	0.021
2879028	GNPDA1	⇩	1.48	0.028
2331679	MFSD2A	⇩	1.48	9.46E-03
2888879	DOK3	⇩	1.48	7.98E-04
2979056	N⇧43	⇩	1.48	1.19E-03
2428796	PTPN22	⇩	1.48	8.06E-04
3719112	ZNHIT3	⇧	1.48	9.97E-03
2369557	SOAT1	⇩	1.48	0.029
3547375	GPR65	⇩	1.48	0.027
3825823	NDUFA13	⇧	1.48	0.021
3490741	SUGT1	⇧	1.48	0.013
3936442	PEX26	⇧	1.48	9.34E-03
2805176	C5orf22	⇩	1.47	0.021
3521484	UGGT2	⇧	1.47	0.049
3444195	MAGOHB	⇧	1.47	1.02E-03
3494137	LMO7	⇧	1.47	0.046
3705412	C17orf97	⇧	1.47	1.99E-03
2626167	PXK	⇩	1.47	0.030
2409368	HYI	⇩	1.47	0.027
2708407	ALG3	⇩	1.47	7.26E-03
2633773	TFG	⇩	1.47	0.011
2692411	PTPLB	⇩	1.46	0.040
3221543	CDC26	⇧	1.46	5.90E-03
3845647	MKNK2	⇧	1.46	2.64E-03
2845274	CCDC127	⇩	1.46	0.035
2744674	RAB33B	⇩	1.46	0.031
3609592	MCTP2	⇧	1.46	0.018
2495446	INPP4A	⇩	1.46	0.026
3260423	CUTC	⇧	1.46	0.012
2464129	LOC100506975	⇧	1.46	0.011
3009198	RHBDD2	⇩	1.46	0.016
3978819	RRAGB	⇧	1.46	4.80E-03
2621583	ZNF589	⇩	1.46	0.035
2342576	ACADM	⇩	1.46	3.71E-03
3347615	ACAT1	⇩	1.46	0.039
3595846	FAM63B	⇧	1.46	0.029
3451264	YAF2	⇧	1.46	7.09E-03
3216529	ZNF782	⇧	1.46	0.018
3475324	TMEM120B	⇧	1.46	9.55E-03
3829768	UBA2	⇧	1.46	2.57E-03
3464967	GALNT4	⇧	1.46	1.60E-03
3507962	KATNAL1	⇧	1.46	0.026
3111695	EBAG9	⇩	1.45	5.52E-03
3996083	TMEM187	⇧	1.45	2.63E-03
2831519	C5orf32	⇩	1.45	0.037
2394784	NOL9	⇩	1.45	0.015

Table B19: C9-LongvShort Gene List (n=1,024) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2871176	REEP5	⇩	1.45	0.026
2954022	TRERF1	⇧	1.45	0.032
3762625	MBTD1	⇧	1.45	5.91E-04
2378180	C1orf107	⇩	1.45	1.64E-03
2845078	TRIM52	⇧	1.45	0.023
2820893	RFESD	⇩	1.44	0.017
2792069	NAF1	⇩	1.44	0.016
3335124	TIGD3	⇧	1.44	0.045
3035892	GNA12	⇧	1.44	0.015
3438027	RAN	⇧	1.44	1.77E-03
2639309	SEC22A	⇩	1.44	6.79E-03
3020273	CAV2	⇧	1.44	0.026
3025740	TMEM140	⇩	1.43	0.042
2636185	SLC35A5	⇩	1.43	0.030
2608469	ITPR1	⇩	1.43	4.68E-03
2743370	C4orf33	⇩	1.43	7.49E-03
2409770	TMEM53	⇩	1.43	0.014
2333658	ATP6V0B	⇩	1.43	0.046
2452977	FAIM3	⇩	1.43	0.046
3488942	NUDT15	⇧	1.43	2.67E-03
2668035	DYNC1LI1	⇩	1.43	4.74E-03
3706651	OR3A3	⇩	1.43	0.029
2870397	PJA2	⇩	1.43	5.50E-03
3061456	SAMD9L	⇩	1.43	0.043
2841699	CPEB4	⇩	1.43	9.14E-03
2446198	TOR1AIP2	⇩	1.43	1.37E-03
2878474	HARS	⇩	1.43	5.34E-03
3005956	C7orf42	⇩	1.43	1.87E-03
2588827	NFE2L2	⇩	1.42	9.86E-03
3283920	ARHGAP12	⇧	1.42	8.24E-04
3458911	CTDSP2	⇧	1.42	0.017
2336963	C1orf83	⇩	1.42	6.64E-03
2750594	SC4MOL	⇩	1.42	0.026
3005684	KCTD7	⇩	1.42	8.00E-03
2522439	BZW1	⇩	1.42	0.032
2616932	MLH1	⇩	1.42	0.018
3384321	RAB30	⇩	1.42	0.027
3807753	MBD1	⇧	1.42	0.023
3354879	HYLS1	⇧	1.42	4.01E-04
3942384	MTFP1	⇧	1.42	0.033
2425212	DBT	⇩	1.42	0.010
3464912	POC1B	⇧	1.41	9.95E-03
3470689	ALKBH2	⇧	1.41	7.77E-03
2411228	STIL	⇩	1.41	0.023
2970985	TSPYL4	⇩	1.41	8.86E-03
2777070	HSD17B11	⇩	1.41	0.044
3396770	CDON	⇧	1.41	8.47E-03
3221633	HDHD3	⇩	1.41	6.62E-03
3179669	C9orf89	⇧	1.41	5.58E-03
3864430	ETHE1	⇩	1.41	0.037
2436228	GATAD2B	⇩	1.41	1.05E-06
3098977	LYN	⇩	1.41	5.79E-03
2807862	C5orf51	⇩	1.41	0.015
3168700	ZCCHC7	⇧	1.41	0.012
2682568	SHQ1	⇩	1.41	0.012
3292634	RUFY2	⇧	1.41	0.013
3584728	SNRPN	⇧	1.41	0.049
2531377	SP100	⇩	1.41	0.045
2773348	PF4	⇧	1.40	0.025
3807261	SMAD7	⇧	1.40	5.76E-03
2690900	CD80	⇩	1.40	0.028
2894663	PAK1IP1	⇩	1.40	0.037
3716664	SUZ12P	⇧	1.40	0.024
2433209	PRKAB2	⇩	1.40	0.017
3428088	ACTR6	⇧	1.40	0.013
2363919	ATF6	⇩	1.40	7.38E-03
3421706	RAB3IP	⇧	1.40	5.23E-03
2973168	ECHDC1	⇩	1.40	0.022
3540353	CHURC1	⇧	1.40	0.013
3841901	NLRP2	⇩	1.40	4.23E-03
2363202	SLAMF7	⇩	1.40	0.028
2796911	CCDC110	⇧	1.40	0.025
2731831	USO1	⇩	1.40	0.011
2876257	SAR1B	⇩	1.39	0.039
3426257	SOCS2	⇧	1.39	0.016
2900269	ZSCAN16	⇩	1.39	0.011
4002148	EIF1AX	⇧	1.39	0.023
3554592	BTBD6	⇩	1.39	0.023
3361811	STK33	⇧	1.39	6.28E-03
2366156	SFT2D2	⇩	1.39	0.010
2506903	MGAT5	⇩	1.39	0.041
3537030	RPL13AP3	⇧	1.39	0.036
2784113	CCNA2	⇩	1.39	0.019
2437401	FDPS	⇩	1.39	6.95E-03
3784509	ZNF271	⇧	1.39	7.91E-03
3462630	CAPS2	⇧	1.39	8.11E-05
2770427	C4orf14	⇩	1.39	0.030
3756856	KRTAP17-1	⇧	1.39	0.027
3998632	PNPLA4	⇧	1.39	4.14E-04
3359751	ZNF195	⇧	1.39	6.76E-03
2596162	INO80D	⇩	1.39	1.79E-04
3439063	ZNF26	⇧	1.39	7.02E-03
4043943	INPP5B	⇩	1.39	3.20E-03
3344861	C11orf54	⇧	1.39	0.038
2348702	SLC35A3	⇩	1.38	0.031
3749432	RNFT1	⇧	1.38	0.011

Table B19: C9-LongvShort Gene List (n=1,024) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3487095	DGKH	⇧	1.38	0.039	3846742	SH3GL1	⇧	1.37	0.034	3402978	DSTNP2	⇧	1.36	0.013
2334459	TMEM69	⇩	1.38	9.21E-04	2442134	TMCO1	⇩	1.37	0.031	2523213	BMPR2	⇩	1.36	0.036
3788833	POLI	⇧	1.38	5.59E-03	2738146	TET2	⇩	1.37	6.46E-03	3332131	STX3	⇧	1.36	1.75E-03
3636956	WDR73	⇧	1.38	5.38E-03	2522509	NIF3L1	⇩	1.37	5.88E-03	3716579	LRRC37BP1	⇧	1.36	0.036
3414440	C12orf62	⇧	1.38	0.021	3836317	VASP	⇧	1.37	9.33E-03	2911413	PRIM2	⇩	1.36	0.035
2903435	HLA-DPB2	⇩	1.38	0.023	3853453	RASAL3	⇧	1.37	0.047	3409127	ARNTL2	⇧	1.36	0.045
3994451	CXorf40A	⇧	1.38	0.039	2820925	RHOBTB3	⇩	1.37	0.035	3781124	MIB1	⇧	1.36	1.22E-03
2866590	LYSMD3	⇩	1.38	0.036	2369796	TOR1AIP1	⇩	1.37	0.012	2835021	PCYOX1L	⇩	1.36	0.049
3353914	VWA5A	⇩	1.38	0.035	2351940	DDX20	⇩	1.37	0.026	3939545	MIF	⇧	1.36	8.34E-03
2608765	ARL8B	⇩	1.38	2.21E-03	3914286	SOX18	⇧	1.37	0.036	2356181	RBM8A	⇩	1.36	0.011
3822216	IER2	⇧	1.38	4.17E-03	2899022	TRIM38	⇩	1.37	6.49E-04	2524743	FASTKD2	⇩	1.36	5.41E-03
3417457	MYL6	⇧	1.38	0.044	2899243	HIST1H4F	⇩	1.37	0.031	2457261	DUSP10	⇩	1.36	0.047
3368398	CCDC73	⇧	1.38	0.023	2386747	GPR137B	⇩	1.37	0.026	2544164	C2orf44	⇩	1.36	0.047
3753500	SLFN11	⇧	1.38	0.022	2413484	YIPF1	⇩	1.37	0.036	2474322	C2orf28	⇩	1.36	5.42E-03
2321849	DNAJC16	⇩	1.38	0.026	2649113	TIPARP	⇩	1.37	0.026	3454680	TFCP2	⇧	1.36	2.59E-03
2814642	MCCC2	⇩	1.38	9.52E-03	2476075	SPAST	⇩	1.37	6.47E-03	3985644	TCEAL3	⇩	1.36	0.039
2956438	MUT	⇩	1.38	0.030	3444525	TAS2R46	⇧	1.37	0.014	2829562	TXNDC15	⇩	1.36	0.042
3434413	RNF10	⇧	1.38	7.12E-03	2372781	RGS1	⇩	1.37	0.028	3589141	SPRED1	⇧	1.36	0.021
2451544	MYOG	⇩	1.38	0.026	3738205	MRPL12	⇧	1.37	0.018	3851150	ZNF433	⇧	1.36	2.54E-03
3840372	ZNF701	⇧	1.38	0.045	3416943	GDF11	⇧	1.37	0.039	2902348	MICB	⇩	1.36	0.022
3431220	MVK	⇧	1.38	9.02E-04	2599433	USP37	⇩	1.37	0.010	2457573	AIDA	⇧	1.36	0.019
4027532	GAB3	⇧	1.38	0.029	2678367	PDHB	⇩	1.37	5.90E-03	2604254	HJURP	⇩	1.36	0.047
2855443	LOC100132356	⇩	1.37	0.014	2859195	DIMT1L	⇩	1.37	0.010	2494484	NCAPH	⇩	1.36	0.047
2575949	TUBA3E	⇧	1.37	1.54E-03	2336913	LRRC42	⇩	1.37	2.91E-03	2501697	ACTR3	⇩	1.36	1.66E-04
2429338	SIKE1	⇩	1.37	4.50E-03	3044753	LSM5	⇩	1.37	0.033	3227454	QRFP	⇧	1.36	0.048
3854756	RAB3A	⇩	1.37	0.020	3869714	ZNF611	⇧	1.37	0.026	3761054	COPZ2	⇧	1.36	8.49E-04
3726960	NME2	⇧	1.37	9.19E-03	2527253	IGFBP2	⇧	1.37	0.049	2892277	NQO2	⇩	1.36	0.015
2551786	MCFD2	⇩	1.37	0.015	3830277	USF2	⇧	1.36	8.24E-03	2784131	BBS7	⇩	1.35	0.011
2818454	XRCC4	⇩	1.37	1.19E-03	3662444	NLRC5	⇧	1.36	7.37E-03	3230490	EDF1	⇧	1.35	5.01E-03
2495782	LIPT1	⇩	1.37	0.022	3644887	TBC1D24	⇩	1.36	0.027	2330334	THRAP3	⇩	1.35	5.42E-03
3738629	SLC16A3	⇧	1.37	0.047	3668898	ZFP1	⇧	1.36	9.63E-03	3223551	MEGF9	⇩	1.35	0.045
2713555	KIAA0226	⇩	1.37	2.40E-03	3426301	CRADD	⇧	1.36	2.54E-04	3142932	C8orf59	⇧	1.35	0.015

Table B19: C9-LongvShort Gene List (n=1,024) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3029030	CASP2	⇩	1.35	0.017
2642791	DNAJC13	⇩	1.35	2.04E-03
2835006	GRPEL2	⇩	1.35	0.029
2316245	PRKCZ	⇩	1.35	0.033
3468925	NFYB	⇧	1.35	5.14E-04
3666649	VPS4A	⇧	1.35	0.014
2425118	SASS6	⇩	1.35	0.013
2355615	SEC22B	⇩	1.35	2.53E-03
3739162	TBCD	⇧	1.35	7.60E-03
3119376	C8orf31	⇩	1.35	0.015
3108433	MTDH	⇩	1.35	0.046
3182409	ZNF189	⇧	1.35	0.016
3673091	BANP	⇧	1.35	5.70E-04
3824395	PGLS	⇧	1.35	2.64E-03
2636726	QTRTD1	⇩	1.35	7.39E-03
2385258	C1orf124	⇩	1.35	0.026
2447993	C1orf25	⇩	1.35	5.97E-04
3191338	GPR107	⇩	1.35	0.032
3456313	ATP5G2	⇧	1.35	0.035
3816264	DOT1L	⇧	1.35	0.034
2439345	OR6Y1	⇩	1.35	5.79E-03
3476665	SCARB1	⇧	1.35	0.012
2559807	MOBKL1B	⇩	1.35	0.020
2318637	VAMP3	⇩	1.35	5.88E-03
2603395	HTR2B	⇩	1.34	0.031
3752097	C17orf42	⇧	1.34	0.036
3564210	PYGL	⇧	1.34	0.048
3929395	GCFC1	⇧	1.34	0.044
3726772	LUC7L3	⇧	1.34	0.019
2893895	BMP6	⇧	1.34	0.011
2986084	PHF10	⇧	1.34	0.045
2367086	FMO4	⇩	1.34	0.016
3490251	WDFY2	⇧	1.34	3.56E-03
3644541	TRAF7	⇧	1.34	0.015
2546008	S⇧T7L	⇩	1.34	5.45E-03
3884793	SLC32A1	⇧	1.34	0.043
2676219	PBRM1	⇩	1.34	0.019
3665997	DUS2L	⇩	1.34	0.026
3225096	NR6A1	⇧	1.34	0.026
2954527	ZNF318	⇩	1.34	0.015
3510858	FOXO1	⇧	1.34	0.047
2708817	TMEM41A	⇩	1.34	0.033
3346584	BIRC2	⇧	1.34	4.57E-03
2366184	TBX19	⇩	1.34	7.12E-03
2362394	IFI16	⇩	1.34	4.80E-04
2673902	QRICH1	⇩	1.34	6.02E-03
3421762	RAB3IP	⇧	1.34	2.84E-03
2434892	VPS72	⇩	1.34	0.019
3195296	SSNA1	⇧	1.34	0.036
3989678	XIAP	⇧	1.34	0.011
2757319	SLBP	⇩	1.34	0.049
3346147	ARHGAP42	⇧	1.34	0.028
2899146	HIST1H4C	⇧	1.34	0.048
2404254	PUM1	⇩	1.33	1.76E-06
2342665	MSH4	⇧	1.33	4.84E-03
3837464	GLTSCR2	⇧	1.33	0.044
2456849	RAB3GAP2	⇩	1.33	7.80E-04
3985665	TCEAL1	⇧	1.33	0.016
3409432	CCDC91	⇧	1.33	0.038
3836044	GEMIN7	⇧	1.33	0.027
3864286	PSG9	⇧	1.33	0.033
4019465	NKRF	⇧	1.33	0.039
2997952	STARD3NL	⇩	1.33	0.040
2974188	MED23	⇩	1.33	4.09E-03
3385003	CREBZF	⇧	1.33	0.021
3705967	SERPINF1	⇧	1.33	0.043
2512330	MARCH7	⇩	1.33	1.92E-03
3835966	RELB	⇧	1.33	0.034
2477302	CCDC75	⇧	1.33	0.031
3571542	PNMA1	⇧	1.33	2.50E-03
3315024	ADAM8	⇧	1.33	0.016
3851703	C19orf43	⇧	1.33	0.019
2517737	PLEKHA3	⇧	1.33	0.033
2460519	EXOC8	⇩	1.33	0.014
2734018	MRPS18C	⇧	1.33	0.018
2906607	NFYA	⇩	1.32	3.62E-03
3892660	RPS21	⇧	1.32	0.018
2541944	SMC6	⇩	1.32	3.27E-03
3770699	MIF4GD	⇩	1.32	0.011
2835531	NDST1	⇩	1.32	0.032
2986493	PSMB1	⇩	1.32	3.30E-03
3468301	PMCH	⇧	1.32	1.38E-03
3204261	CCL27	⇧	1.32	0.020
2339511	ATG4C	⇩	1.32	0.019
3421824	C12orf28	⇧	1.32	0.016
3448428	C12orf11	⇧	1.32	4.28E-03
2519756	WDR75	⇩	1.32	0.030
3870162	ZNF665	⇧	1.32	4.48E-04
2575196	SAP130	⇩	1.32	3.22E-03
3334501	PRDX5	⇧	1.32	0.034
3601840	CSK	⇧	1.32	0.026
3855071	FKBP8	⇧	1.32	4.37E-03
3825838	YJEFN3	⇧	1.32	5.28E-03
2841184	ERGIC1	⇩	1.32	0.020
3103494	TMEM70	⇩	1.32	0.015
3143330	FAM82B	⇧	1.32	5.33E-03

