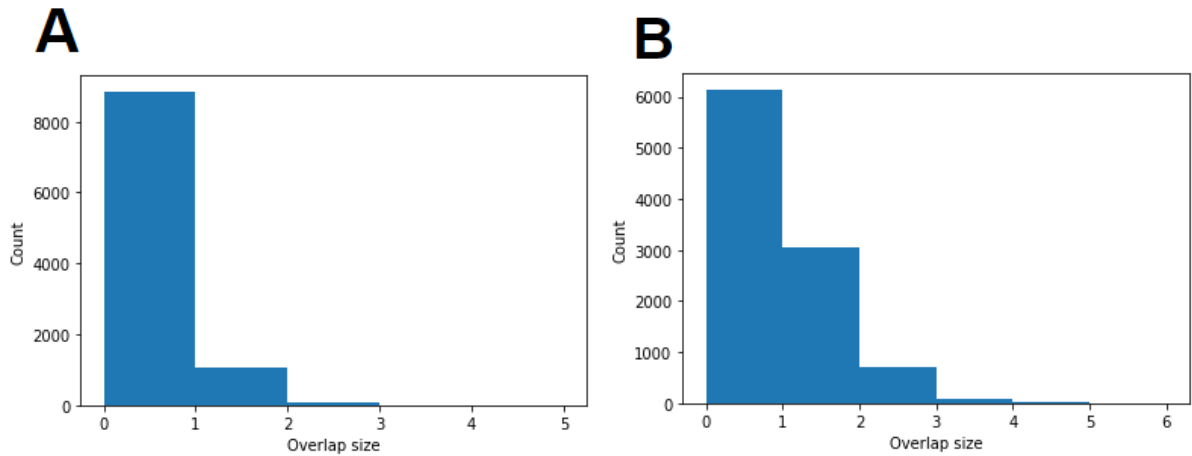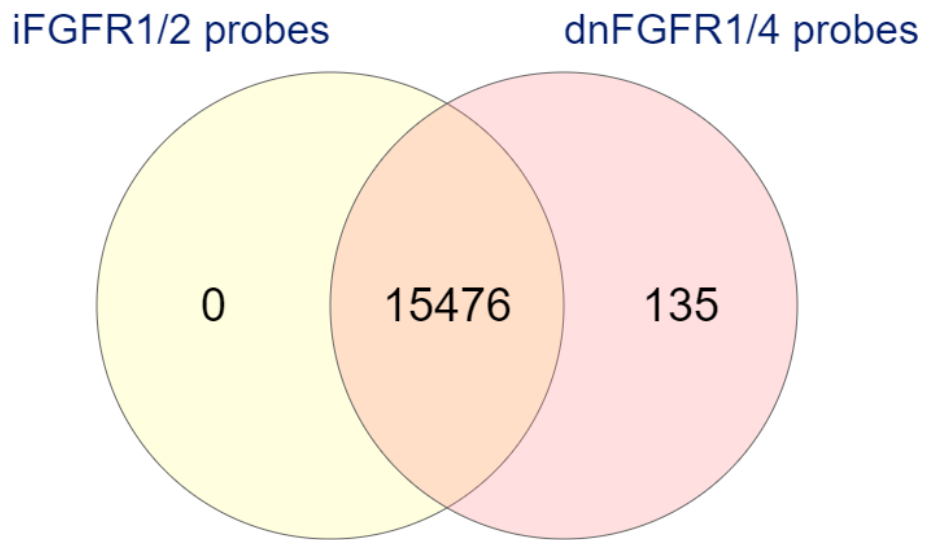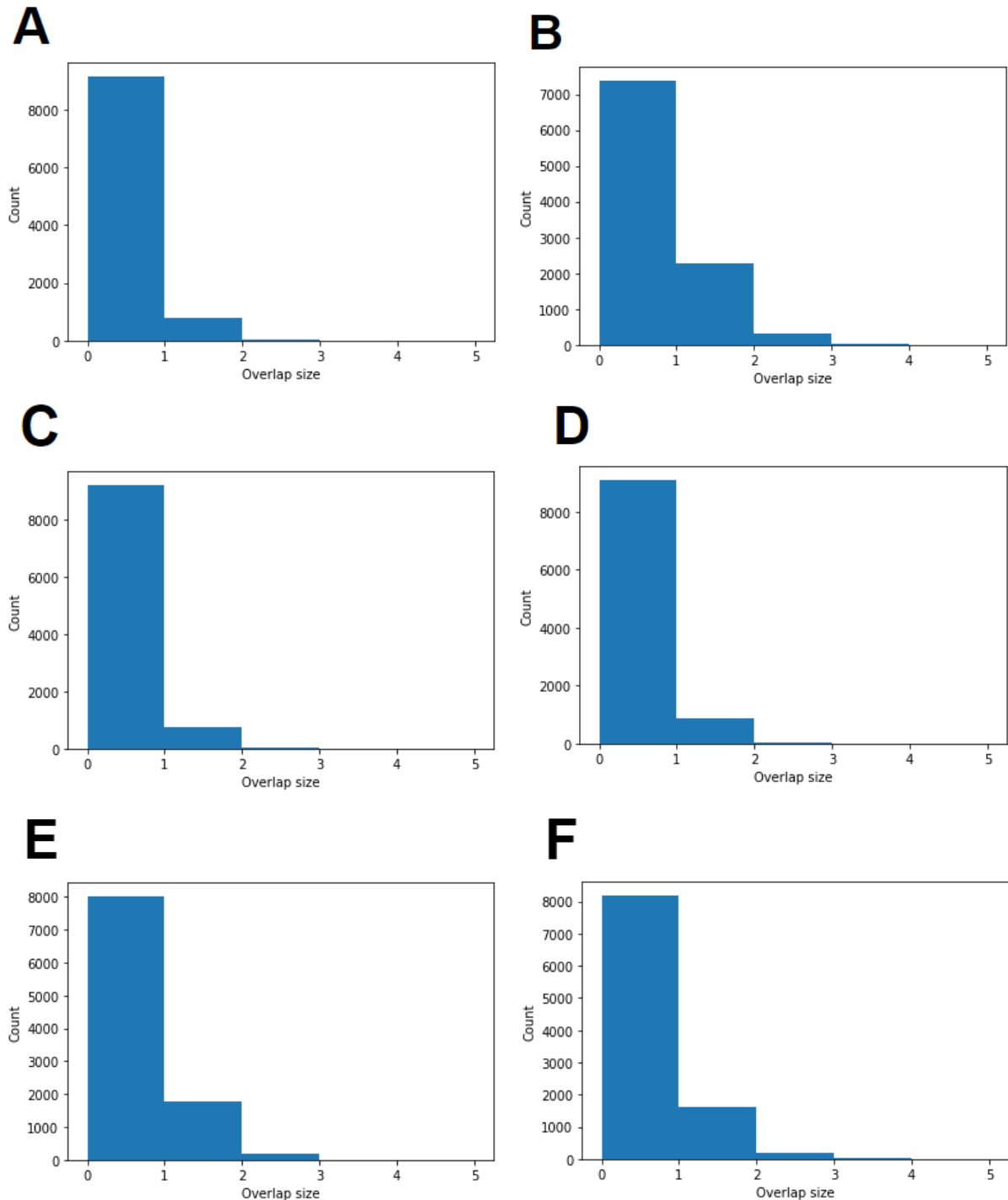**Figure S1: Expected size of overlaps modelling dnFGFR microarray data using Python. (A)** Up regulated probes: 18 and 30 gene probes satisfied high stringency filtering (p ≤ 0.05, fold change ≥ 2) in *X. laevis* subject to FGF inhibition by dnFGFR1 and dnFGFR4 respectively, with an overlap of 14. Histogram shows size of overlaps generated by random sampling of sets of 18 and 30 numbers between 1 and 15,611 (number of probes in the microarray) in 10,000 iterations. **(B)** Down regulated probes: 59 and 75 gene probes satisfied high stringency filtering (p ≤ 0.05, fold change ≤ 0.5) in *X. laevis* subject to FGF inhibition by dnFGFR1 and dnFGFR4 respectively, with an overlap of 57. Histogram shows size of overlaps generated by random sampling of sets of 59 and 75 numbers between 1 and 15,611 (number of probes in the microarray) in 10,000 iterations.

Figure S2: Expected size of overlaps modelling iFGFR microarray data using Python. (A) Up regulated probes: 45 and 41 gene probes satisfied high stringency filtering (arbitrary unit ≥ 20, fold change ≥ 2) in *X. laevis* subject to increased FGF signalling by iFGFR1 and iFGFR2 respectively, with an overlap of 25. Histogram shows size of overlaps generated by random sampling of sets of 41 and 45 numbers between 1 and 15,476 (number of probes in the microarray) in 10,000 iterations. **(B)** Down regulated probes: 154 and 48 gene probes satisfied high stringency filtering (arbitrary unit ≥ 20, fold change ≤ 0.5) in *X. laevis* subject to increased FGF signalling by iFGFR1 and iFGFR2 respectively, with an overlap of 41. Histogram shows size of overlaps generated by random sampling of sets of 154 and 48 numbers between 1 and 15,476 (number of probes in the microarray) in 10,000 iterations.

Figure S3: Number of gene probes present in both dnFGFR and iFGFR microarray data sets. Lists of probe sets were compared. List analysis was performed using Multiple List Comparator (http://www.molbiotools.com/listcompare.html).
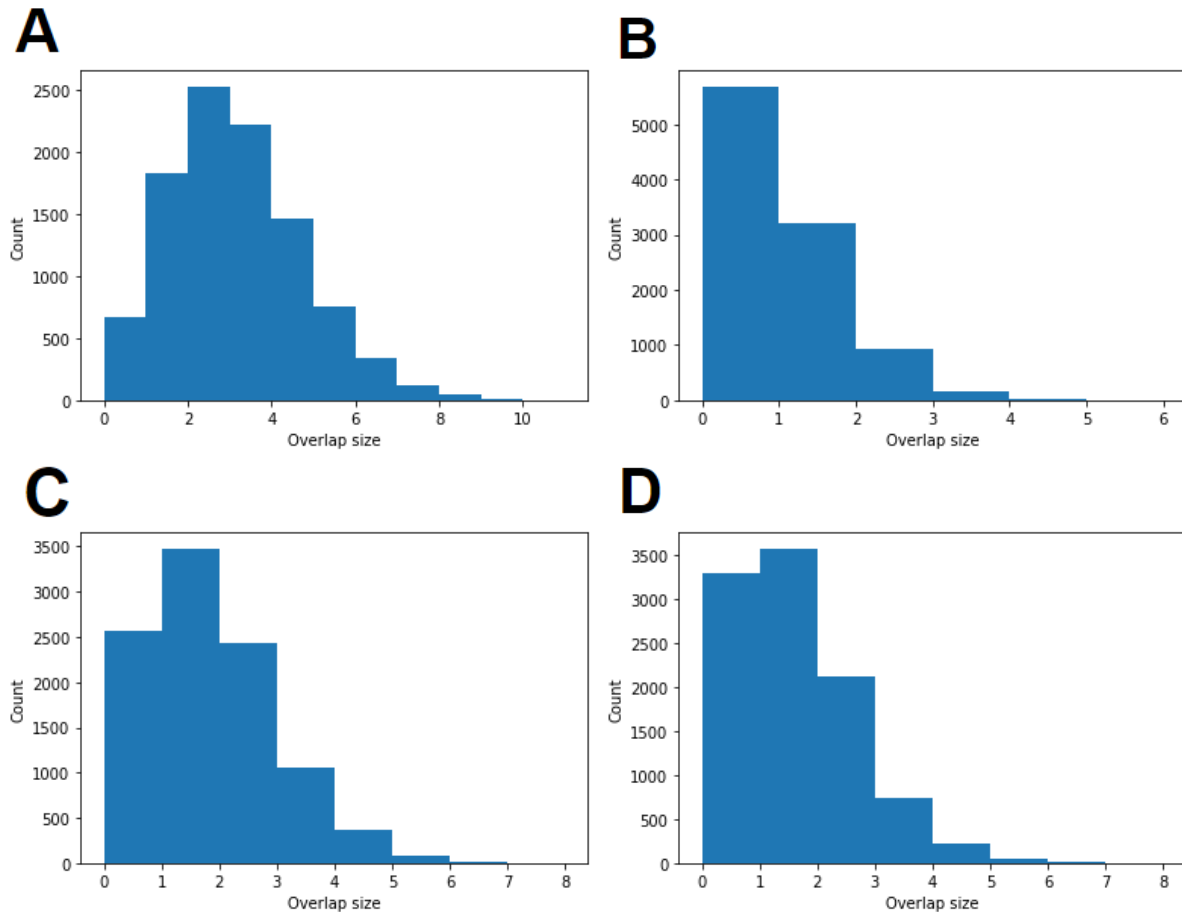
Figure S4: Expected size of overlaps modelling dnFGFR and iFGFR microarray data using Python. (A) Up regulated probes by dnFGFR4 and iFGFR1: 30 and 45 gene probes satisfied high stringency filtering in *X. laevis* by dnFGFR4 and iFGFR1 respectively, with an overlap of 4. Histogram shows size of overlaps generated by random sampling of sets of 30 and 45 numbers between 1 and 15,476 (number of probes present in both microarrays) in 10,000 iterations. **(B)** Probes up regulated by dnFGFR4 and down regulated by iFGFR1: 30 and 154 gene probes satisfied high stringency filtering in *X. laevis* by dnFGFR4 and iFGFR1 respectively, with an overlap of 3. Histogram shows size of overlaps generated by random sampling of sets of 30 and 154 numbers between 1 and 15,476 (number of probes present in both microarrays) in 10,000 iterations. **(C)** Up regulated probes by dnFGFR4 and iFGFR2: 30 and 41 gene probes satisfied high stringency filtering in *X. laevis* by dnFGFR4 and iFGFR1 respectively, with an overlap of 4. Histogram shows size of overlaps generated by random sampling of sets of 30 and 41 numbers between 1 and 15,476 (number of probes present in both microarrays) in

10,000 iterations. **(D)** Probes up regulated by dnFGFR4 and down regulated by iFGFR2: 30 and 48 gene probes satisfied high stringency filtering in *X. laevis* by dnFGFR4 and iFGFR1 respectively, with an overlap of 2. Histogram shows size of overlaps generated by random sampling of sets of 30 and 48 numbers between 1 and 15,476 (number of probes present in both microarrays) in 10,000 iterations. **(E)** Probes down regulated by dnFGFR4 and up regulated by iFGFR1: 75 and 45 gene probes satisfied high stringency filtering in *X. laevis* by dnFGFR4 and iFGFR1 respectively, with an overlap of 5. Histogram shows size of overlaps generated by random sampling of sets of 75 and 45 numbers between 1 and 15,476 (number of probes present in both microarrays) in 10,000 iterations. **(F)** Probes down regulated by dnFGFR4 and up regulated by iFGFR2: 75 and 41 gene probes satisfied high stringency filtering in *X. laevis* by dnFGFR4 and iFGFR1 respectively, with an overlap of 6. Histogram shows size of overlaps generated by random sampling of sets of 75 and 41 numbers between 1 and 15,476 (number of probes present in both microarrays) in 10,000 iterations.

Figure S5: Overlap of differentially expressed genes in embryos subject to decreased FGF signalling by dnFGFR4 and increased by iFGFR1 or iFGFR2, from low stringency filtering. Up and down regulated probe lists were compiled to produce differentially expressed gene lists, containing 112, 199 and 90 for dnFGFR4, iFGFR1 and iFGFR2 respectively. List analysis was performed using Multiple List Comparator (http://www.molbiotools.com/listcompare.html).