Table B19: C9-LongvShort Gene List (n=1,024) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3348189	FDX1	⇧	1.32	5.30E-03	2723710	PGM2	⇩	1.31	0.028	2694785	MBD4	⇩	1.30	0.011
3828162	C19orf2	⇧	1.32	7.18E-03	3418513	MARCH9	⇧	1.31	9.44E-03	2811745	IPO11	⇩	1.30	0.037
2328936	ZBTB8A	⇩	1.32	0.048	2892341	RIPK1	⇩	1.31	0.046	3075550	ZC3HAV1L	⇧	1.30	0.049
2550959	PREPL	⇩	1.32	3.36E-03	2545092	HADHA	⇩	1.31	0.017	3831168	CAPNS1	⇩	1.30	0.047
3761313	HOXB3	⇧	1.32	0.023	2358221	RPRD2	⇩	1.31	0.023	3409364	KLHDC5	⇧	1.30	0.014
2901660	PRR3	⇩	1.32	0.014	3197014	GLIS3	⇩	1.31	0.029	2950515	VPS52	⇩	1.30	0.038
3693837	GOT2	⇧	1.32	0.045	3578089	C14orf49	⇧	1.31	0.030	2430370	GDAP2	⇩	1.30	0.010
3947627	TSPO	⇧	1.32	0.049	2636272	GTPBP8	⇩	1.31	0.025	3923896	KRTAP10-12	⇧	1.30	9.09E-03
2516332	SCRN3	⇩	1.32	0.027	3229591	UBAC1	⇧	1.30	0.012	2429069	TRIM33	⇩	1.30	1.23E-03
3081707	MNX1	⇧	1.32	7.74E-03	2930753	C6orf72	⇩	1.30	0.032	3766960	SMURF2	⇧	1.30	0.042
3337168	GSTP1	⇧	1.32	6.93E-03	3673684	CDT1	⇧	1.30	0.020	2555630	CCT4	⇩	1.30	1.24E-03
2909723	CENPQ	⇩	1.32	0.037	3809671	NARS	⇩	1.30	0.010	3670772	CMIP	⇧	1.30	0.025
2659887	FYTTD1	⇩	1.32	0.029	3655723	MVP	⇧	1.30	6.94E-03	3402935	TPI1	⇧	1.30	0.042
2662491	TMEM111	⇩	1.31	0.044	2595443	WDR12	⇩	1.30	0.037	3608787	SLCO3A1	⇧	1.30	8.82E-03
3418298	KIF5A	⇧	1.31	8.72E-03	2949210	BAT4	⇩	1.30	0.024	3135184	RB1CC1	⇧	1.30	4.99E-03
3697090	ST3GAL2	⇧	1.31	0.033	2631845	CHMP2B	⇩	1.30	0.032	2458649	C1orf55	⇩	1.30	0.022
2826064	SRFBP1	⇩	1.31	6.21E-03	3432333	PTPN11	⇧	1.30	0.043	3737647	CHMP6	⇧	1.29	0.012
3712098	SNORD49A	⇧	1.31	0.014	3636879	UBE2Q2P1	⇧	1.30	9.41E-03	3530002	KHNYN	⇧	1.29	6.36E-03
2398789	SDHB	⇩	1.31	0.012	2446244	TOR1AIP1	⇩	1.30	0.037	3611126	MEF2A	⇧	1.29	5.06E-03
3503224	⇧F3A	⇧	1.31	3.68E-03	2336706	CPT2	⇩	1.30	0.013	3822723	PKN1	⇧	1.29	0.015
3784727	ELP2	⇧	1.31	0.012	3423184	ZDHHC17	⇧	1.30	0.022	3642604	MPG	⇧	1.29	4.58E-04
3821847	ASNA1	⇧	1.31	8.07E-03	2676319	GLT8D1	⇩	1.30	0.041	3642390	TARSL2	⇧	1.29	0.026
3707715	RPAIN	⇧	1.31	8.62E-03	4026842	ARHGAP4	⇧	1.30	0.025	3424442	TMTC2	⇧	1.29	0.041
3947310	C22orf32	⇧	1.31	0.029	3308864	RAB11FIP2	⇧	1.30	0.038	3570599	MAP3K9	⇧	1.29	1.13E-03
2623515	ALAS1	⇩	1.31	8.37E-03	3338552	CTTN	⇧	1.30	0.016	2726323	SLAIN2	⇩	1.29	0.011
2325526	SRRM1	⇩	1.31	0.016	2344542	RPF1	⇩	1.30	0.021	2328990	RBBP4	⇩	1.29	0.046
2876046	PPP2CA	⇩	1.31	0.021	3476457	NCOR2	⇧	1.30	7.62E-03	3713195	SMCR8	⇩	1.29	0.035
3292413	DNAJC12	⇧	1.31	0.015	2437645	GON4L	⇩	1.30	4.30E-03	2822407	PPIP5K2	⇩	1.29	0.032
2548274	STRN	⇩	1.31	5.60E-03	3026599	TRIM24	⇩	1.30	8.24E-03	3417435	MYL6B	⇧	1.29	0.018
3882720	RALY	⇧	1.31	0.017	2542737	LAPTM4A	⇩	1.30	0.036	3304718	PCGF6	⇧	1.29	0.010
3465409	BTG1	⇧	1.31	9.38E-04	3834519	ARHGEF1	⇧	1.30	0.018	3241601	C10orf68	⇧	1.29	0.048
2708610	MAGEF1	⇧	1.31	0.041	2336302	ZFYVE9	⇧	1.30	0.027	2963614	CGA	⇩	1.29	0.031

Table B19: C9-LongvShort Gene List (n=1,024) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3829020	PDCD5	⇧	1.29	0.039	2745288	IL15	⇧	1.28	6.72E-03	3348891	C11orf57	⇧	1.28	0.024
3161566	KDM4C	⇧	1.29	0.016	3218496	OR13C9	⇧	1.28	0.030	2744597	NAA15	⇩	1.28	0.018
2396121	DFFA	⇩	1.29	0.021	3331129	OR5AK2	⇧	1.28	0.015	3303530	NDUFB8	⇧	1.28	3.94E-03
2336099	OSBPL9	⇩	1.29	6.17E-03	2548402	EIF2AK2	⇩	1.28	0.020	2559649	DUSP11	⇩	1.28	0.035
3537164	PELI2	⇧	1.29	0.028	2360083	UBAP2L	⇩	1.28	1.62E-04	2363444	USP21	⇩	1.28	0.021
3088983	XPO7	⇩	1.29	6.96E-03	3015178	ZSCAN21	⇩	1.28	0.025	2570616	BUB1	⇩	1.28	0.049
3389745	CWF19L2	⇧	1.29	0.025	3381241	ARAP1	⇧	1.28	0.040	3747324	ZNF624	⇧	1.28	1.48E-03
2928392	VTA1	⇩	1.29	0.017	3243078	ZNF33A	⇧	1.28	0.031	3415812	ZNF740	⇧	1.28	5.93E-03
3697125	COG4	⇧	1.29	0.041	3229943	SDCCAG3	⇧	1.28	6.68E-03	3538789	SLC38A6	⇧	1.27	0.039
3396883	RPUSD4	⇧	1.29	0.015	3614087	UBE3A	⇧	1.28	0.018	3992148	DDX26B	⇧	1.27	0.020
3535515	FRMD6	⇧	1.29	0.013	3578069	C14orf139	⇧	1.28	0.028	2601021	FARSB	⇩	1.27	0.027
3177563	NAA35	⇧	1.29	6.44E-03	2349086	DPH5	⇧	1.28	0.043	2522728	CASP8	⇩	1.27	0.033
3037142	PMS2	⇩	1.29	0.011	3195174	MAN1B1	⇧	1.28	3.14E-03	3018484	GPR22	⇧	1.27	9.27E-04
3687715	TBC1D10B	⇧	1.29	0.021	3865511	EML2	⇧	1.28	0.018	3851267	ZNF625	⇧	1.27	0.047
3472225	DDX54	⇧	1.29	7.96E-03	3390852	C11orf92	⇧	1.28	0.038	3191176	USP20	⇧	1.27	5.65E-04
3181193	TDRD7	⇧	1.29	0.026	3383081	INTS4	⇩	1.28	0.026	2528020	TTLL4	⇩	1.27	0.014
2484305	PAPOLG	⇩	1.29	0.023	3761127	CBX1	⇧	1.28	7.23E-03	3730899	DDX42	⇧	1.27	0.028
3829857	ZNF302	⇧	1.29	7.44E-03	3403224	LOC283314	⇧	1.28	0.024	3349014	PTS	⇧	1.27	0.010
2436338	CRTC2	⇩	1.29	6.15E-04	2474527	NRBP1	⇩	1.28	0.033	2681157	TMF1	⇩	1.27	0.030
3416344	HOXC9	⇧	1.29	6.41E-03	3386638	SLC36A4	⇧	1.28	0.048	3942161	UQCR10	⇧	1.27	5.85E-03
3088544	ATP6V1B2	⇩	1.29	0.020	3382015	CHRDL2	⇧	1.28	0.029	3429555	EID3	⇧	1.27	4.09E-03
3067080	COG5	⇩	1.29	0.015	3320604	USP47	⇧	1.28	4.16E-03	2671652	ZDHHC3	⇩	1.27	0.041
2877465	ETF1	⇩	1.29	0.045	2693937	TPRA1	⇩	1.28	0.014	3243164	ZNF37A	⇧	1.27	0.032
4013224	ATRX	⇧	1.29	0.010	2950329	HLA-DPA1	⇩	1.28	0.040	2714230	PCGF3	⇩	1.27	0.032
3932148	BRWD1	⇧	1.29	0.024	2531522	CAB39	⇩	1.28	0.048	2717059	LOC93622	⇧	1.27	0.021
3464622	CEP290	⇧	1.29	5.10E-03	2356205	PEX11B	⇩	1.28	0.012	3803418	KLHL14	⇧	1.27	0.034
2866225	MEF2C	⇩	1.28	2.81E-03	3292735	SLC25A16	⇧	1.28	7.85E-03	3474228	RAB35	⇧	1.27	7.94E-03
3831698	ZNF420	⇧	1.28	1.59E-03	2320210	UBIAD1	⇩	1.28	0.035	3009959	PTPN12	⇩	1.27	0.025
3345774	JRKL	⇧	1.28	0.023	2827388	PRRC1	⇩	1.28	0.022	3424379	C12orf26	⇧	1.27	0.020
2515183	DCAF17	⇩	1.28	0.024	3447129	KIAA0528	⇧	1.28	2.01E-03	2347788	RWDD3	⇧	1.27	8.87E-03
2920962	FIG4	⇩	1.28	0.020	3272795	PAOX	⇧	1.28	5.97E-03	3975987	RBM10	⇧	1.27	0.014
2924898	RNF146	⇩	1.28	0.011	3657318	ZNF720	⇧	1.28	0.023	3819401	LASS4	⇧	1.27	0.031

Table B19: C9-LongvShort Gene List (n=1,024) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2384375	DUSP5P	⇧	1.27	0.024	4007734	TFE3	⇧	1.26	0.029	3962165	CENPM	⇧	1.25	0.031
3655877	INO80E	⇧	1.27	7.36E-03	2721809	ZCCHC4	⇩	1.26	0.016	3847515	NDUFA11	⇧	1.25	6.94E-03
2596201	NDUFS1	⇩	1.27	0.021	2436132	ILF2	⇩	1.26	0.038	3982560	P2RY10	⇩	1.25	0.047
2421782	CCBL2	⇩	1.27	0.046	3757602	DHX58	⇧	1.26	0.045	3735346	C17orf106	⇧	1.25	0.011
2600068	TUBA4A	⇩	1.27	0.034	2411638	LOC100128922	⇧	1.26	0.033	3271220	CTAGE7P	⇧	1.25	0.027
3504134	GJA3	⇧	1.27	0.040	2943808	N⇧153	⇩	1.26	4.44E-03	2359036	SNX27	⇩	1.25	0.019
3914230	ZNF512B	⇧	1.27	4.61E-03	2741768	EXOSC9	⇩	1.26	9.17E-03	3489957	RNASEH2B	⇧	1.25	0.032
2662520	CIDECP	⇩	1.27	6.96E-03	3815493	HMHA1	⇧	1.26	0.019	3756344	SMARCE1	⇧	1.25	0.022
3514711	CTAGE3P	⇧	1.27	0.016	2766359	RFC1	⇩	1.26	0.031	3939707	CABIN1	⇧	1.25	0.018
2695200	PIK3R4	⇩	1.27	0.047	2772968	COX18	⇩	1.26	0.033	3459956	C12orf66	⇧	1.25	0.017
3466826	CDK17	⇧	1.27	8.12E-03	3846114	AES	⇧	1.26	0.049	3228097	TTF1	⇧	1.25	0.046
3476012	MPHOSPH9	⇧	1.27	0.022	3320717	MICAL2	⇩	1.26	0.038	2862716	GFM2	⇩	1.25	0.017
3955940	CRYBB1	⇩	1.27	0.014	3015216	COPS6	⇩	1.26	0.036	2641263	RAB7A	⇩	1.25	0.013
3110171	ATP6V1C1	⇩	1.27	0.026	3859622	ZNF792	⇧	1.26	0.025	3816686	ZNF556	⇧	1.25	4.84E-03
3457315	WIBG	⇧	1.26	0.034	3849688	ZNF266	⇧	1.26	0.025	3944620	MPST	⇧	1.25	0.024
2616317	PDCD6IP	⇩	1.26	5.02E-03	3866302	AP2S1	⇧	1.26	0.025	3808096	MEX3C	⇧	1.25	0.030
2860614	CCDC125	⇩	1.26	0.042	2466039	ZNF692	⇩	1.26	0.026	2908100	POLH	⇩	1.25	0.015
3372235	RAPSN	⇩	1.26	0.022	2688070	GUCA1C	⇧	1.26	0.028	3317223	IGF2AS	⇧	1.25	0.021
3674559	DEF8	⇧	1.26	0.044	3169043	RG9MTD3	⇧	1.26	0.041	3886050	SRSF6	⇧	1.25	1.25E-03
3768880	ABCA10	⇧	1.26	0.040	3212728	AGTPBP1	⇧	1.26	0.020	2621949	NDUFAF3	⇩	1.25	0.020
2821417	LNPEP	⇩	1.26	0.033	4053462	KLHL17	⇧	1.26	5.62E-04	3830002	GRAMD1A	⇧	1.25	0.013
4000269	GEMIN8	⇧	1.26	0.032	3478457	STX2	⇧	1.26	0.030	3202224	LRRC19	⇧	1.25	7.29E-03
3214359	AUH	⇧	1.26	1.89E-03	3299782	FLJ37201	⇧	1.26	0.019	2526759	ATIC	⇩	1.25	0.034
3949097	TRMU	⇧	1.26	5.11E-04	3708160	ALOX12	⇧	1.25	1.51E-03	3352813	TBCEL	⇧	1.25	0.025
3704896	CHMP1A	⇧	1.26	7.89E-03	2541230	NBAS	⇩	1.25	0.011	3923632	PFKL	⇧	1.25	1.70E-03
3197479	INSL6	⇧	1.26	0.022	3343202	EED	⇧	1.25	0.035	3710681	MAP2K4	⇧	1.25	0.031
3741383	OR1E2	⇧	1.26	5.36E-03	3735847	SEPT9	⇧	1.25	0.046	3224650	DENND1A	⇧	1.25	0.040
3056292	CLDN3	⇧	1.26	3.53E-03	2963929	RNGTT	⇩	1.25	6.19E-03	2595252	SUMO1	⇧	1.25	0.024
2462456	HEATR1	⇩	1.26	0.028	3846783	UBXN6	⇧	1.25	8.89E-03	3702689	ZDHHC7	⇧	1.25	0.025
2978989	LATS1	⇩	1.26	0.014	2712632	TFRC	⇩	1.25	0.047	3870054	ZNF160	⇧	1.25	0.033
3729123	DHX40	⇧	1.26	0.018	3817167	MRPL54	⇧	1.25	0.041	3199790	PSIP1	⇧	1.25	0.027
3720322	PPP1R1B	⇩	1.26	0.014	2527939	BCS1L	⇩	1.25	0.044	2454532	INTS7	⇩	1.25	0.045

Table B19: C9-LongvShort Gene List (n=1,024) MALE ONLY SAMPLES [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

3671850	KLHL36	⇧	1.25	0.014	3637006	SEC11A	⇧	1.24	0.044	2396480	EXOSC10	⇩	1.23	6.36E-04
3394183	H2AFX	⇧	1.25	0.035	3804143	RPRD1A	⇧	1.24	0.027	3758845	HDAC5	⇧	1.23	0.027
3030448	ZNF398	⇩	1.25	0.044	3427876	APAF1	⇧	1.24	0.036	3833323	ZNF546	⇧	1.23	0.035
2852333	ZFR	⇩	1.25	3.52E-03	2525272	PIKFYVE	⇩	1.24	0.014	3747966	SREBF1	⇧	1.23	0.017
2882555	FAM114A2	⇩	1.25	0.014	3716337	CCDC55	⇧	1.24	0.047	2659918	LRCH3	⇩	1.23	0.032
3761348	HOXB4	⇧	1.24	0.041	2544925	ASXL2	⇩	1.24	0.013	3713874	MAPK7	⇧	1.23	1.83E-03
2759857	ACOX3	⇩	1.24	0.038	3416114	TARBP2	⇧	1.24	0.011	2843619	HNRNPAB	⇩	1.23	0.040
3845365	TCF3	⇧	1.24	0.021	3045739	HERPUD2	⇩	1.24	0.034	3481543	SPATA13	⇧	1.23	0.046
3949229	TBC1D22A	⇧	1.24	0.016	3724989	CDK5RAP3	⇧	1.24	0.045	3303913	FBXW4	⇧	1.23	4.40E-03
2890859	MGAT1	⇧	1.24	0.025	2392421	PEX10	⇩	1.24	0.035	2564816	ANKRD36B	⇧	1.23	0.039
2729884	UGT2B10	⇧	1.24	0.027	2389789	SCCPDH	⇩	1.24	0.030	3414632	DIP2B	⇧	1.23	0.045
3431426	IFT81	⇧	1.24	0.015	3027808	AGK	⇩	1.24	0.026	2456746	EPRS	⇩	1.23	0.022
2331511	BMP8A	⇧	1.24	0.046	3046556	TARP	⇧	1.24	0.032	3412008	PPHLN1	⇧	1.23	0.031
3671448	HSBP1	⇧	1.24	0.026	2742093	BBS12	⇩	1.24	9.65E-03	3015778	EPO	⇩	1.23	0.029
2612175	NR2C2	⇩	1.24	1.94E-03	3791168	KIAA1468	⇧	1.24	0.023	2320374	FBXO6	⇩	1.23	0.022
3829575	LSM14A	⇧	1.24	0.032	2678029	DNAH12	⇧	1.24	0.019	3131720	BRF2	⇧	1.23	0.019
3843525	ZNF586	⇧	1.24	0.022	3018652	CBLL1	⇩	1.24	0.033	2975680	BCLAF1	⇩	1.23	0.044
3662170	MT1DP	⇧	1.24	1.67E-03	3747657	FLCN	⇧	1.24	0.013	2693569	ZXDC	⇩	1.23	0.010
2796384	IRF2	⇩	1.24	0.026	3874249	ITPA	⇩	1.24	0.035	2504645	MYO7B	⇩	1.23	0.024
3601675	ARID3B	⇧	1.24	0.040	3860596	ZNF461	⇧	1.23	0.027	3740201	MYO1C	⇧	1.23	0.027
2815331	BTF3	⇧	1.24	0.034	3834651	ZNF526	⇧	1.23	6.27E-03	2675628	VPRBP	⇩	1.23	0.031
3359469	NAP1L4	⇧	1.24	0.023	3474344	RPLP0	⇧	1.23	0.013	2535927	GPR35	⇩	1.23	0.024
2647898	MED12L	⇧	1.24	0.043	2604223	DNAJB3	⇧	1.23	0.036	3687849	ZNF764	⇧	1.23	0.044
3928534	KRTAP19-4	⇧	1.24	0.048	3851250	ZNF20	⇧	1.23	0.032	2831719	ANKHD1	⇩	1.23	6.43E-03
3960827	SUN2	⇧	1.24	0.035	3185205	HSDL2	⇩	1.23	0.026	3946563	RBX1	⇧	1.23	2.85E-04
3419239	MON2	⇧	1.24	2.31E-03	2739079	SEC24B	⇩	1.23	0.011	3421446	CPSF6	⇧	1.23	5.81E-03
3145953	RPL30	⇧	1.24	0.029	3378867	TMEM134	⇧	1.23	0.028	3018696	DLD	⇩	1.23	0.019
4019900	CUL4B	⇧	1.24	0.028	3245783	WDFY4	⇧	1.23	0.035	3701297	CDYL2	⇩	1.23	0.037
3272027	LRRC27	⇧	1.24	0.011	3642707	ITFG3	⇧	1.23	0.032	3358174	IRF7	⇧	1.23	0.038
2851274	CDH10	⇧	1.24	1.72E-03	3894098	C20orf96	⇩	1.23	0.041	3540862	GPHN	⇧	1.23	0.046
3856720	ZNF99	⇧	1.24	0.038	2901841	ATAT1	⇩	1.23	0.011	2950242	PPP1R2P1	⇧	1.23	8.19E-03
3965833	SBF1	⇧	1.24	0.010	2529627	KCNE4	⇧	1.23	0.032	3956290	PITPNB	⇧	1.23	0.014

Table B19: C9-LongvShort Gene List (n=1,024) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2419235	FUBP1	⇩	1.23	4.11E-05	3401099	FKBP4	⇧	1.22	0.037	3893796	DNAJC5	⇧	1.21	0.049
2837499	LSM11	⇧	1.23	8.67E-03	3479438	CHFR	⇧	1.22	0.040	3908786	STAU1	⇧	1.21	0.028
3276421	KIN	⇧	1.23	0.045	2408855	FOXJ3	⇩	1.22	0.026	3817222	ITGB1BP3	⇧	1.21	0.023
3592366	SPATA5L1	⇧	1.22	0.033	2400373	EIF4G3	⇩	1.22	8.98E-03	3824713	ARRDC2	⇧	1.21	4.12E-03
3708462	ACAP1	⇧	1.22	6.82E-03	2333907	RNF220	⇩	1.22	3.58E-03	3478957	DDX51	⇧	1.21	3.80E-03
3119735	ZNF623	⇩	1.22	0.032	2971692	MCM9	⇧	1.22	0.026	3419849	TBK1	⇧	1.21	0.011
2878446	NDUFA2	⇩	1.22	0.034	3458783	CDK4	⇧	1.22	0.046	4009062	KDM5C	⇧	1.21	0.015
2909404	CD2AP	⇩	1.22	0.012	3696016	PSMB10	⇧	1.22	2.28E-03	3938113	HIC2	⇧	1.21	0.043
2877314	CDC23	⇩	1.22	6.26E-03	3135156	FAM150A	⇧	1.22	0.037	2502952	TMEM177	⇩	1.21	0.036
2470654	DDX1	⇩	1.22	0.039	2532510	GIGYF2	⇩	1.22	2.12E-03	2545750	EIF2B4	⇩	1.21	0.026
3589947	BAHD1	⇧	1.22	0.026	3892409	LSM14B	⇧	1.22	0.020	2459866	N⇧133	⇩	1.21	0.038
2352228	CAPZA1	⇩	1.22	3.27E-03	3260957	LZTS2	⇧	1.22	0.010	3667902	DHX38	⇧	1.21	0.012
2662020	RAD18	⇩	1.22	0.030	3407229	AEBP2	⇧	1.22	0.015	3063727	TAF6	⇩	1.21	0.025
3850409	KRI1	⇧	1.22	0.039	2717049	MRFAP1	⇧	1.22	0.044	3840642	ZNF818P	⇧	1.21	0.024
3962293	CYP2D7P1	⇧	1.22	0.047	3602569	C15orf27	⇧	1.22	0.035	3279410	FAM188A	⇧	1.21	0.020
3668834	ZNRF1	⇧	1.22	0.045	2618940	CTNNB1	⇩	1.22	8.41E-03	2806231	BRIX1	⇩	1.21	0.041
3869761	ZNF600	⇧	1.22	0.033	2435044	POGZ	⇩	1.22	0.010	2507495	UBXN4	⇩	1.21	0.033
3438417	SFSWAP	⇧	1.22	0.016	3250726	KIAA1274	⇧	1.22	0.038	3347549	CUL5	⇧	1.21	0.040
3924100	C21orf89	⇧	1.22	0.048	3159754	DMRT2	⇧	1.22	1.27E-03	3292448	HERC4	⇧	1.21	0.027
2358171	PRPF3	⇩	1.22	8.26E-03	3770588	NT5C	⇧	1.22	6.42E-03	3816988	FZR1	⇧	1.21	0.015
2947572	TRIM27	⇩	1.22	0.038	3662265	N⇧93	⇩	1.22	0.038	2835960	G3BP1	⇩	1.21	3.30E-03
2594569	ORC2	⇩	1.22	0.027	2452319	RBBP5	⇩	1.21	9.16E-04	3566304	EXOC5	⇧	1.21	0.043
3216476	ZNF510	⇧	1.22	0.037	2775756	SEC31A	⇩	1.21	2.46E-03	3230371	LCN10	⇩	1.21	5.27E-03
3980981	ITGB1BP2	⇧	1.22	0.013	3959829	IFT27	⇧	1.21	0.043	3202293	C9orf11	⇧	1.21	0.019
3916576	GABPA	⇧	1.22	7.22E-03	2773756	G3BP2	⇩	1.21	0.031	2319881	PEX14	⇩	1.21	0.011
3674349	ZNF276	⇧	1.22	0.034	3358361	PDDC1	⇧	1.21	0.048	3603295	CRABP1	⇧	1.21	0.017
2477980	GEMIN6	⇩	1.22	0.042	2800906	MTRR	⇩	1.21	0.033	2964327	LYRM2	⇧	1.21	0.038
3358262	DEAF1	⇧	1.22	0.043	3658980	GPT2	⇧	1.21	0.013	2545653	MPV17	⇩	1.21	5.25E-03
3504526	LATS2	⇧	1.22	0.035	2407191	GNL2	⇩	1.21	0.045	3267273	GRK5	⇧	1.21	0.044
2519140	ZC3H15	⇩	1.22	0.025	2461786	ARID4B	⇩	1.21	0.041	2464499	HNRNPU	⇩	1.21	0.017
2815043	TNPO1	⇩	1.22	5.05E-03	2695941	TOPBP1	⇩	1.21	0.031	3844656	POLRMT	⇧	1.21	0.037
3337329	ALDH3B1	⇧	1.22	9.57E-03	2709235	DGKG	⇩	1.21	0.041	3302360	MMS19	⇧	1.21	0.017

Table B19: C9-LongvShort Gene List (n=1,024) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2756831	SLC26A1	⇩	1.21	9.71E-03
2367154	BAT2L2	⇩	1.21	1.55E-03
3281068	PIP4K2A	⇧	1.21	0.011
3559497	STRN3	⇧	1.21	0.031
2512601	TANK	⇩	1.21	0.040
3406195	C12orf60	⇧	1.21	4.83E-03
3441955	MRPL51	⇧	1.21	0.038
3923498	PWP2	⇧	1.21	0.028
3503976	PSPC1	⇧	1.21	0.037
3862167	FBL	⇧	1.21	0.019
3832830	PAK4	⇧	1.21	1.77E-03
3825201	UBA52	⇧	1.21	0.011
3029213	TAS2R41	⇩	1.21	0.043
3849190	ACTL9	⇧	1.21	0.042
2336383	PRPF38A	⇩	1.21	0.030
2321911	DDI2	⇩	1.21	0.044
3699133	FA2H	⇩	1.21	0.015
2895159	HIVEP1	⇩	1.21	0.019
3074362	CNOT4	⇩	1.21	0.021
2508611	ARHGAP15	⇩	1.21	0.031
3727499	TOM1L1	⇧	1.21	0.026
3290368	IPMK	⇧	1.20	0.032
3060450	C7orf62	⇧	1.20	0.021
2902013	GTF2H4	⇩	1.20	0.048
2451139	ARL8A	⇩	1.20	0.036
3832865	NCCRP1	⇧	1.20	0.029
3514488	INTS6	⇧	1.20	0.021
3299469	ANKRD22	⇧	1.20	0.014
2440143	COPA	⇩	1.20	0.013
3157901	PLEC	⇧	1.20	0.038
3740479	PRPF8	⇩	1.20	9.92E-03
3362934	ZBED5	⇧	1.20	0.036
3339423	INPPL1	⇧	1.20	3.16E-03
3334257	FERMT3	⇧	1.20	0.033
3458337	STAT6	⇧	1.20	0.022
2602901	TRIP12	⇩	1.20	1.98E-03
3091628	ELP3	⇩	1.20	0.023
3633109	ULK3	⇧	1.20	0.011
2333599	IPO13	⇩	1.20	0.049
3315835	PTDSS2	⇧	1.20	0.025
2514441	PPIG	⇩	1.20	0.033
3572869	C14orf4	⇧	1.20	0.037
3075566	ZC3HAV1	⇩	1.20	0.013
2396201	CASZ1	⇩	1.20	0.026
3576545	SMEK1	⇧	1.20	0.024
3060300	SRI	⇩	1.20	0.048
2993639	CBX3	⇧	1.20	0.014
3545403	GSTZ1	⇧	1.20	0.019
3977083	CCDC22	⇧	1.20	0.014
3929272	TCP10L	⇧	1.20	0.031
3532560	BRMS1L	⇧	1.20	0.028
2536531	FARP2	⇩	1.20	0.047
3732885	PRKAR1A	⇩	1.20	0.024
3330919	OR5T3	⇧	1.20	0.018
3157311	LY6H	⇧	1.20	0.011
3873185	RBCK1	⇧	1.20	0.011
3955327	C22orf13	⇧	1.20	0.026
3742727	DHX33	⇧	1.20	0.049
3739867	NXN	⇧	1.20	0.016
3488253	COG3	⇧	1.20	0.032
2908572	CDC5L	⇩	1.20	0.036
2684851	VGLL3	⇧	1.20	0.011
3468080	SYCP3	⇧	1.20	0.011
2832431	PCDHB11	⇩	1.20	0.047
2921086	CDC40	⇩	1.20	6.63E-03
3629272	PIF1	⇧	1.20	0.016
2479640	PPM1B	⇧	1.20	0.037

Table B20: C9-Long Specific Gene List (n=894) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value
3369249	APIP	⇧	2.93	5.73E-04	3743734	C17orf61	⇧	1.75	4.87E-04	3035892	GNA12	⇧	1.62	1.62E-03
3403841	RIMKLB	⇧	2.43	9.61E-03	3208355	CBWD3	⇧	1.75	0.027	2638789	CD86	⇩	1.62	0.026
3617574	GOLGA8B	⇧	2.42	0.014	3444336	PRR4	⇧	1.75	0.023	3760945	MRPL10	⇧	1.61	0.012
3385175	PICALM	⇧	2.27	5.14E-04	2363618	SDHC	⇩	1.74	0.017	3074039	SLC35B4	⇩	1.61	0.016
2899095	HIST1H4A	⇧	2.17	8.67E-03	2946364	HIST1H3F	⇧	1.74	0.029	2514122	LASS6	⇩	1.61	0.027
2671101	ANO10	⇩	2.17	0.021	2437247	GBA	⇩	1.73	0.036	2727762	SRD5A3	⇩	1.61	0.021
2913694	CD109	⇩	2.00	0.021	2735362	HERC6	⇩	1.73	0.027	3564919	FERMT2	⇧	1.61	3.24E-03
3945545	APOBEC3B	⇩	2.00	7.73E-03	3324713	METT5D1	⇧	1.72	0.040	2766893	APBB2	⇧	1.60	0.037
2878246	PFDN1	⇩	1.97	0.020	3507962	KATNAL1	⇧	1.71	1.77E-03	2668205	GLB1	⇩	1.60	0.018
2638077	PLA1A	⇩	1.96	0.013	2501317	LOC654433	⇧	1.71	8.02E-03	2788511	SLC10A7	⇩	1.59	0.019
3577443	ASB2	⇩	1.96	0.038	2946319	HIST1H4D	⇧	1.70	0.011	2820865	ARSK	⇩	1.58	0.041
2708855	LIPH	⇩	1.93	0.012	3188111	PTGS1	⇩	1.70	0.049	2836451	MFAP3	⇩	1.58	0.011
2633191	GPR15	⇩	1.92	0.033	3403077	C12orf57	⇧	1.68	2.50E-04	3818395	ALKBH7	⇧	1.58	0.030
3942472	TCN2	⇩	1.92	0.028	2991233	AHR	⇩	1.67	0.015	3260423	CUTC	⇧	1.58	2.82E-03
2409069	CCDC23	⇧	1.90	0.042	3470689	ALKBH2	⇧	1.67	1.47E-04	3619165	SRP14	⇧	1.58	9.88E-03
2893392	LY86	⇩	1.90	3.16E-04	3410695	DNM1L	⇧	1.66	0.019	2325192	RPL11	⇧	1.58	0.021
2399743	AKR7A3	⇩	1.89	0.022	2514563	KLHL23	⇧	1.66	0.017	3166844	CHMP5	⇧	1.57	0.046
3518086	TBC1D4	⇧	1.88	0.011	3160658	SLC1A1	⇩	1.65	0.033	3633699	NRG4	⇧	1.57	8.72E-03
3617458	GOLGA8A	⇧	1.85	0.044	2505993	POTEKP	⇧	1.65	0.017	3903361	AHCY	⇧	1.56	0.015
3275729	IL2RA	⇩	1.83	0.049	3173479	FOXD4L3	⇧	1.64	8.54E-03	3927226	APP	⇩	1.56	0.033
3142217	PAG1	⇩	1.82	0.043	3797295	L3MBTL4	⇧	1.64	0.046	3253438	RPS24	⇧	1.56	0.027
3841621	LILRB4	⇩	1.81	0.023	2468622	ID2	⇩	1.64	0.020	3020273	CAV2	⇧	1.56	6.81E-03
2418929	PIGK	⇩	1.80	0.026	3427014	SNRPF	⇧	1.64	0.016	3513995	DLEU2	⇧	1.56	0.027
2369557	SOAT1	⇩	1.80	1.43E-03	3761632	SNF8	⇧	1.64	7.65E-04	3420854	DYRK2	⇧	1.55	0.037
2395564	SLC2A5	⇩	1.78	0.040	3226097	ENG	⇩	1.64	0.020	3851072	ACP5	⇩	1.55	0.036
2963859	CNR1	⇩	1.78	0.031	4002148	EIF1AX	⇧	1.63	1.06E-03	2766192	TLR10	⇩	1.55	6.06E-03
2944025	TPMT	⇩	1.78	0.026	3490741	SUGT1	⇧	1.63	1.97E-03	2587618	OLA1	⇧	1.55	3.61E-03
2845274	CCDC127	⇩	1.77	2.06E-03	3462843	NAP1L1	⇧	1.63	0.012	3892452	LSM14B	⇧	1.55	0.036
2950145	HLA-DOB	⇩	1.76	0.027	3288013	BMS1P1	⇧	1.63	2.42E-03	3770944	H3F3B	⇧	1.55	0.015
3362468	SBF2	⇧	1.76	2.50E-03	2792800	DDX60	⇩	1.63	0.046	3842301	ZNF581	⇧	1.55	0.012
2950307	HLA-DOA	⇩	1.76	8.27E-03	2424102	CNN3	⇩	1.62	0.046	3458400	NDUFA4L2	⇧	1.55	0.012

Table B20: C9-Long Specific Gene List (n=894) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3405515	APOLD1	⇧	1.54	9.47E-03
2370317	MR1	⇩	1.54	0.013
3854454	BST2	⇩	1.54	0.042
3733911	SSTR2	⇩	1.54	0.038
2930243	SASH1	⇩	1.54	0.013
3221543	CDC26	⇧	1.54	2.04E-03
3542145	KIAA0247	⇩	1.53	9.98E-03
3438027	RAN	⇧	1.53	3.09E-04
3595846	FAM63B	⇧	1.53	0.014
3169331	ALDH1B1	⇧	1.53	0.021
3072435	TMEM209	⇩	1.53	0.017
2542795	SDC1	⇧	1.53	0.033
3864551	PLAUR	⇩	1.53	0.029
2977621	PLAGL1	⇩	1.53	0.017
3263624	MXI1	⇧	1.53	0.027
2960955	SLC17A5	⇩	1.52	0.011
2865050	RPS23	⇧	1.52	0.049
2330773	CDCA8	⇩	1.52	0.016
2454661	TMEM206	⇩	1.52	0.025
3263944	PDCD4	⇧	1.52	0.012
3185063	UGCG	⇩	1.52	0.011
3742708	C1QBP	⇧	1.52	0.019
2796911	CCDC110	⇧	1.51	5.96E-03
3475324	TMEM120B	⇧	1.51	4.39E-03
3453837	TUBA1A	⇧	1.51	0.041
3388914	DCUN1D5	⇧	1.51	0.020
3147020	ZNF706	⇧	1.51	0.031
2946681	HIST1H2BJ	⇧	1.51	0.029
3712197	CCDC144A	⇧	1.51	3.70E-03
2324616	HSPC157	⇧	1.50	0.021
3433843	SUDS3	⇧	1.50	0.047
3770632	SUMO2	⇧	1.50	9.03E-03
3512527	TPT1	⇧	1.50	6.16E-03
3444195	MAGOHB	⇧	1.50	5.36E-04
3634811	CTSH	⇩	1.50	0.038
3513856	EBPL	⇧	1.50	0.010
3916527	JAM2	⇩	1.50	0.023
2628682	ARL6IP5	⇩	1.50	0.031
3784509	ZNF271	⇧	1.50	1.32E-03
3435490	DENR	⇧	1.50	0.019
3447863	KRAS	⇧	1.49	6.10E-03
3250019	DDX50	⇧	1.49	6.95E-03
3103523	LY96	⇩	1.49	0.038
2692411	PTPLB	⇩	1.49	0.032
3962448	RRP7A	⇧	1.49	0.015
3053691	GUSB	⇩	1.48	3.26E-03
3951732	CECR5	⇧	1.48	5.59E-03
2363919	ATF6	⇩	1.48	2.10E-03
3837464	GLTSCR2	⇧	1.48	5.85E-03
3167383	NUDT2	⇧	1.48	0.046
3025740	TMEM140	⇩	1.48	0.027
2352106	CTTNBP2NL	⇩	1.48	3.93E-03
3414440	C12orf62	⇧	1.48	5.67E-03
3812385	CD226	⇩	1.48	0.028
3254337	C10orf57	⇩	1.48	0.038
3939545	MIF	⇧	1.48	1.10E-03
3468925	NFYB	⇧	1.47	1.41E-05
3061456	SAMD9L	⇩	1.47	0.027
2523213	BMPR2	⇩	1.47	8.64E-03
3726960	NME2	⇧	1.47	1.97E-03
3989678	XIAP	⇧	1.47	1.29E-03
3463522	PAWR	⇧	1.46	0.024
2403261	IFI6	⇩	1.46	0.018
3845352	UQCR11	⇧	1.46	0.040
2608469	ITPR1	⇩	1.46	2.85E-03
3824212	DDA1	⇧	1.46	0.021
3827218	RPSAP58	⇧	1.46	0.042
3704495	APRT	⇧	1.46	0.019
2835021	PCYOX1L	⇩	1.46	0.017
3451264	YAF2	⇧	1.46	6.90E-03
2899022	TRIM38	⇩	1.46	7.33E-05
2320411	AGTRAP	⇩	1.45	0.025
2442134	TMCO1	⇩	1.45	0.010
2970897	FRK	⇧	1.45	0.046
3458911	CTDSP2	⇧	1.45	0.012
3917204	C21orf7	⇧	1.45	0.045
3556966	HAUS4	⇧	1.45	0.025
3712041	UBB	⇧	1.45	0.016
3289392	FLJ31958	⇧	1.44	0.033
3341440	RN28S1	⇧	1.44	0.030
2705748	NCEH1	⇩	1.44	0.046
3189311	PBX3	⇩	1.44	6.07E-03
3407793	PYROXD1	⇧	1.44	0.043
2415084	JUN	⇩	1.44	0.042
3336378	RBM14	⇩	1.44	0.035
3510963	SUGT1P3	⇧	1.44	0.024
3391255	IL18	⇧	1.44	0.042
3868905	CTU1	⇧	1.44	0.014
2437736	RIT1	⇩	1.44	0.034
3770290	CD300LB	⇩	1.44	0.033
3923702	TRPM2	⇩	1.44	0.047
3547375	GPR65	⇩	1.44	0.038
2820925	RHOBTB3	⇩	1.43	0.016
2841184	ERGIC1	⇩	1.43	3.03E-03
2989435	C1GALT1	⇩	1.43	0.032
3027204	TBXAS1	⇩	1.43	0.046

Table B20: C9-Long Specific Gene List (n=894) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3345107	ANKRD49	⇧	1.43	6.11E-03
3892812	SLCO4A1	⇩	1.43	0.028
3373487	OR5M1	⇧	1.43	4.61E-03
3589141	SPRED1	⇧	1.43	7.47E-03
2370123	XPR1	⇩	1.43	0.018
3942161	UQCR10	⇧	1.43	7.00E-05
3475838	VPS37B	⇧	1.43	0.036
3928534	KRTAP19-4	⇧	1.43	1.55E-03
3221633	HDHD3	⇩	1.43	4.77E-03
2409368	HYI	⇩	1.43	0.037
3460584	LLPH	⇧	1.43	0.035
2321849	DNAJC16	⇩	1.43	0.014
3466284	NDUFA12	⇧	1.42	7.30E-03
3864286	PSG9	⇧	1.42	9.19E-03
2899146	HIST1H4C	⇧	1.42	0.018
2726483	OCIAD1	⇩	1.42	0.016
3722739	G6PC3	⇩	1.42	0.038
2336302	ZFYVE9	⇧	1.42	3.49E-03
3824395	PGLS	⇧	1.42	4.49E-04
2369796	TOR1AIP1	⇩	1.42	5.67E-03
3878934	NAA20	⇧	1.42	5.16E-03
3430389	C12orf23	⇧	1.42	0.023
3936442	PEX26	⇧	1.42	0.018
3368398	CCDC73	⇧	1.42	0.014
3738205	MRPL12	⇧	1.41	9.07E-03
3774385	SIRT7	⇧	1.41	0.046
2527253	IGFBP2	⇧	1.41	0.029
3712098	SNORD49A	⇧	1.41	2.24E-03
3729123	DHX40	⇧	1.41	5.61E-04
3428088	ACTR6	⇧	1.41	0.011
3630099	TIPIN	⇧	1.41	0.012
3866302	AP2S1	⇧	1.41	1.34E-03
2939034	SERPINB9	⇩	1.41	0.035
3985644	TCEAL3	⇩	1.41	0.021
2437645	GON4L	⇩	1.41	2.86E-04
3130113	GTF2E2	⇧	1.41	7.46E-03
3748659	GRAP	⇧	1.41	0.049
3886050	SRSF6	⇧	1.41	3.21E-06
3829857	ZNF302	⇧	1.41	4.51E-04
3720322	PPP1R1B	⇩	1.41	3.98E-04
3948047	PARVG	⇩	1.40	0.025
3473727	WSB2	⇧	1.40	0.042
2876257	SAR1B	⇩	1.40	0.036
2398736	ATP13A2	⇩	1.40	0.040
2941784	NEDD9	⇩	1.40	0.024
2363202	SLAMF7	⇩	1.40	0.027
2949801	AGPAT1	⇩	1.40	5.05E-03
2830638	KIF20A	⇩	1.40	0.037
2372781	RGS1	⇩	1.40	0.020
3207241	FLJ20444	⇧	1.40	0.038
2899413	BTN3A3	⇩	1.40	0.016
3636956	WDR73	⇧	1.40	3.45E-03
2835792	GM2A	⇩	1.40	0.031
3396770	CDON	⇧	1.40	8.80E-03
3705412	C17orf97	⇧	1.40	5.50E-03
2868904	ST8SIA4	⇩	1.40	0.030
2973995	EPB41L2	⇩	1.40	0.043
2773655	RCHY1	⇧	1.40	9.77E-03
4019465	NKRF	⇧	1.40	0.016
2922215	MARCKS	⇧	1.40	0.029
3432333	PTPN11	⇧	1.40	0.011
2384375	DUSP5P	⇧	1.39	2.38E-03
3331487	CTNND1	⇩	1.39	0.014
3444252	CSDA	⇧	1.39	0.015
2520138	MFSD6	⇩	1.39	0.026
3474344	RPLP0	⇧	1.39	1.70E-04
3580769	CKB	⇧	1.39	0.033
3997946	PRKX	⇧	1.39	0.012
3916576	GABPA	⇧	1.39	3.09E-05
3962000	PMM1	⇧	1.39	1.30E-03
2815331	BTF3	⇧	1.39	1.67E-03
2367843	DARS2	⇩	1.39	0.013
3857171	ZNF675	⇩	1.39	0.029
3762625	MBTD1	⇧	1.39	1.85E-03
3468301	PMCH	⇧	1.39	2.19E-04
3665857	NUTF2	⇧	1.39	1.57E-03
2386867	LGALS8	⇩	1.39	0.011
3417345	RPL41	⇧	1.39	0.010
3390852	C11orf92	⇧	1.39	7.21E-03
3042001	CYCS	⇧	1.39	2.06E-03
3470964	GLTP	⇧	1.39	0.018
3454740	PHB	⇧	1.39	0.021
3304004	NPM3	⇧	1.38	0.039
4015693	TIMM8A	⇧	1.38	7.68E-04
2488596	EMX1	⇩	1.38	0.019
2462589	MT1H	⇩	1.38	0.037
3223551	MEGF9	⇩	1.38	0.030
3952703	C22orf39	⇧	1.38	0.017
2708407	ALG3	⇩	1.38	0.020
3417457	MYL6	⇧	1.38	0.042
3947310	C22orf32	⇧	1.38	9.75E-03
2750594	SC4MOL	⇩	1.38	0.038
3441955	MRPL51	⇧	1.38	8.08E-04
3435681	ARL6IP4	⇧	1.38	6.08E-03
2875929	C5orf15	⇩	1.38	0.048
2955025	MRPL14	⇧	1.38	0.026

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3121228	ERICH1	⇧	1.38	0.038	2474322	C2orf28	⇩	1.36	4.85E-03	2964327	LYRM2	⇧	1.35	1.95E-03
3108901	VPS13B	⇩	1.38	9.62E-03	3426257	SOCS2	⇧	1.36	0.024	3687698	CD2BP2	⇧	1.35	0.042
2542226	RDH14	⇩	1.38	0.019	3869714	ZNF611	⇧	1.36	0.027	3394488	PVRL1	⇩	1.35	0.017
2482683	RPL23AP32	⇩	1.38	0.029	3413787	TUBA1C	⇧	1.36	0.034	3468103	GNPTAB	⇩	1.35	0.044
3376867	TRMT112	⇧	1.38	6.01E-03	2878662	DIAPH1	⇩	1.36	0.029	3815566	STK11	⇧	1.35	0.032
3119339	LY6E	⇩	1.38	0.013	2708610	MAGEF1	⇧	1.36	0.019	3292634	RUFY2	⇧	1.35	0.027
2986084	PHF10	⇧	1.38	0.028	3804143	RPRD1A	⇧	1.36	1.92E-03	2716655	MSX1	⇧	1.35	0.047
3056292	CLDN3	⇧	1.38	8.99E-05	2813060	PIK3R1	⇩	1.36	0.026	3422703	ATXN7L3B	⇧	1.35	0.013
2558150	AAK1	⇩	1.38	0.033	2930863	PCMT1	⇩	1.36	0.047	3716993	RNF135	⇧	1.34	0.021
3856554	ZNF100	⇧	1.38	0.042	3195296	SSNA1	⇧	1.36	0.029	3372235	RAPSN	⇩	1.34	4.00E-03
2423017	EVI5	⇧	1.37	0.042	3346147	ARHGAP42	⇧	1.36	0.022	3056656	GTF2IRD2	⇧	1.34	3.92E-03
2457573	AIDA	⇧	1.37	0.014	3292735	SLC25A16	⇧	1.36	1.27E-03	2386747	GPR137B	⇩	1.34	0.036
2331511	BMP8A	⇧	1.37	4.16E-03	2902736	C6orf48	⇧	1.36	0.021	3728509	DYNLL2	⇧	1.34	0.012
3462630	CAPS2	⇧	1.37	1.43E-04	4011844	IL2RG	⇩	1.35	8.47E-03	2428796	PTPN22	⇩	1.34	8.95E-03
3434413	RNF10	⇧	1.37	8.16E-03	2427074	PSMA5	⇧	1.35	0.032	3060182	ABCB1	⇩	1.34	0.040
2671652	ZDHHC3	⇩	1.37	6.57E-03	3822805	TECR	⇩	1.35	0.032	3018484	GPR22	⇧	1.34	6.82E-05
3332131	STX3	⇧	1.37	1.11E-03	3442785	CLEC4C	⇧	1.35	0.025	3459956	C12orf66	⇧	1.34	1.99E-03
3210179	C9orf95	⇧	1.37	0.012	3716579	LRRC37BP1	⇧	1.35	0.035	3191338	GPR107	⇩	1.34	0.037
3872441	ZNF552	⇧	1.37	0.029	3665116	CBFB	⇧	1.35	0.023	3522225	STK24	⇧	1.34	0.013
3799615	PTPN2	⇧	1.37	0.042	2842570	FAF2	⇩	1.35	0.040	3225096	NR6A1	⇧	1.34	0.024
2908052	POLR1C	⇧	1.37	1.45E-03	3338552	CTTN	⇧	1.35	6.18E-03	3005956	C7orf42	⇩	1.34	8.80E-03
2541230	NBAS	⇩	1.37	5.41E-04	2559696	TPRKB	⇧	1.35	9.06E-03	2465324	AHCTF1	⇧	1.34	0.017
3996083	TMEM187	⇧	1.37	9.45E-03	3752097	C17orf42	⇧	1.35	0.031	2864237	HOMER1	⇧	1.34	0.049
3540353	CHURC1	⇧	1.37	0.018	3464967	GALNT4	⇧	1.35	9.39E-03	3474228	RAB35	⇧	1.34	1.28E-03
3828162	C19orf2	⇧	1.37	2.39E-03	2868131	ERAP1	⇩	1.35	0.043	3749432	RNFT1	⇧	1.34	0.021
3716664	SUZ12P	⇧	1.37	0.035	3066751	SYPL1	⇩	1.35	0.030	3725083	SNX11	⇧	1.33	0.026
3829768	UBA2	⇧	1.37	0.010	2415910	DOCK7	⇩	1.35	0.024	3978819	RRAGB	⇧	1.33	0.029
3406421	STRAP	⇧	1.37	9.11E-03	3292413	DNAJC12	⇧	1.35	6.99E-03	2717518	AFAP1	⇧	1.33	0.015
3046556	TARP	⇧	1.37	2.06E-03	3391234	TIMM8B	⇧	1.35	0.042	3758148	CCDC56	⇧	1.33	0.024
2342665	MSH4	⇧	1.36	1.92E-03	3944620	MPST	⇧	1.35	2.77E-03	3135184	RB1CC1	⇧	1.33	2.04E-03
3421523	YEATS4	⇧	1.36	0.041	3464912	POC1B	⇧	1.35	0.024	2544925	ASXL2	⇩	1.33	1.22E-03
2437401	FDPS	⇩	1.36	9.98E-03	3145953	RPL30	⇧	1.35	3.06E-03	3129121	CCDC25	⇧	1.33	0.024

Table B20: C9-Long Specific Gene List (n=894) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3308864	RAB11FIP2	⇧	1.33	0.025
3642815	NME4	⇧	1.33	0.026
3494102	UCHL3	⇧	1.33	0.040
3435902	DDX55	⇧	1.33	5.83E-03
2950515	VPS52	⇩	1.33	0.023
2883878	EBF1	⇩	1.33	0.020
3892660	RPS21	⇧	1.33	0.014
3741305	OR1D2	⇧	1.33	0.018
2954527	ZNF318	⇩	1.33	0.016
2893895	BMP6	⇧	1.33	0.014
3361041	TPP1	⇩	1.33	0.043
3563814	L2HGDH	⇧	1.33	3.97E-03
2545645	UCN	⇧	1.33	0.029
3961664	ST13	⇧	1.33	0.020
3403299	PEX5	⇧	1.33	8.49E-03
2961317	TMEM30A	⇩	1.33	0.049
2729884	UGT2B10	⇧	1.33	4.20E-03
3608113	IQGAP1	⇩	1.33	0.024
3838665	RCN3	⇩	1.33	6.86E-03
3420497	HELB	⇧	1.33	0.036
3821847	ASNA1	⇧	1.33	5.20E-03
3624448	GNB5	⇧	1.32	0.021
3051928	CHCHD2	⇧	1.32	0.010
2565246	TMEM127	⇩	1.32	0.015
2971692	MCM9	⇧	1.32	2.55E-03
3739108	FN3KRP	⇧	1.32	0.027
2508520	KYNU	⇩	1.32	0.015
2871717	CCDC112	⇧	1.32	0.018
3781124	MIB1	⇧	1.32	2.78E-03
2916825	ANKRD6	⇧	1.32	2.10E-04
2437307	SCAMP3	⇩	1.32	0.047
2466039	ZNF692	⇩	1.32	7.89E-03
3518169	COMMD6	⇧	1.32	0.047
3695359	FAM96B	⇧	1.32	0.023
2477302	CCDC75	⇧	1.32	0.033
3668898	ZFP1	⇧	1.32	0.018
3829020	PDCD5	⇧	1.32	0.024
3784727	ELP2	⇧	1.32	0.010
2501697	ACTR3	⇩	1.32	4.80E-04
3439063	ZNF26	⇧	1.32	0.019
3535515	FRMD6	⇧	1.32	6.79E-03
3378790	PPP1CA	⇧	1.32	0.038
3402978	DSTNP2	⇧	1.32	0.022
3197014	GLIS3	⇩	1.31	0.024
3334847	C11orf2	⇧	1.31	0.018
2425212	DBT	⇩	1.31	0.040
3385003	CREBZF	⇧	1.31	0.025
3415915	PFDN5	⇧	1.31	0.029
3488942	NUDT15	⇧	1.31	0.019
3472225	DDX54	⇧	1.31	4.50E-03
2411638	LOC100128922	⇧	1.31	0.012
2777447	NAP1L5	⇧	1.31	0.019
3190659	SET	⇧	1.31	9.40E-03
3820906	C19orf52	⇧	1.31	1.40E-03
3218496	OR13C9	⇧	1.31	0.017
2548402	EIF2AK2	⇩	1.31	9.94E-03
3159040	RPL8	⇧	1.31	2.94E-04
3998632	PNPLA4	⇧	1.31	2.64E-03
3457523	RNF41	⇧	1.31	0.013
2415728	TM2D1	⇩	1.31	0.039
3225292	SCAI	⇧	1.31	2.20E-03
3451318	ZCRB1	⇧	1.31	0.027
3243078	ZNF33A	⇧	1.31	0.017
3014411	TRRAP	⇩	1.31	0.010
3323443	PRMT3	⇧	1.31	0.012
2977265	HIVEP2	⇩	1.31	0.028
2707824	MCCC1	⇩	1.31	0.023
3633550	IMP3	⇧	1.31	0.033
3402935	TPI1	⇧	1.31	0.035
2447993	C1orf25	⇩	1.31	1.64E-03
3862167	FBL	⇧	1.30	1.47E-03
3730899	DDX42	⇧	1.30	0.014
3741383	OR1E2	⇧	1.30	1.44E-03
2676219	PBRM1	⇩	1.30	0.029
2835531	NDST1	⇩	1.30	0.041
3421706	RAB3IP	⇧	1.30	0.024
2742009	ADAD1	⇧	1.30	0.012
3257670	PCGF5	⇧	1.30	0.044
2654855	ATP11B	⇩	1.30	0.036
3136129	RPS20	⇧	1.30	0.038
2734018	MRPS18C	⇧	1.30	0.025
3453556	PRKAG1	⇧	1.30	0.030
3860596	ZNF461	⇧	1.30	6.14E-03
3094778	TACC1	⇩	1.30	1.50E-03
3418513	MARCH9	⇧	1.30	9.71E-03
3566304	EXOC5	⇧	1.30	4.93E-03
2438504	MRPL24	⇧	1.30	0.048
2717049	MRFAP1	⇧	1.30	8.00E-03
3471704	BRAP	⇧	1.30	0.011
2639309	SEC22A	⇩	1.30	0.043
2362394	IFI16	⇩	1.30	1.53E-03
2748198	KIAA0922	⇩	1.30	2.51E-03
3409364	KLHDC5	⇧	1.30	0.013
3750685	SLC46A1	⇩	1.30	0.025
3890109	C20orf108	⇧	1.30	0.014
2756831	SLC26A1	⇩	1.30	6.92E-04

Table B20: C9-Long Specific Gene List (n=894) MALE ONLY SAMPLES [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

2499158	RANBP2	⇩	1.30	0.016
3929931	ATP5O	⇧	1.30	0.045
2888879	DOK3	⇩	1.30	0.020
2915268	DOPEY1	⇩	1.30	9.31E-03
3444525	TAS2R46	⇧	1.30	0.039
3396883	RPUSD4	⇧	1.30	0.012
3502829	GAS6	⇧	1.30	2.70E-03
2330334	THRAP3	⇩	1.30	0.014
3636442	C15orf40	⇧	1.30	8.38E-03
2545092	HADHA	⇩	1.29	0.020
2521479	HSPE1	⇧	1.29	0.044
3673684	CDT1	⇧	1.29	0.023
3421630	CCT2	⇧	1.29	0.028
2993639	CBX3	⇧	1.29	7.78E-04
3937743	SERPIND1	⇩	1.29	0.040
2489440	DOK1	⇧	1.29	0.015
2946845	ZNF204P	⇩	1.29	0.040
2349086	DPH5	⇧	1.29	0.037
2599371	TMBIM1	⇩	1.29	0.038
2376799	IKBKE	⇩	1.29	0.029
2369325	C1orf220	⇧	1.29	2.21E-03
3413950	SPATS2	⇧	1.29	0.045
2514566	SSB	⇧	1.29	0.011
2601230	SCG2	⇧	1.29	0.026
3534923	KLHDC2	⇧	1.29	0.028
3204261	CCL27	⇧	1.29	0.032
3883941	TGIF2	⇧	1.29	0.028
3977646	GSPT2	⇧	1.29	0.040
3962054	NHP2L1	⇧	1.29	0.026
3530982	G2E3	⇧	1.29	0.020
2821417	LNPEP	⇩	1.29	0.020
3644541	TRAF7	⇧	1.29	0.031
3307680	DCLRE1A	⇧	1.29	0.020
3825201	UBA52	⇧	1.29	1.10E-03
2599433	USP37	⇩	1.29	0.036
3530002	KHNYN	⇧	1.29	6.02E-03
2573641	CLASP1	⇩	1.29	7.98E-04
3898224	ESF1	⇧	1.29	4.23E-03
3053827	NCRNA00174	⇩	1.29	0.032
2731831	USO1	⇩	1.28	0.049
3375147	VPS37C	⇧	1.28	0.015
2706938	GNB4	⇧	1.28	0.023
3143330	FAM82B	⇧	1.28	0.011
3676156	IGFALS	⇩	1.28	0.046
3821701	ZNF788	⇧	1.28	8.36E-03
3761054	COPZ2	⇧	1.28	5.26E-03
3386638	SLC36A4	⇧	1.28	0.047
3742727	DHX33	⇧	1.28	7.02E-03
3233547	RBM17	⇧	1.28	0.025
2648378	RAP2B	⇧	1.28	0.020
2958117	HMGCLL1	⇧	1.28	6.84E-03
3673091	BANP	⇧	1.28	3.22E-03
3849797	ZNF561	⇧	1.28	0.024
2688070	GUCA1C	⇧	1.28	0.020
2359444	LCE1B	⇧	1.28	0.023
3332325	MS4A6E	⇧	1.28	0.015
2541944	SMC6	⇩	1.28	8.82E-03
2347732	TMEM56	⇧	1.28	0.019
3855071	FKBP8	⇧	1.28	0.011
3203482	BAG1	⇧	1.28	0.023
2698738	XRN1	⇩	1.28	9.40E-04
3250726	KIAA1274	⇧	1.28	0.010
3576545	SMEK1	⇧	1.28	3.41E-03
3142932	C8orf59	⇧	1.28	0.043
2915133	TPBG	⇧	1.28	0.029
3131844	LSM1	⇧	1.28	0.045
2534483	RBM44	⇧	1.28	0.029
2867432	ANKRD32	⇧	1.28	0.026
3961253	RPS19BP1	⇧	1.28	0.038
3707715	RPAIN	⇧	1.28	0.015
2715476	FAM193A	⇩	1.28	0.012
3976519	RBM3	⇧	1.28	0.020
3562721	FKBP3	⇧	1.28	0.037
2542737	LAPTM4A	⇩	1.28	0.044
3033397	RBM33	⇩	1.28	0.021
3279857	TRDMT1	⇧	1.28	0.038
3458783	CDK4	⇧	1.28	0.013
3080033	MLL3	⇩	1.28	0.011
3580947	C14orf2	⇧	1.28	0.022
2436228	GATAD2B	⇩	1.27	1.89E-04
3779756	SEH1L	⇧	1.27	0.037
3229591	UBAC1	⇧	1.27	0.020
2353021	SYCP1	⇧	1.27	0.017
4012868	RLIM	⇧	1.27	8.89E-03
3923896	KRTAP10-12	⇧	1.27	0.014
3831698	ZNF420	⇧	1.27	1.80E-03
3873160	TRIB3	⇧	1.27	0.043
3838795	BCL2L12	⇧	1.27	0.013
3416344	HOXC9	⇧	1.27	8.85E-03
3747236	C17orf76	⇩	1.27	3.75E-03
2781693	CASP6	⇧	1.27	0.048
3761127	CBX1	⇧	1.27	9.09E-03
2550122	COX7A2L	⇧	1.27	0.024
2978989	LATS1	⇩	1.27	1.00E-02
2659918	LRCH3	⇩	1.27	0.014
2482505	SPTBN1	⇩	1.27	0.011

Table B20: C9-Long Specific Gene List (n=894) MALE ONLY SAMPLES [Partek® unadjusted $p<0.05$, FC ≥ ±1.20]

3676649	DCI	⇧	1.27	0.011	2328909	TSSK3	⇧	1.26	0.013	2405284	TMEM54	⇧	1.25	5.90E-03
3431220	MVK	⇧	1.27	0.010	3817167	MRPL54	⇧	1.26	0.035	3347549	CUL5	⇧	1.25	0.016
3421824	C12orf28	⇧	1.27	0.037	3932148	BRWD1	⇧	1.26	0.039	2713555	KIAA0226	⇩	1.25	0.023
3671448	HSBP1	⇧	1.27	0.015	3315549	PSMD13	⇧	1.26	5.96E-03	3675815	C16orf42	⇧	1.25	0.024
2945677	C6orf62	⇧	1.27	0.034	3062576	ASNS	⇧	1.26	0.031	2363902	DUSP12	⇧	1.25	0.049
2596162	INO80D	⇩	1.27	4.22E-03	3403224	LOC283314	⇧	1.26	0.037	2731417	MTHFD2L	⇧	1.25	9.26E-03
3351166	IL10RA	⇩	1.27	0.041	3960875	DNAL4	⇧	1.26	6.89E-03	3417435	MYL6B	⇧	1.25	0.037
4046481	ING5	⇧	1.27	0.035	3656622	CTF1	⇧	1.26	8.13E-03	2629693	PPP4R2	⇧	1.25	0.035
3229943	SDCCAG3	⇧	1.27	7.66E-03	3318390	TRIM6-TRIM34	⇩	1.26	0.045	3226181	ST6GALNAC4	⇧	1.25	0.014
3821727	ZNF136	⇧	1.27	0.029	2642791	DNAJC13	⇩	1.26	0.015	2684851	VGLL3	⇧	1.25	2.17E-03
3923312	RRP1	⇧	1.27	0.016	3177563	NAA35	⇧	1.26	0.013	2903488	HSD17B8	⇧	1.25	0.034
3529064	BCL2L2	⇧	1.27	0.010	3454680	TFCP2	⇧	1.26	0.022	3581386	CDCA4	⇧	1.25	0.017
3890870	RAB22A	⇧	1.27	0.026	2436920	PMVK	⇧	1.26	0.014	2479640	PPM1B	⇧	1.25	0.012
3718382	ZNF830	⇧	1.27	0.016	3654614	SULT1A1	⇩	1.26	2.21E-03	3407229	AEBP2	⇧	1.25	6.39E-03
3401099	FKBP4	⇧	1.26	0.015	2899437	BTN2A1	⇩	1.26	0.044	2674526	NICN1	⇩	1.25	0.022
2655168	YEATS2	⇩	1.26	0.038	2644333	SOX14	⇧	1.26	4.53E-03	2380554	RRP15	⇧	1.25	0.036
3288337	ARHGAP22	⇩	1.26	0.045	3227645	UCK1	⇧	1.26	8.20E-03	2978026	FBXO30	⇧	1.25	0.020
3259253	ENTPD1	⇩	1.26	0.044	3346584	BIRC2	⇧	1.25	0.025	3642390	TARSL2	⇧	1.25	0.046
3230490	EDF1	⇧	1.26	0.026	3228097	TTF1	⇧	1.25	0.040	3352813	TBCEL	⇧	1.25	0.022
3819104	TRAPPC5	⇧	1.26	0.012	3465409	BTG1	⇧	1.25	4.25E-03	2500615	TMEM87B	⇩	1.25	0.049
3837504	SEPW1	⇧	1.26	0.046	3870162	ZNF665	⇧	1.25	3.29E-03	2369843	CEP350	⇩	1.25	9.84E-04
2597010	IDH1	⇩	1.26	0.034	3812589	GTSCR1	⇧	1.25	0.023	3404496	KLRF1	⇧	1.25	0.036
2427688	C1orf103	⇩	1.26	0.032	2723391	MGC42157	⇧	1.25	0.046	2762334	QDPR	⇧	1.25	0.042
3558226	RIPK3	⇩	1.26	0.018	3336351	CCS	⇧	1.25	7.60E-03	3221571	RNF183	⇧	1.25	0.025
2900453	PGBD1	⇧	1.26	9.51E-03	3642604	MPG	⇧	1.25	1.59E-03	3503224	UPF3A	⇧	1.25	0.016
3212728	AGTPBP1	⇧	1.26	0.021	2851274	CDH10	⇧	1.25	9.29E-04	2828115	LYRM7	⇧	1.25	0.033
3300869	PIPSL	⇧	1.26	0.033	3330927	OR5T1	⇧	1.25	0.015	3555492	TMEM55B	⇧	1.25	0.013
2678367	PDHB	⇩	1.26	0.038	3478457	STX2	⇧	1.25	0.033	3657318	ZNF720	⇧	1.25	0.039
3358262	DEAF1	⇧	1.26	0.021	2324743	ZBTB40	⇩	1.25	0.037	2772375	UGT2A1	⇧	1.25	0.031
3676209	C16orf73	⇧	1.26	0.036	3999395	MID1	⇧	1.25	0.036	3348891	C11orf57	⇧	1.25	0.041
2837499	LSM11	⇧	1.26	3.26E-03	3892941	OGFR	⇧	1.25	0.043	2437417	ASH1L	⇩	1.25	0.037
3486807	WBP4	⇧	1.26	0.035	3416114	TARBP2	⇧	1.25	8.46E-03	3442396	PHB2	⇧	1.25	4.42E-03

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2320762	VPS13D	⇩	1.25	0.024
2834574	SPINK14	⇧	1.25	5.88E-03
3334783	SNX15	⇧	1.25	0.025
3200689	RPS6	⇧	1.25	0.042
2448232	TPR	⇩	1.24	2.44E-03
2451139	ARL8A	⇩	1.24	0.014
3348189	FDX1	⇧	1.24	0.024
3469844	MTERFD3	⇧	1.24	0.037
2373494	CFHR2	⇧	1.24	0.037
2951057	C6orf1	⇧	1.24	0.020
2903189	HLA-DRA	⇩	1.24	0.042
2954678	XPO5	⇩	1.24	0.036
3712517	NT5M	⇧	1.24	0.012
2336271	BTF3L4	⇧	1.24	0.036
2745288	IL15	⇧	1.24	0.014
2532699	INPP5D	⇩	1.24	5.36E-03
3272027	LRRC27	⇧	1.24	9.65E-03
3435653	OGFOD2	⇧	1.24	0.024
2878630	SLC25A2	⇧	1.24	4.73E-03
3969115	TLR8	⇧	1.24	5.37E-03
3747324	ZNF624	⇧	1.24	4.89E-03
3882720	RALY	⇧	1.24	0.049
2815139	FCHO2	⇧	1.24	0.014
2576788	ANKRD30BL	⇧	1.24	1.03E-03
3850040	EIF3G	⇧	1.24	0.013
3016211	ZNHIT1	⇧	1.24	0.033
2840036	DOCK2	⇩	1.24	6.66E-04
3843525	ZNF586	⇧	1.24	0.021
3854877	JUND	⇧	1.24	0.048
2391465	MXRA8	⇧	1.24	3.15E-03
3971877	EIF2S3	⇧	1.24	0.018
3379390	SUV420H1	⇧	1.24	0.042
2612175	NR2C2	⇩	1.24	1.95E-03
2581430	STAM2	⇩	1.24	0.017
3824153	C19orf62	⇧	1.24	0.048
2476219	BIRC6	⇩	1.24	1.58E-03
2832115	PCDHA12	⇧	1.24	0.045
3471374	PPP1CC	⇧	1.24	0.016
3476012	MPHOSPH9	⇧	1.24	0.038
2977949	EPM2A	⇧	1.24	0.016
2895159	HIVEP1	⇩	1.24	8.89E-03
2966636	ASCC3	⇩	1.24	0.047
3337168	GSTP1	⇧	1.24	0.032
2389789	SCCPDH	⇩	1.24	0.028
3012910	GNGT1	⇧	1.24	0.040
3349014	PTS	⇧	1.24	0.020
3424379	C12orf26	⇧	1.24	0.039
3647632	C16orf72	⇧	1.24	8.96E-03
2564816	ANKRD36B	⇧	1.24	0.033
2633631	NIT2	⇩	1.24	0.045
3513953	C13orf1	⇧	1.23	0.038
3317223	IGF2AS	⇧	1.23	0.027
2334459	TMEM69	⇩	1.23	0.025
2923270	PLN	⇧	1.23	0.018
3376529	PLA2G16	⇧	1.23	0.045
2435044	POGZ	⇩	1.23	6.69E-03
3145567	UQCRB	⇧	1.23	5.75E-03
4007734	TFE3	⇧	1.23	0.046
3846538	EEF2	⇧	1.23	4.04E-03
2418700	ASB17	⇧	1.23	0.016
2987410	NUDT1	⇧	1.23	0.012
2664891	TBC1D5	⇩	1.23	0.011
3157844	NRBP2	⇩	1.23	0.010
2359817	INTS3	⇩	1.23	5.51E-03
2790652	FGG	⇧	1.23	9.01E-03
2835166	ARHGEF37	⇧	1.23	0.011
2377427	CD46	⇩	1.23	0.047
2514365	BBS5	⇧	1.23	4.12E-03
3202293	C9orf11	⇧	1.23	0.010
2730281	ODAM	⇧	1.23	6.95E-03
3191113	PRRX2	⇩	1.23	8.60E-04
2572601	CCDC93	⇩	1.23	0.019
2711139	ATP13A5	⇧	1.23	0.047
3418298	KIF5A	⇧	1.23	0.044
2943808	NUP153	⇩	1.23	9.51E-03
3183757	RAD23B	⇧	1.23	0.022
2693937	TPRA1	⇩	1.23	0.039
2691718	GOLGB1	⇩	1.23	7.89E-03
3271220	CTAGE7P	⇧	1.23	0.040
3882854	ITCH	⇧	1.23	0.020
3792952	SOCS6	⇧	1.23	0.037
2974188	MED23	⇩	1.23	0.035
3131720	BRF2	⇧	1.23	0.020
2828146	CDC42SE2	⇧	1.23	0.046
2400373	EIF4G3	⇩	1.23	5.54E-03
3360982	RRP8	⇧	1.23	0.035
2346657	BTBD8	⇧	1.23	0.036
3440017	FBXL14	⇩	1.23	0.047
3135156	FAM150A	⇧	1.23	0.031
3064024	C7orf61	⇧	1.23	0.047
3331129	OR5AK2	⇧	1.23	0.040
3665846	THAP11	⇧	1.23	0.044
3591909	CTDSPL2	⇧	1.23	0.026
2608765	ARL8B	⇩	1.23	0.039
3258997	CYP2C19	⇧	1.23	0.020
3672455	COX4I1	⇧	1.23	0.044

Table B20: C9-Long Specific Gene List (n=894) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3045739	HERPUD2	⇩	1.23	0.035	3029213	TAS2R41	⇩	1.22	0.036	3257750	HECTD2	⇧	1.21	0.026
3114358	FAM91A1	⇧	1.22	0.031	2519038	FSIP2	⇧	1.22	0.026	2618702	ZNF620	⇧	1.21	0.017
3715809	NEK8	⇧	1.22	0.011	3584443	SNRPN	⇧	1.22	0.040	3713874	MAPK7	⇧	1.21	4.06E-03
2512330	MARCH7	⇩	1.22	0.027	2830742	KDM3B	⇩	1.22	1.04E-03	3956290	PITPNB	⇧	1.21	0.022
3907373	WFDC9	⇧	1.22	0.046	3894194	TBC1D20	⇧	1.22	0.027	3236395	HSPA14	⇧	1.21	5.16E-03
4021149	SMARCA1	⇧	1.22	0.040	2486851	APLF	⇧	1.22	0.044	2544238	ITSN2	⇩	1.21	9.07E-03
2318736	PARK7	⇧	1.22	0.044	2550959	PREPL	⇩	1.22	0.031	3464622	CEP290	⇧	1.21	0.027
2575949	TUBA3E	⇧	1.22	0.038	3662170	MT1DP	⇧	1.22	3.87E-03	3330961	OR8J1	⇧	1.21	8.52E-03
3974838	DDX3X	⇧	1.22	0.042	3514488	INTS6	⇧	1.22	0.013	3874023	PTPRA	⇩	1.21	0.029
3704896	CHMP1A	⇧	1.22	0.020	3466826	CDK17	⇧	1.21	0.029	3507003	LNX2	⇧	1.21	0.042
2347788	RWDD3	⇧	1.22	0.029	3430552	PWP1	⇧	1.21	0.047	3846783	UBXN6	⇧	1.21	0.022
3892409	LSM14B	⇧	1.22	0.016	2862716	GFM2	⇩	1.21	0.036	2516780	HOXD13	⇧	1.21	6.56E-03
2404254	PUM1	⇩	1.22	2.25E-04	3511817	ENOX1	⇧	1.21	5.76E-03	2413203	LRP8	⇩	1.21	0.046
3121023	C8orf33	⇧	1.22	0.038	2676397	ITIH4	⇩	1.21	0.031	3832865	NCCRP1	⇧	1.21	0.023
3735346	C17orf106	⇧	1.22	0.019	2817576	THBS4	⇧	1.21	0.024	3149754	EIF3H	⇧	1.21	0.033
2367154	BAT2L2	⇩	1.22	9.55E-04	2351572	CD53	⇩	1.21	0.019	3488253	COG3	⇧	1.21	0.024
3476130	SBNO1	⇧	1.22	0.036	3835339	ZNF230	⇧	1.21	0.037	3982410	COX7B	⇧	1.21	0.040
2546008	SUPT7L	⇩	1.22	0.047	3300115	PPP1R3C	⇧	1.21	0.033	2692909	HEG1	⇩	1.20	0.040
3829575	LSM14A	⇧	1.22	0.045	3226311	NAIF1	⇧	1.21	0.044	3360702	OR52L1	⇧	1.20	0.028
3899641	HSPC072	⇧	1.22	0.037	7385683	VPS41	⇩	1.21	0.045	3727499	TOM1L1	⇧	1.20	0.031
3429555	EID3	⇧	1.22	0.013	3407629	SLCO1B3	⇧	1.21	0.017	3447129	KIAA0528	⇧	1.20	0.017
3758845	HDAC5	⇧	1.22	0.031	2559849	SLC4A5	⇧	1.21	0.032	2961647	HTR1B	⇧	1.20	0.034
3954746	IGLL1	⇩	1.22	5.85E-03	3856908	ZNF99	⇧	1.21	0.044	2573570	TFCP2L1	⇧	1.20	0.040
3026599	TRIM24	⇩	1.22	0.038	3721851	COASY	⇧	1.21	0.012	3555272	TTC5	⇧	1.20	2.10E-03
2816030	POLK	⇩	1.22	0.041	2607923	CNTN4	⇧	1.21	3.39E-03	2340819	TCTEX1D1	⇧	1.20	9.05E-03
3127610	PEBP4	⇩	1.22	0.014	3871576	FIZ1	⇧	1.21	0.014	2780296	TACR3	⇧	1.20	0.018
2556667	RAB1A	⇧	1.22	0.033	3419849	TBK1	⇧	1.21	9.99E-03	3154185	TMEM71	⇧	1.20	0.036
3923498	PWP2	⇧	1.22	0.022	3202224	LRRC19	⇧	1.21	0.019	2519480	GULP1	⇧	1.20	0.034
2675088	IFRD2	⇧	1.22	0.013	2423422	BCAR3	⇧	1.21	0.022	2678029	DNAH12	⇧	1.20	0.038
2907190	UBR2	⇩	1.22	2.75E-03	3928545	KRTAP19-6	⇧	1.21	7.33E-04	2950242	PPP1R2P1	⇧	1.20	0.015
3431426	IFT81	⇧	1.22	0.024	3223605	FBXW2	⇧	1.21	0.011	2717757	C4orf23	⇩	1.20	0.042
2399409	UBR4	⇩	1.22	2.53E-03	2456849	RAB3GAP2	⇩	1.21	0.021	2468138	LOC400940	⇧	1.20	6.70E-03

Table B20: C9-Long Specific Gene List (n=894) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3955327	C22orf13	⇧	1.20	0.020	2977122	NMBR	⇧	1.20	0.016	3696194	DDX28	⇧	1.20	6.19E-03
3348990	TEX12	⇧	1.20	0.035	2672532	SETD2	⇩	1.20	2.76E-03	2318416	THAP3	⇧	1.20	0.017
2326640	ARID1A	⇩	1.20	0.036	3453348	RND1	⇧	1.20	0.034	2811145	PART1	⇧	1.20	0.033
2620315	TMEM42	⇧	1.20	0.049	2327418	MED18	⇧	1.20	0.047	2880463	C5orf46	⇧	1.20	0.043
3934903	NCRNA00205	⇩	1.20	0.038	3344897	MED17	⇩	1.20	0.037	2353477	ATP1A1	⇩	1.20	0.041
3788560	DCC	⇧	1.20	0.021	2627390	ATXN7	⇩	1.20	7.66E-03	3702352	HSDL1	⇧	1.20	3.66E-03
2761321	BOD1L	⇩	1.20	0.026	3834651	ZNF526	⇧	1.20	0.016	2824144	FLJ11235	⇧	1.20	0.040
2525272	PIKFYVE	⇩	1.20	0.035	3833827	EGLN2	⇧	1.20	1.16E-03	3755359	PIP4K2B	⇧	1.20	0.045
3836266	FOSB	⇧	1.20	0.043	2594569	ORC2	⇩	1.20	0.042	2491046	FUNDC2P2	⇧	1.20	0.030
3337329	ALDH3B1	⇧	1.20	0.018	3321269	FAR1	⇧	1.20	0.045	2959596	EYS	⇧	1.20	8.56E-03
3569778	C14orf181	⇧	1.20	0.019	3868472	FAM71E1	⇩	1.20	3.05E-03	2927255	PEX7	⇧	1.20	0.043

Table B21: C9-Short Specific Gene List (n=916) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value	Transcript ID	Symbol		Fold	p-value
3566383	C14orf105	⇩	2.69	2.33E-03	3754797	HNF1B	⇩	1.87	6.98E-03	3852880	EMR2	⇩	1.61	0.031
2459042	CDC42BPA	⇩	2.53	2.29E-03	3496409	GPC5	⇩	1.86	9.06E-04	2899243	HIST1H4F	⇧	1.60	2.19E-05
2440385	CD244	⇩	2.45	2.61E-03	3129361	FBXO16	⇧	1.86	9.40E-03	2362333	MNDA	⇧	1.60	0.027
3718555	SLFN5	⇩	2.39	3.18E-03	2973376	PTPRK	⇩	1.85	0.023	2371547	C1orf21	⇩	1.60	0.034
3393446	FXYD2	⇩	2.30	2.16E-03	3382216	ARRB1	⇩	1.85	0.027	3344142	NAALAD2	⇩	1.59	0.033
3388673	MMP7	⇩	2.25	0.044	3996598	NCRNA00204	⇧	1.82	0.026	3944404	APOL1	⇩	1.59	5.96E-03
2607568	CHL1	⇩	2.22	0.027	2924253	RNF217	⇩	1.82	0.020	2730746	SLC4A4	⇩	1.58	0.026
3456805	GTSF1	⇧	2.19	0.027	3560403	EGLN3	⇩	1.82	2.41E-03	3841357	LILRA2	⇩	1.58	0.012
2569908	SEPT10	⇧	2.15	0.028	3944129	HMOX1	⇧	1.80	2.53E-04	3174510	GDA	⇩	1.58	0.041
3445908	EPS8	⇩	2.13	0.010	2477073	CRIM1	⇩	1.79	0.034	2902707	HSPA1A	⇧	1.58	0.010
2731636	PARM1	⇩	2.13	2.22E-03	2571483	IL1A	⇧	1.79	0.045	2973232	C6orf174	⇩	1.58	0.015
3623031	FBN1	⇩	2.13	3.10E-04	3209384	TMEM2	⇩	1.78	0.024	3609592	MCTP2	⇩	1.57	1.38E-04
3507282	FLT1	⇩	2.12	2.93E-03	3955102	GSTT1	⇧	1.78	0.015	4005859	CASK	⇩	1.56	6.24E-03
3150579	ENPP2	⇩	2.10	3.12E-03	3599709	GLCE	⇩	1.76	8.10E-03	3396593	FEZ1	⇧	1.56	0.034
3132016	FGFR1	⇩	2.06	9.91E-04	2403446	PTAFR	⇩	1.74	0.018	2584018	DPP4	⇩	1.56	0.037
2898746	LRRC16A	⇩	2.04	3.14E-03	2485406	HSPC159	⇧	1.73	9.30E-04	2378068	G0S2	⇧	1.55	0.011
2699564	PLOD2	⇩	2.02	8.64E-03	3494137	LMO7	⇩	1.72	1.53E-04	2879105	SPRY4	⇩	1.55	2.46E-03
2635741	CD96	⇩	2.02	0.022	3351675	CXCR5	⇧	1.70	0.022	2899223	HIST1H2AE	⇧	1.55	0.036
4022370	GPC4	⇩	2.02	0.014	3972929	GK	⇩	1.70	2.19E-03	2895244	EDN1	⇩	1.54	0.034
3512948	C13orf18	⇧	2.01	6.44E-03	3791254	TNFRSF11A	⇩	1.68	0.031	3420442	IRAK3	⇩	1.54	0.037
3778504	RAB31	⇧	2.01	0.011	2615360	TGFBR2	⇩	1.68	7.10E-03	3082590	LOC286161	⇧	1.54	1.62E-03
3569814	ACTN1	⇩	2.01	4.22E-03	2705445	PLD1	⇩	1.68	0.022	2351854	C1orf162	⇧	1.54	0.027
3933566	TMPRSS3	⇩	1.99	0.042	3724545	ITGB3	⇩	1.66	0.015	3644191	FAHD1	⇧	1.54	5.11E-04
2915828	NT5E	⇩	1.98	0.035	3941848	EMID1	⇩	1.66	3.73E-03	2633691	TMEM45A	⇩	1.54	0.013
3449068	TMTC1	⇩	1.98	5.42E-03	2986999	GPR146	⇩	1.65	8.46E-03	3450899	SLC2A13	⇩	1.54	7.46E-03
2853102	PRLR	⇩	1.97	0.011	3323891	GAS2	⇩	1.64	0.031	3197955	GLDC	⇧	1.53	0.048
2459173	PRO2012	⇩	1.95	9.66E-04	2662581	C3orf10	⇧	1.64	0.015	3164825	IFNA1	⇩	1.53	7.19E-03
4002081	MAP7D2	⇩	1.91	1.41E-03	3409605	FAR2	⇩	1.63	0.045	2879028	GNPDA1	⇧	1.53	1.06E-03
3692999	MT1G	⇧	1.89	0.017	3139580	SLCO5A1	⇩	1.63	3.23E-04	2439001	FCRL3	⇧	1.53	0.030
2664209	SH3BP5	⇧	1.87	6.83E-04	3417583	RBMS2	⇧	1.62	0.028	3132940	ANK1	⇩	1.52	0.011
3284596	PARD3	⇩	1.87	6.65E-03	2462160	NID1	⇩	1.61	4.17E-03	2910868	TINAG	⇩	1.52	2.70E-03

Table B21: C9-Short Specific Gene List (n=916) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3624145	DMXL2	⇩	1.52	4.26E-05
3054165	SBDS	⇧	1.52	0.011
3136178	PLAG1	⇧	1.51	9.63E-03
3899173	RRBP1	⇩	1.51	8.97E-05
3225855	ANGPTL2	⇩	1.51	0.022
3887210	MMP9	⇩	1.50	0.024
2338625	HOOK1	⇩	1.50	0.020
2849992	FAM134B	⇩	1.50	0.024
2932508	TIAM2	⇧	1.49	3.28E-03
3403244	CLSTN3	⇩	1.49	1.08E-03
3273667	ADARB2	⇩	1.49	9.47E-03
2422035	GBP5	⇩	1.49	0.015
2902725	HSPA1B	⇧	1.48	4.61E-03
3184218	C9orf6	⇧	1.48	0.015
3946095	GRAP2	⇧	1.48	0.016
2933175	ZDHHC14	⇩	1.48	0.021
2829275	UBE2B	⇧	1.48	9.66E-04
3252071	VCL	⇩	1.48	0.014
3101622	RRS1	⇧	1.48	2.44E-03
2362351	PYHIN1	⇧	1.47	0.031
3727449	TOM1L1	⇩	1.47	0.024
3538213	DAAM1	⇩	1.47	0.017
2626167	PXK	⇧	1.47	2.10E-03
3543619	C14orf169	⇧	1.47	6.04E-03
3825013	SSBP4	⇩	1.47	1.60E-03
2651835	GPR160	⇧	1.47	0.037
2956052	TNFRSF21	⇩	1.47	0.040
2912649	COL19A1	⇩	1.47	0.012
3914273	SAMD10	⇩	1.47	1.57E-03
3230141	NOTCH1	⇩	1.47	1.40E-04
2369339	RALGPS2	⇧	1.47	0.035
2796484	CASP3	⇧	1.47	1.40E-03
2396461	SRM	⇧	1.47	6.74E-05
3245881	WDFY4	⇩	1.47	1.21E-03
3091077	DPYSL2	⇧	1.46	0.019
2331178	NDUFS5	⇧	1.46	5.48E-03
3402757	LAG3	⇩	1.46	8.55E-03
2336585	SCP2	⇧	1.46	3.38E-03
3851493	ZNF443	⇩	1.45	3.59E-03
3101153	BHLHE22	⇩	1.45	0.047
3663074	MMP15	⇩	1.45	0.017
3352438	POU2F3	⇩	1.45	0.028
2427208	GSTM3	⇧	1.45	0.034
3687789	DCTPP1	⇧	1.45	1.29E-03
3447348	SOX5	⇩	1.44	9.78E-03
3234277	GATA3	⇩	1.44	3.68E-03
2946219	HIST1H2AB	⇧	1.44	0.027
3838094	FTL	⇧	1.44	0.036
3351841	HMBS	⇧	1.44	0.013
2327677	EPB41	⇧	1.44	6.56E-03
4007164	CFP	⇩	1.44	0.043
2626258	KCTD6	⇧	1.44	5.42E-04
3766533	CD79B	⇩	1.44	0.017
2449711	DENND1B	⇧	1.44	0.029
3734379	CD300A	⇩	1.44	1.66E-04
3753500	SLFN11	⇩	1.44	4.12E-04
2826295	SNX2	⇧	1.44	1.65E-03
3761313	HOXB3	⇩	1.43	6.58E-05
3236538	RPP38	⇧	1.43	0.044
3020302	CAV1	⇧	1.43	0.036
3011838	STEAP1	⇩	1.43	9.03E-03
4027176	FLNA	⇩	1.43	4.33E-03
2437893	UBQLN4	⇩	1.42	6.86E-03
2443989	VAMP4	⇧	1.42	2.89E-03
3712062	TRPV2	⇩	1.42	4.59E-04
3424442	TMTC2	⇩	1.42	1.19E-04
2351004	GSTM5	⇧	1.42	0.010
3302177	ARHGAP19	⇧	1.42	0.037
4018080	CHRDL1	⇩	1.42	0.029
2471978	RHOB	⇩	1.42	0.048
3005444	TPST1	⇩	1.41	0.046
2371346	RGL1	⇧	1.41	0.017
2325479	RCAN3	⇧	1.41	2.55E-03
2732844	ANXA3	⇩	1.41	0.042
3714068	ALDH3A2	⇧	1.41	3.72E-04
2316245	PRKCZ	⇧	1.41	7.76E-04
3203382	SMU1	⇧	1.41	0.026
2385696	C1orf57	⇧	1.40	0.026
2586744	METTL8	⇧	1.40	1.29E-03
2692060	PARP9	⇧	1.40	0.012
2767295	BEND4	⇩	1.40	0.040
3708644	FGF11	⇩	1.40	0.025
2601287	AP1S3	⇧	1.40	8.20E-04
2885099	NUDCD2	⇧	1.40	1.86E-05
3887302	CD40	⇩	1.40	3.58E-03
3840327	ZNF808	⇧	1.40	8.51E-03
3103818	HNF4G	⇩	1.40	0.027
3734355	GPRC5C	⇩	1.39	0.042
3067302	LAMB1	⇩	1.39	0.033
2848265	CMBL	⇧	1.39	0.030
2319225	H6PD	⇩	1.39	0.032
2323559	MRTO4	⇧	1.39	6.75E-03
3738629	SLC16A3	⇩	1.39	3.45E-03
3453252	ADCY6	⇩	1.39	1.87E-03
2992863	IGF2BP3	⇧	1.39	8.80E-04
2866576	MBLAC2	⇧	1.39	6.75E-04

Table B21: C9-Short Specific Gene List (n=916) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3450655	CPNE8	⇩	1.39	0.014
3592484	PLDN	⇧	1.39	6.37E-03
2855443	LOC100132356	⇧	1.38	4.82E-04
3848243	INSR	⇩	1.38	0.015
3687494	MAPK3	⇧	1.38	0.010
2871241	MCC	⇩	1.38	6.29E-03
3628923	FAM96A	⇧	1.38	2.85E-03
2531522	CAB39	⇧	1.38	4.41E-04
3538087	DACT1	⇩	1.38	5.88E-03
3937755	SNAP29	⇧	1.38	7.15E-03
3245783	WDFY4	⇩	1.38	1.93E-05
3278813	FAM107B	⇧	1.38	0.018
2999640	UBE2D4	⇧	1.38	4.44E-03
3288518	C10orf72	⇩	1.38	0.026
2558483	C2orf42	⇧	1.38	4.93E-03
2341645	HHLA3	⇧	1.38	7.48E-03
2713111	MFI2	⇩	1.38	0.010
2626141	RPP14	⇧	1.38	9.26E-03
3748323	SHMT1	⇧	1.38	0.016
3926138	C21orf91	⇧	1.38	8.50E-03
2538600	ADI1	⇧	1.38	0.027
2805176	C5orf22	⇧	1.38	6.78E-03
2362537	FCER1A	⇧	1.37	0.033
2902178	TCF19	⇧	1.37	6.68E-03
3009399	HSPB1	⇧	1.37	0.041
2676182	NT5DC2	⇧	1.37	1.07E-03
3048869	H2AFV	⇧	1.37	4.14E-04
2514441	PPIG	⇧	1.37	2.68E-06
2427791	DENND2D	⇩	1.37	0.027
2682568	SHQ1	⇧	1.37	1.05E-03
2425400	EXTL2	⇩	1.37	0.018
3887107	ZSWIM1	⇧	1.37	5.67E-03
2495806	MRPL30	⇧	1.37	2.44E-03
3788049	SKA1	⇧	1.37	0.016
2492496	NCRNA00152	⇧	1.37	0.021
3199207	NFIB	⇩	1.37	0.037
3564872	GNPNAT1	⇧	1.37	6.51E-03
2604390	ARL4C	⇧	1.37	0.011
3004768	ZNF273	⇧	1.37	0.020
3396107	ESAM	⇩	1.37	9.47E-03
3816827	S1PR4	⇩	1.37	0.030
3429566	CHST11	⇩	1.37	4.31E-05
3168385	GLIPR2	⇧	1.36	0.011
3900091	RALGAPA2	⇩	1.36	0.013
2712906	RNF168	⇧	1.36	6.66E-03
3761291	HOXB2	⇩	1.36	0.024
3892918	C20orf20	⇧	1.36	0.022
2842561	HIGD2A	⇧	1.36	0.017
2775735	SCD5	⇩	1.36	0.029
2376894	DYRK3	⇧	1.36	5.84E-03
3333247	FADS2	⇩	1.36	5.75E-03
2777487	FAM13A	⇩	1.36	0.029
3833238	LGALS14	⇧	1.36	0.028
2636272	GTPBP8	⇧	1.36	4.08E-04
4003895	CXorf21	⇩	1.36	0.027
2350489	KIAA1324	⇩	1.36	0.041
2997907	EPDR1	⇩	1.35	0.021
3005717	RABGEF1	⇧	1.35	6.78E-04
2724338	LIAS	⇧	1.35	9.75E-03
3011492	ADAM22	⇩	1.35	0.022
3289235	SGMS1	⇩	1.35	5.85E-03
3259978	PI4K2A	⇧	1.35	0.036
3336402	RBM14	⇩	1.35	8.23E-03
3016636	SH2B2	⇧	1.35	0.020
3286975	ANUBL1	⇧	1.35	1.42E-03
2608419	SETMAR	⇧	1.35	1.33E-03
3758510	ETV4	⇩	1.35	0.017
2715440	RNF4	⇧	1.35	0.021
2549260	MAP4K3	⇧	1.35	3.63E-03
3893849	PRPF6	⇩	1.35	9.82E-03
3824890	MPV17L2	⇧	1.35	0.038
2478748	EML4	⇧	1.35	7.56E-03
3161113	PDCD1LG2	⇩	1.35	0.035
2929036	LTV1	⇧	1.35	3.40E-03
3988987	NDUFA1	⇧	1.35	0.029
2443518	C1orf156	⇧	1.34	2.63E-03
3414695	ATF1	⇧	1.34	0.035
3651955	METTL9	⇧	1.34	2.28E-03
3553531	TNFAIP2	⇩	1.34	0.023
2835006	GRPEL2	⇧	1.34	2.49E-03
3402736	PTMS	⇩	1.34	0.029
3332886	TMEM138	⇧	1.34	0.025
3130850	RNF122	⇩	1.34	0.023
3875195	MCM8	⇧	1.34	2.71E-03
3279982	PTPLA	⇩	1.34	0.043
3816264	DOT1L	⇩	1.34	3.86E-03
3118451	CHRAC1	⇧	1.34	6.19E-03
3508898	STARD13	⇩	1.34	0.032
2778980	EIF4E	⇧	1.34	0.018
3074912	DGKI	⇩	1.34	0.011
2327375	ATPIF1	⇧	1.34	2.00E-03
3944690	CYTH4	⇩	1.34	0.014
3015395	PVRIG	⇩	1.34	0.046
3803120	B4GALT6	⇩	1.34	4.39E-03
2655113	KLHL24	⇧	1.34	0.045
3864430	ETHE1	⇧	1.34	0.012

Table B21: C9-Short Specific Gene List (n=916) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3267382	INPP5F	⇧	1.33	0.027
2746024	ABCE1	⇧	1.33	9.82E-03
2515183	DCAF17	⇧	1.33	2.94E-04
3733590	SOX9	⇩	1.33	0.043
2674168	C3orf62	⇧	1.33	4.17E-04
2560141	MRPL53	⇧	1.33	3.93E-04
2659887	FYTTD1	⇧	1.33	1.53E-03
3539724	SYNE2	⇩	1.33	0.014
3379708	MRPL21	⇧	1.33	0.017
2389016	PPPDE1	⇧	1.33	0.014
2548459	CEBPZ	⇧	1.33	1.15E-03
2332767	C1orf50	⇧	1.33	4.58E-03
3635198	BCL2A1	⇧	1.33	0.031
2827525	SLC12A2	⇩	1.33	0.017
2491676	VAMP5	⇧	1.33	0.039
2638962	DTX3L	⇧	1.33	0.027
3106243	RIPK2	⇧	1.33	0.038
3836317	VASP	⇩	1.33	9.36E-04
3438617	EP400	⇩	1.33	2.44E-03
3649890	ABCC1	⇩	1.32	7.34E-04
4019412	CXorf56	⇧	1.32	1.32E-03
3761348	HOXB4	⇩	1.32	3.51E-04
2367743	PRDX6	⇧	1.32	3.63E-04
2343289	DNAJB4	⇧	1.32	0.018
3002873	LANCL2	⇧	1.32	0.033
2325274	C1orf128	⇧	1.32	4.69E-04
3707199	PSMB6	⇧	1.32	0.042
3583541	GOLGA6L1	⇧	1.32	0.019
2396121	DFFA	⇧	1.32	5.04E-04
2696379	ANAPC13	⇧	1.32	0.025
2494749	CNNM3	⇩	1.32	2.13E-03
3677612	ZNF597	⇧	1.32	1.63E-03
3934407	ICOSLG	⇩	1.32	1.08E-03
3005684	KCTD7	⇧	1.32	2.70E-03
3521484	UGGT2	⇩	1.32	0.042
2945645	TDP2	⇧	1.32	5.18E-03
3377933	EFEMP2	⇩	1.32	0.029
3329343	MDK	⇩	1.32	0.039
3057650	YWHAG	⇧	1.32	2.53E-04
2723710	PGM2	⇧	1.32	1.58E-03
3596109	FAM81A	⇧	1.32	5.63E-03
2477980	GEMIN6	⇧	1.32	1.55E-04
2654069	NDUFB5	⇧	1.32	8.17E-03
3079803	PRKAG2	⇧	1.32	8.91E-04
2523478	NBEAL1	⇧	1.32	0.012
3741800	ATP2A3	⇩	1.32	0.025
3044129	GGCT	⇧	1.32	0.027
3255938	OPN4	⇧	1.32	0.030
3485292	NBEA	⇩	1.32	0.022
2548617	CDC42EP3	⇧	1.32	0.044
3771602	RHBDF2	⇩	1.31	6.76E-03
2766456	UGDH	⇧	1.31	0.012
2562271	CAPG	⇩	1.31	0.037
3740432	SCARF1	⇩	1.31	0.020
3996306	RPL10	⇧	1.31	0.045
2403470	DNAJC8	⇧	1.31	0.024
2779408	MAPKSP1	⇧	1.31	3.05E-03
3340589	SERPINH1	⇩	1.31	0.046
2758686	LYAR	⇧	1.31	1.35E-03
3035682	FTSJ2	⇧	1.31	9.17E-04
4027345	LAGE3	⇧	1.31	1.20E-03
2815455	UTP15	⇧	1.31	3.52E-03
2775909	PLAC8	⇩	1.31	0.034
2905404	PIM1	⇧	1.31	0.027
3982612	GPR174	⇩	1.31	0.026
3284188	ITGB1	⇩	1.31	0.027
3417371	ESYT1	⇩	1.31	0.028
2352743	DCLRE1B	⇧	1.31	2.36E-03
3866094	PTGIR	⇩	1.31	0.030
3164601	KIAA1797	⇩	1.30	2.55E-03
2544164	C2orf44	⇧	1.30	0.014
2900059	HIST1H2BM	⇧	1.30	0.011
3698055	TXNL4B	⇧	1.30	0.024
3318666	SMPD1	⇩	1.30	0.031
4024160	ATP11C	⇩	1.30	0.014
3498837	PCCA	⇩	1.30	0.016
2320581	PLOD1	⇩	1.30	0.021
2559494	C2orf7	⇧	1.30	7.97E-03
3317915	STIM1	⇩	1.30	2.38E-03
3073981	AKR1B1	⇧	1.30	0.048
2356142	LIX1L	⇧	1.30	0.046
2412988	C1orf163	⇧	1.30	6.12E-04
3015769	POP7	⇧	1.30	0.018
3635125	MTHFS	⇧	1.30	0.023
2877465	ETF1	⇧	1.30	3.39E-03
2596763	FZD5	⇩	1.30	0.039
3654956	LAT	⇩	1.30	1.81E-03
2447148	RGS16	⇩	1.30	0.027
3146103	STK3	⇩	1.30	6.13E-03
3845944	GNG7	⇧	1.30	0.016
2773872	NAAA	⇧	1.30	0.029
3094286	PROSC	⇧	1.30	0.015
3489481	PHF11	⇩	1.30	1.13E-03
3670668	ATMIN	⇧	1.30	0.011
3205488	ZBTB5	⇧	1.30	0.018
2927722	HEBP2	⇧	1.30	0.010

Table B21: C9-Short Specific Gene List (n=916) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2745220	ZNF330	⇧	1.30	8.23E-03
2898562	ACOT13	⇧	1.30	0.026
3714659	DHRS7B	⇩	1.30	0.015
2582124	NR4A2	⇧	1.30	0.033
3487095	DGKH	⇩	1.30	0.018
2821761	RGMB	⇧	1.30	2.34E-05
2603531	C2orf52	⇧	1.30	3.77E-03
2706985	MRPL47	⇧	1.30	0.031
3193900	MRPS2	⇧	1.30	0.024
3662444	NLRC5	⇩	1.30	1.55E-03
3798291	PPP4R1	⇧	1.30	0.020
2773907	SDAD1	⇧	1.30	0.041
3101385	MTFR1	⇧	1.29	0.019
4007216	UXT	⇧	1.29	0.042
3708938	ATP1B2	⇧	1.29	0.018
3945133	POLR2F	⇧	1.29	0.025
3272205	INPP5A	⇩	1.29	0.025
3350775	SIDT2	⇩	1.29	4.34E-04
3849752	ZNF426	⇧	1.29	7.36E-03
3721926	TUBG1	⇧	1.29	0.015
2689208	NAA50	⇧	1.29	7.67E-03
2767378	ATP8A1	⇩	1.29	0.014
2957462	GSTA4	⇧	1.29	0.014
2538000	RNASEH1	⇧	1.29	0.018
2465493	ZNF670	⇧	1.29	0.011
2961300	COX7A2	⇧	1.29	0.015
2360257	IL6R	⇧	1.29	0.016
2924492	HEY2	⇧	1.29	0.013
3074260	WDR91	⇩	1.29	4.18E-03
3535922	STYX	⇧	1.29	0.012
2842911	FGFR4	⇩	1.29	5.97E-03
3342426	C11orf82	⇧	1.29	0.043
2505957	PLEKHB2	⇧	1.29	0.020
3655574	SPN	⇩	1.29	3.99E-03
2931683	C6orf211	⇧	1.29	0.013
2730313	CSN3	⇧	1.29	0.023
2621122	NBEAL2	⇩	1.29	2.67E-03
2438482	ISG20L2	⇧	1.29	5.36E-03
3766960	SMURF2	⇩	1.29	4.85E-03
2820893	RFESD	⇧	1.29	0.018
2472914	UBXN2A	⇧	1.29	8.28E-03
2432607	GNRHR2	⇧	1.29	8.29E-04
3139722	NCOA2	⇩	1.29	8.64E-03
3690034	C16orf87	⇧	1.29	8.57E-03
3323052	NAV2	⇩	1.29	6.22E-03
3697090	ST3GAL2	⇩	1.29	5.34E-03
3704376	FAM38A	⇩	1.29	0.011
3939707	CABIN1	⇩	1.29	2.24E-04
3561110	RALGAPA1	⇩	1.29	0.030
2838688	MAT2B	⇧	1.29	5.87E-03
3751042	TLCD1	⇧	1.29	0.037
3015178	ZSCAN21	⇧	1.29	1.31E-03
3940992	ASPHD2	⇩	1.29	0.031
3548929	RIN3	⇩	1.29	0.025
3020444	CAPZA2	⇧	1.29	0.045
2908144	MAD2L1BP	⇧	1.29	2.14E-03
3529908	NFATC4	⇩	1.29	0.014
2847264	MED10	⇧	1.28	0.010
2754538	SLC25A4	⇧	1.28	0.043
3736162	TMC8	⇩	1.28	2.27E-03
2475407	CLIP4	⇧	1.28	3.31E-03
2595443	WDR12	⇧	1.28	5.55E-03
3822347	C19orf53	⇧	1.28	0.032
3018652	CBLL1	⇧	1.28	5.52E-04
3251298	CHST3	⇩	1.28	0.035
2802398	TRIO	⇩	1.28	5.47E-04
3542689	PCNX	⇩	1.28	3.43E-03
2798915	TRIP13	⇧	1.28	0.039
2769512	RPL21P44	⇧	1.28	3.51E-03
2861952	MRPS27	⇧	1.28	3.18E-03
2942578	CCDC90A	⇧	1.28	3.56E-03
2336913	LRRC42	⇧	1.28	8.33E-04
2564599	MRPS5	⇧	1.28	0.021
3590108	GCHFR	⇧	1.28	0.043
3893458	PPDPF	⇧	1.28	0.023
3476665	SCARB1	⇩	1.28	3.48E-03
2409770	TMEM53	⇧	1.28	0.015
3766651	ERN1	⇩	1.28	0.017
4026669	BCAP31	⇩	1.28	0.018
3316234	NS3BP	⇧	1.28	2.47E-03
2633460	C3orf26	⇧	1.28	0.032
2317317	TP73	⇧	1.28	0.045
2873785	ALDH7A1	⇧	1.28	0.037
3040454	TWISTNB	⇧	1.28	1.36E-04
2954324	MEA1	⇧	1.28	0.030
2492938	RPIA	⇧	1.28	0.015
3545311	KIAA1737	⇧	1.28	2.88E-03
3837731	EMP3	⇩	1.28	2.98E-04
3850817	RAB3D	⇩	1.28	8.01E-03
3832383	PSMD8	⇧	1.28	0.011
3831514	ZNF567	⇧	1.28	0.017
2814642	MCCC2	⇧	1.28	4.83E-03
2709486	RFC4	⇧	1.27	0.045
2979679	ZBTB2	⇧	1.27	0.014
2649113	TIPARP	⇧	1.27	0.014
3685306	NDUFAB1	⇧	1.27	6.88E-03

Table B21: C9-Short Specific Gene List (n=916) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2484970	EHBP1	⇩	1.27	0.021
2360818	HCN3	⇩	1.27	0.014
3740367	SLC43A2	⇩	1.27	0.044
2465182	TFB2M	⇧	1.27	2.48E-03
3340449	SLCO2B1	⇩	1.27	0.038
3304746	USMG5	⇧	1.27	0.015
2458629	LEFTY2	⇧	1.27	0.018
3101802	SGK3	⇧	1.27	1.24E-03
2374422	C1orf106	⇩	1.27	5.45E-03
2351872	RAP1A	⇧	1.27	5.66E-03
2434490	ENSA	⇧	1.27	0.041
2721809	ZCCHC4	⇧	1.27	5.07E-04
3540862	GPHN	⇩	1.27	1.17E-03
2434862	LYSMD1	⇧	1.27	0.012
2378180	C1orf107	⇧	1.27	3.07E-03
3660175	NOD2	⇩	1.27	7.90E-03
2895721	NOL7	⇧	1.27	0.022
3995254	GABRQ	⇧	1.27	0.047
2339414	USP1	⇧	1.27	0.012
2404521	PEF1	⇧	1.27	0.012
2954489	C6orf108	⇧	1.27	0.035
3740201	MYO1C	⇩	1.27	4.26E-04
2555630	CCT4	⇧	1.27	4.22E-05
3941010	SRRD	⇧	1.27	0.023
2385258	C1orf124	⇧	1.27	0.011
2534126	COPS8	⇧	1.27	1.88E-05
2336383	PRPF38A	⇧	1.27	2.58E-04
2383550	ZNF678	⇧	1.27	1.21E-03
2523354	FAM117B	⇧	1.27	0.011
3325820	DEPDC7	⇩	1.27	0.019
2562821	VPS24	⇧	1.27	0.018
2900269	ZSCAN16	⇧	1.27	9.39E-03
2911903	PTP4A1	⇧	1.27	5.98E-03
3969455	OFD1	⇩	1.27	0.014
3712675	RAI1	⇩	1.27	0.016
3283920	ARHGAP12	⇩	1.27	1.20E-03
2960872	C6orf150	⇧	1.27	0.012
3228463	RALGDS	⇩	1.27	4.69E-03
2346863	RPL5	⇧	1.27	0.017
2319802	PGD	⇧	1.27	0.027
2889753	ZNF354A	⇧	1.27	0.026
2934308	IGF2R	⇩	1.27	9.66E-03
3728325	FLJ11710	⇩	1.26	0.034
2588827	NFE2L2	⇧	1.26	0.013
2417272	GNG12	⇧	1.26	5.62E-03
2786657	SETD7	⇧	1.26	5.63E-03
2597273	C2orf67	⇩	1.26	8.21E-03
3417574	SPRYD4	⇧	1.26	0.016
2988459	RBAK	⇧	1.26	0.028
2336497	ZYG11B	⇧	1.26	4.71E-03
3175597	VPS13A	⇩	1.26	0.013
2700828	SIAH2	⇧	1.26	9.84E-03
2636483	SIDT1	⇩	1.26	0.020
3578089	C14orf49	⇩	1.26	7.28E-03
4026842	ARHGAP4	⇩	1.26	5.34E-03
2407128	MEAF6	⇧	1.26	0.013
3527684	RNASE3	⇧	1.26	0.018
2819747	POLR3G	⇧	1.26	7.93E-03
3742067	UBE2G1	⇧	1.26	0.031
2408681	HIVEP3	⇩	1.26	0.016
3829313	CEBPG	⇧	1.26	0.048
2694644	CNBP	⇧	1.26	0.020
3456260	ATF7	⇩	1.26	6.69E-03
2703217	KPNA4	⇧	1.26	8.67E-03
2435849	SPRR2D	⇧	1.26	0.034
3485074	RFC3	⇧	1.26	0.026
2642325	ATP2C1	⇩	1.26	6.33E-03
2519140	ZC3H15	⇧	1.26	4.04E-04
3454006	FMNL3	⇩	1.26	6.24E-03
2574798	MAP3K2	⇧	1.26	3.07E-03
2407729	RRAGC	⇧	1.26	0.010
2619323	SS18L2	⇧	1.26	0.042
2331959	DEM1	⇧	1.26	2.74E-04
2618640	RPL14	⇧	1.26	2.58E-03
2379132	ATF3	⇧	1.26	0.016
3489538	ARL11	⇧	1.26	0.012
3316344	CD151	⇧	1.26	0.047
2334279	UROD	⇧	1.26	5.72E-03
2435195	MRPL9	⇧	1.26	0.013
2859494	SREK1IP1	⇧	1.26	0.020
3631214	TLE3	⇩	1.26	3.51E-03
4054117	TAF13	⇧	1.26	0.039
2773756	G3BP2	⇧	1.26	4.07E-04
3864597	C19orf61	⇩	1.26	3.86E-03
2635983	ABHD10	⇧	1.26	0.017
2460325	C1orf198	⇧	1.26	3.59E-03
2700500	COMMD2	⇧	1.25	0.028
3829160	C19orf40	⇧	1.25	3.68E-03
3662265	NUP93	⇧	1.25	9.11E-04
2519860	ASNSD1	⇧	1.25	0.015
2320657	MIIP	⇧	1.25	4.13E-04
3818897	PNPLA6	⇩	1.25	1.45E-03
2601341	WDFY1	⇧	1.25	0.025
3904527	NDRG3	⇧	1.25	0.048
2364189	UAP1	⇧	1.25	0.039
3516639	PCDH9	⇩	1.25	1.37E-03

Table B21: C9-Short Specific Gene List (n=916) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2662473	PRRT3	⇩	1.25	0.043
2489806	MRPL19	⇧	1.25	0.028
2612278	CAPN7	⇧	1.25	8.60E-03
3131741	RAB11FIP1	⇧	1.25	0.031
2342576	ACADM	⇧	1.25	0.013
3195174	MAN1B1	⇩	1.25	2.81E-04
3415763	SOAT2	⇩	1.25	1.08E-03
3963676	C22orf9	⇩	1.25	0.025
2685776	MINA	⇧	1.25	8.74E-03
2833286	ARHGAP26	⇩	1.25	0.032
3747717	COPS3	⇧	1.25	2.77E-03
2367086	FMO4	⇧	1.25	7.62E-03
2371694	RNF2	⇧	1.25	0.023
3611744	LRRK1	⇩	1.25	0.026
3382972	RSF1	⇧	1.25	0.039
2963614	CGA	⇧	1.25	7.28E-03
2831567	PURA	⇧	1.25	2.85E-04
3157901	PLEC	⇩	1.25	4.47E-04
2904000	HMGA1	⇧	1.25	4.79E-04
2905327	FGD2	⇩	1.25	8.58E-03
3707352	RNF167	⇩	1.25	1.03E-03
3044753	LSM5	⇧	1.25	0.028
3153428	ASAP1	⇧	1.25	0.011
2830010	SMAD5	⇧	1.25	3.58E-03
3197318	AK3	⇧	1.25	0.018
3709244	CHD3	⇩	1.25	2.18E-03
3959986	IL2RB	⇩	1.25	0.028
3417767	GPR182	⇧	1.25	9.06E-03
3020804	NAA38	⇧	1.25	0.016
2489071	TET3	⇩	1.25	0.015
3959451	MYH9	⇩	1.25	6.69E-04
2986906	GET4	⇧	1.25	9.46E-03
3748026	TOM1L2	⇩	1.25	8.61E-04
3715874	ERAL1	⇧	1.25	0.022
3161566	KDM4C	⇩	1.24	3.33E-03
4009315	HUWE1	⇩	1.24	3.07E-04
3063337	ZNF394	⇧	1.24	3.13E-03
2934167	MRPL18	⇧	1.24	8.22E-03
3185205	HSDL2	⇧	1.24	1.27E-03
3383322	NARS2	⇧	1.24	0.019
3847959	TUBB4	⇧	1.24	0.019
3216023	C9orf130	⇧	1.24	0.011
3710870	ARHGAP44	⇧	1.24	0.012
2401275	HNRNPR	⇧	1.24	4.34E-04
2886977	FBXW11	⇧	1.24	1.63E-03
2639874	UMPS	⇧	1.24	0.032
2921374	RPF2	⇧	1.24	0.035
3923354	AGPAT3	⇩	1.24	8.41E-04
3537264	C14orf101	⇩	1.24	8.67E-03
2950214	TAP1	⇩	1.24	4.62E-03
2709414	TBCCD1	⇧	1.24	8.95E-04
3058156	TMEM60	⇧	1.24	0.027
3629206	OAZ2	⇧	1.24	0.023
2979056	NUP43	⇧	1.24	8.28E-03
2906607	NFYA	⇧	1.24	1.12E-03
2343231	NEXN	⇧	1.24	0.046
2460487	C1orf131	⇧	1.24	7.67E-04
2739160	CCDC109B	⇧	1.24	0.025
2805581	SUB1	⇧	1.24	0.019
2664288	METTL6	⇧	1.24	0.011
3607183	MRPS11	⇧	1.24	0.011
2413519	HSPB11	⇧	1.24	0.018
3307939	ABLIM1	⇧	1.24	0.010
2601414	SERPINE2	⇧	1.24	0.035
2500838	POLR1B	⇧	1.24	0.038
3376235	WDR74	⇧	1.24	2.19E-03
3453592	MLL2	⇩	1.24	0.010
2433209	PRKAB2	⇧	1.24	0.030
3936887	MRPL40	⇧	1.24	0.042
2825629	TNFAIP8	⇧	1.24	9.68E-03
2827388	PRRC1	⇧	1.24	5.19E-03
2693149	SNX4	⇧	1.24	0.026
3591044	HAUS2	⇧	1.24	4.39E-03
3441849	TNFRSF1A	⇩	1.24	0.045
2728189	PAICS	⇧	1.24	0.019
3564210	PYGL	⇩	1.24	0.039
2356181	RBM8A	⇧	1.24	0.012
2317434	TPRG1L	⇧	1.24	0.032
2451544	MYOG	⇧	1.24	0.033
2361279	LMNA	⇩	1.24	0.014
3852783	DNAJB1	⇧	1.24	0.025
2838598	CCNG1	⇧	1.24	0.012
3535000	ARF6	⇧	1.24	0.018
2779486	H2AFZ	⇧	1.23	6.24E-03
2377094	PFKFB2	⇧	1.23	0.016
2934801	MAP3K4	⇩	1.23	0.019
3240095	RAB18	⇧	1.23	0.043
2405893	C1orf212	⇧	1.23	0.013
3693837	GOT2	⇩	1.23	0.030
2982319	SOD2	⇧	1.23	0.030
2901660	PRR3	⇧	1.23	7.67E-03
3368814	LMO2	⇧	1.23	4.97E-03
3434525	MLEC	⇩	1.23	0.017
2857416	IL6ST	⇩	1.23	0.044
2434527	GOLPH3L	⇧	1.23	8.04E-03
2838042	TTC1	⇧	1.23	0.036

Table B21: C9-Short Specific Gene List (n=916) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3325052	EIF2AK2	⇧	1.23	0.026
3334749	PPP2R5B	⇩	1.23	0.025
2486740	PNO1	⇧	1.23	9.50E-03
3601931	CPLX3	⇩	1.23	0.011
3757745	GHDC	⇩	1.23	0.016
3919033	SLC5A3	⇩	1.23	0.011
2610336	VHL	⇧	1.23	6.63E-03
3725456	ATP5G1	⇧	1.23	0.027
3816424	SPPL2B	⇩	1.23	9.98E-03
3869379	ZNF614	⇧	1.23	0.042
3119735	ZNF623	⇧	1.23	2.28E-03
2949210	BAT4	⇧	1.23	0.012
2438344	GPATCH4	⇧	1.23	0.037
2327219	STX12	⇧	1.23	0.011
3267314	BAG3	⇧	1.23	3.61E-03
3854477	TMEM221	⇧	1.23	0.016
3705641	TIMM22	⇧	1.23	4.70E-03
3705491	FAM57A	⇩	1.23	0.014
3204744	TLN1	⇩	1.23	3.27E-03
3261886	C10orf26	⇩	1.23	0.027
3624697	ARPP19	⇧	1.23	0.016
2645579	RASA2	⇧	1.23	0.034
3031827	SLC4A2	⇩	1.23	0.012
2964200	UBE2J1	⇧	1.23	0.037
3041875	OSBPL3	⇩	1.23	0.031
2403215	FGR	⇩	1.23	0.018
3665997	DUS2L	⇧	1.23	0.020
2363444	USP21	⇧	1.23	5.21E-03
3337516	LRP5	⇩	1.23	0.048
3146012	NIPAL2	⇩	1.23	2.60E-03
2708229	PARL	⇧	1.23	0.020
2442980	ANKRD36BP1	⇧	1.23	0.012
2575980	CCDC115	⇧	1.23	0.047
3828887	ZNF507	⇧	1.23	5.96E-03
3056414	RFC2	⇧	1.23	0.024
3739962	ABR	⇩	1.23	7.97E-03
3666282	ZFP90	⇧	1.23	0.031
3110171	ATP6V1C1	⇧	1.23	6.98E-03
3048886	PURB	⇧	1.23	9.65E-03
2743370	C4orf33	⇧	1.22	0.028
3261820	TRIM8	⇩	1.22	0.022
3757154	KRT14	⇩	1.22	0.013
3822657	CD97	⇩	1.22	0.013
3329904	NDUFS3	⇧	1.22	0.011
3098454	MRPL15	⇧	1.22	0.025
3048212	MRPS24	⇧	1.22	3.24E-03
2356205	PEX11B	⇧	1.22	3.89E-03
3362795	RNF141	⇧	1.22	0.024
3017795	RINT1	⇧	1.22	0.029
2812315	C5orf44	⇧	1.22	5.11E-03
3307120	ZDHHC6	⇩	1.22	0.033
3282974	SVIL	⇩	1.22	0.022
3642707	ITFG3	⇩	1.22	4.08E-03
2903782	ITPR3	⇩	1.22	0.019
3926080	BTG3	⇧	1.22	0.034
3426828	VEZT	⇩	1.22	0.048
2807862	C5orf51	⇧	1.22	0.040
3090922	PPP2R2A	⇧	1.22	0.026
2863535	WDR41	⇧	1.22	1.34E-03
3960827	SUN2	⇩	1.22	6.12E-03
3996467	PLXNA3	⇩	1.22	0.019
2503618	TSN	⇧	1.22	0.016
2536800	D2HGDH	⇩	1.22	0.035
3072368	ZC3HC1	⇧	1.22	9.70E-04
2901352	PPP1R11	⇧	1.22	0.027
3377091	MAP4K2	⇩	1.22	0.023
2491788	ATOH8	⇧	1.22	2.23E-04
3304853	SH3PXD2A	⇩	1.22	5.11E-03
2458649	C1orf55	⇧	1.22	0.013
3883971	C20orf24	⇧	1.22	0.015
2859195	DIMT1L	⇧	1.22	0.019
2783484	C4orf3	⇧	1.22	0.039
3536905	KTN1	⇩	1.22	0.012
3335465	SIPA1	⇩	1.22	5.74E-04
3222128	TNFSF15	⇩	1.22	0.011
3544346	DLST	⇧	1.22	0.017
2712858	UBXN7	⇧	1.22	0.020
3830002	GRAMD1A	⇩	1.22	1.26E-03
3354879	HYLS1	⇩	1.22	2.40E-03
3408018	ETNK1	⇩	1.22	0.013
2495782	LIPT1	⇧	1.22	0.032
2602997	SLC16A14	⇧	1.22	0.013
2351940	DDX20	⇧	1.22	0.040
2906824	FOXP4	⇩	1.22	0.034
2472955	MFSD2B	⇧	1.22	0.012
2501238	PSD4	⇩	1.22	0.029
2567242	CHST10	⇧	1.22	0.049
3634458	TBC1D2B	⇩	1.22	7.82E-03
2694785	MBD4	⇧	1.22	5.02E-03
3047202	C7orf11	⇧	1.22	8.50E-03
3922664	SLC37A1	⇩	1.22	5.57E-03
2999816	YKT6	⇧	1.22	0.026
2757720	HAUS3	⇧	1.22	2.26E-03
2903574	B3GALT4	⇩	1.22	9.46E-03
2899206	HIST1H2BF	⇧	1.22	0.013
3698919	GLG1	⇩	1.22	0.018

Table B21: C9-Short Specific Gene List (n=916) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

3100166	RAB2A	⇧	1.22	4.98E-03
2921456	KIAA1919	⇩	1.22	0.032
3675116	TMEM8A	⇩	1.22	6.18E-03
2948648	NCRNA00243	⇧	1.22	0.018
3050367	FIGNL1	⇧	1.22	0.047
2852274	MTMR12	⇧	1.22	6.99E-03
3759778	ARHGAP27	⇩	1.22	0.013
3693533	CSNK2A2	⇩	1.22	4.95E-03
2827156	PHAX	⇧	1.22	6.10E-03
3434374	GATC	⇧	1.22	0.047
2642562	NUDT16	⇧	1.22	4.49E-03
3835645	PVR	⇩	1.21	5.35E-03
3363091	GALNTL4	⇩	1.21	0.011
2822215	PAM	⇩	1.21	0.035
2444790	MRPS14	⇧	1.21	1.25E-03
3978706	PAGE5	⇧	1.21	0.022
3819401	LASS4	⇩	1.21	0.013
3003153	GBAS	⇧	1.21	8.19E-03
2907568	KLHDC3	⇧	1.21	7.02E-03
3830712	MLL4	⇩	1.21	7.87E-03
3564250	TRIM9	⇩	1.21	0.022
3328520	CD82	⇩	1.21	0.010
3189714	GARNL3	⇧	1.21	0.025
3325768	QSER1	⇩	1.21	0.013
3558270	CBLN3	⇩	1.21	0.033
2641577	C3orf37	⇧	1.21	0.022
3775038	C17orf62	⇩	1.21	9.27E-03
3841901	NLRP2	⇧	1.21	0.016
3717452	LRRC37BP1	⇩	1.21	0.015
3048749	DDX56	⇧	1.21	6.52E-03
2845591	BRD9	⇧	1.21	0.012
3347658	ATM	⇩	1.21	9.53E-03
2750227	C4orf43	⇧	1.21	9.65E-03
2927993	HECA	⇧	1.21	2.78E-03
2484752	COMMD1	⇧	1.21	0.036
3880706	ENTPD6	⇩	1.21	6.59E-03
3743486	GABARAP	⇧	1.21	7.52E-03
2903703	SYNGAP1	⇧	1.21	1.29E-03
3032243	GALNT11	⇧	1.21	0.016
2950885	MLN	⇧	1.21	0.041
3855538	MEF2B	⇧	1.21	6.80E-03
2398789	SDHB	⇧	1.21	0.012
2548776	ATL2	⇧	1.21	0.042
3610982	SYNM	⇩	1.21	0.032
3874313	ATRN	⇩	1.21	0.043
2315739	PUSL1	⇧	1.21	1.71E-03
3375545	FADS1	⇩	1.21	0.049
2947572	TRIM27	⇧	1.21	5.78E-03
3884191	SRC	⇩	1.21	7.62E-03
2596955	CRYGC	⇧	1.21	0.047
2327188	FAM76A	⇧	1.21	5.68E-03
2522014	C2orf47	⇧	1.21	1.40E-03
2545509	PREB	⇧	1.21	6.53E-03
2560704	C2orf3	⇧	1.21	0.021
2444451	CENPL	⇧	1.21	4.35E-03
3770029	CDC42EP4	⇩	1.21	4.57E-03
3552847	DYNC1H1	⇩	1.21	0.028
2452311	TMEM81	⇧	1.21	2.70E-03
2318637	VAMP3	⇧	1.21	0.012
3851545	MAN2B1	⇩	1.21	0.015
2916246	C6orf162	⇧	1.21	0.018
2678116	FAM116A	⇧	1.21	6.92E-03
2565143	STARD7	⇧	1.21	0.021
2443537	SCYL3	⇧	1.21	6.12E-04
3614901	HERC2	⇩	1.21	0.011
3753372	RFFL	⇩	1.21	0.010
3851703	C19orf43	⇩	1.21	0.022
3683845	DCUN1D3	⇧	1.21	3.57E-03
2678090	ARF4	⇧	1.21	0.044
3315024	ADAM8	⇩	1.21	0.019
2870397	PJA2	⇧	1.21	0.028
3701297	CDYL2	⇧	1.21	5.71E-03
3934695	PTTG1IP	⇩	1.21	0.041
4017810	ACSL4	⇩	1.21	0.049
3839489	GPR32	⇩	1.21	0.032
2623388	PARP3	⇧	1.21	0.048
3565303	CNIH	⇩	1.21	0.015
3880767	PYGB	⇩	1.20	0.038
3918104	C21orf63	⇩	1.20	5.35E-03
4026722	IDH3G	⇧	1.20	0.021
2843619	HNRNPAB	⇧	1.20	8.60E-03
2451200	UBE2T	⇧	1.20	0.025
3945863	MGAT3	⇩	1.20	0.028
2977471	ADAT2	⇧	1.20	0.033
3639007	HDDC3	⇧	1.20	0.014
3179551	FGD3	⇩	1.20	0.027
3551303	CCNK	⇧	1.20	5.05E-03
2649609	MLF1	⇧	1.20	0.018
3774218	DYSFIP1	⇧	1.20	0.024
3729569	BCAS3	⇩	1.20	0.017
3928477	KRTAP26-1	⇧	1.20	0.049
2641479	GP9	⇩	1.20	0.015
3867400	FUT1	⇩	1.20	0.019
3221135	C9orf80	⇧	1.20	0.030
2855614	C5orf34	⇧	1.20	0.047
2526806	FN1	⇧	1.20	0.026

Table B21: C9-Short Specific Gene List (n=916) MALE ONLY SAMPLES [Partek® unadjusted p<0.05, FC ≥ ±1.20]

2951221	C6orf106	⇧	1.20	0.045
3655723	MVP	⇩	1.20	6.94E-03
3995848	ABCD1	⇩	1.20	2.58E-03
3472000	C12orf51	⇩	1.20	0.043
2663551	NUP210	⇩	1.20	0.036
3375990	INTS5	⇧	1.20	0.024
2832431	PCDHB11	⇧	1.20	5.42E-03
3432678	TPCN1	⇩	1.20	0.013
2949830	AGER	⇩	1.20	5.99E-03
3257559	RPP30	⇧	1.20	0.022
2921296	AMD1	⇧	1.20	0.013
2916952	CASP8AP2	⇧	1.20	0.037
2367287	METTL13	⇧	1.20	0.014
3442514	C1RL	⇩	1.20	0.013
3695541	FHOD1	⇩	1.20	0.018
2403585	TAF12	⇧	1.20	0.046
3014714	ARPC1B	⇧	1.20	0.027
2735027	SPP1	⇧	1.20	0.045
2878446	NDUFA2	⇧	1.20	7.55E-03
3259400	CCNJ	⇧	1.20	1.00E-03
3181728	TGFBR1	⇩	1.20	0.036
3923218	RRP1B	⇧	1.20	0.038
4017519	PSMD10	⇧	1.20	0.020
3396144	C11orf61	⇩	1.20	0.036
2598099	BARD1	⇧	1.20	7.07E-03
3251926	KIAA0913	⇩	1.20	6.55E-03
3190558	SPTAN1	⇩	1.20	0.020
3635456	MESDC2	⇩	1.20	0.042
3865422	RTN2	⇩	1.20	1.91E-04
2878474	HARS	⇧	1.20	0.036
3255220	GHITM	⇧	1.20	0.014
3269587	C10orf137	⇩	1.20	0.011
2877141	HNRNPA0	⇧	1.20	1.11E-03
2662087	SRGAP3	⇧	1.20	0.015
3540136	HSPA2	⇧	1.20	7.83E-03
3933331	C2CD2	⇩	1.20	0.020
4026956	HCFC1	⇩	1.20	0.026
2382336	FBXO28	⇧	1.20	0.015
3816664	ZNF555	⇧	1.20	8.84E-03
3192171	POMT1	⇩	1.20	2.32E-03
3648412	RUNDC2A	⇩	1.20	0.049
3992148	DDX26B	⇩	1.20	0.012
3484005	USPL1	⇧	1.20	0.025
3937294	LOC150197	⇩	1.20	3.34E-03
2695941	TOPBP1	⇧	1.20	4.05E-03
2966232	COQ3	⇧	1.20	5.25E-03
2565579	ANKRD39	⇧	1.20	0.041
3341362	AQP11	⇧	1.20	7.88E-03
2995189	PLEKHA8	⇩	1.20	2.09E-03
2886535	LOC100133106	⇧	1.20	0.041
3029646	ARHGEF5	⇧	1.20	0.010
3352618	GRIK4	⇩	1.20	0.019
3809671	NARS	⇧	1.20	0.012
2724235	WDR19	⇧	1.20	0.022
2437801	ARHGEF2	⇩	1.20	7.97E-03