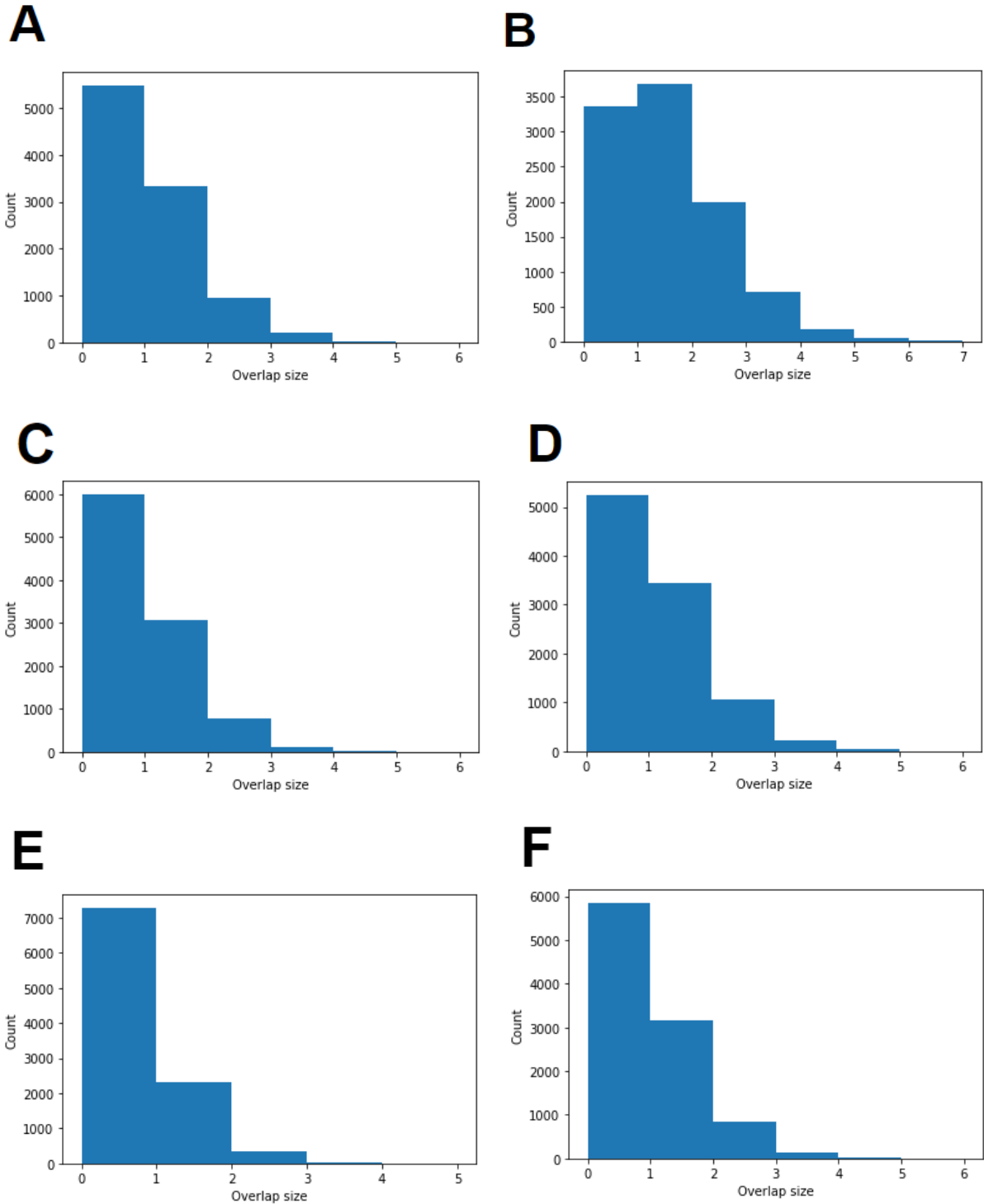
Figure S6: Expected size of overlaps modelling iFGFR RNA-Seq data using Python. (A) Up regulated transcripts: 257 and 368 transcripts satisfied high stringency filtering (FPKM ≥ 20, fold change ≥ 2) in *X. laevis* subject to FGF signalling by iFGFR1 and iFGFR4 respectively, with an overlap of 11. Histogram shows size of overlaps generated by random sampling of sets of 257 and 368 numbers between 1 and 35,532 (number of transcripts in the RNA-Seq) in 10,000 iterations. **(B)** Down regulated transcripts: 108 and 186 transcripts satisfied high stringency filtering (FPKM ≥ 20, fold change ≤ 0.5) in *X. laevis* subject to increased FGF signalling by iFGFR1 and iFGFR4 respectively, with an overlap of 15. Histogram shows size of overlaps generated by random sampling of sets of 108 and 186 numbers between 1 and 35,532 (number of transcripts in the RNA-Seq) in 10,000 iterations. **(C)** Transcripts up regulated by iFGFR1 and down regulated by iFGFR4: 257 and 186 transcripts satisfied high stringency filtering (FPKM ≥ 20, fold change ≥ 2 or ≤ 0.5 respectively) in *X. laevis* subject to FGF signalling by iFGFR1 and iFGFR4 respectively, with an overlap of 4. Histogram shows size of overlaps generated by random sampling of sets of 257 and 186 numbers between 1 and 35,532 (number of transcripts in the RNA-Seq) in 10,000 iterations. **(D)** Transcripts down regulated by iFGFR1 and up regulated by iFGFR4: 108 and 368 transcripts satisfied high stringency filtering (FPKM ≥ 20, fold change ≤ 0.5 or ≥ 2 respectively) in *X. laevis* subject to increased FGF signalling by iFGFR1 and iFGFR4 respectively, with an overlap of 3. Histogram shows size of overlaps generated by random sampling of sets of 108 and 368 numbers between 1 and 35,532 (number of transcripts in the RNA-Seq) in 10,000 iterations.
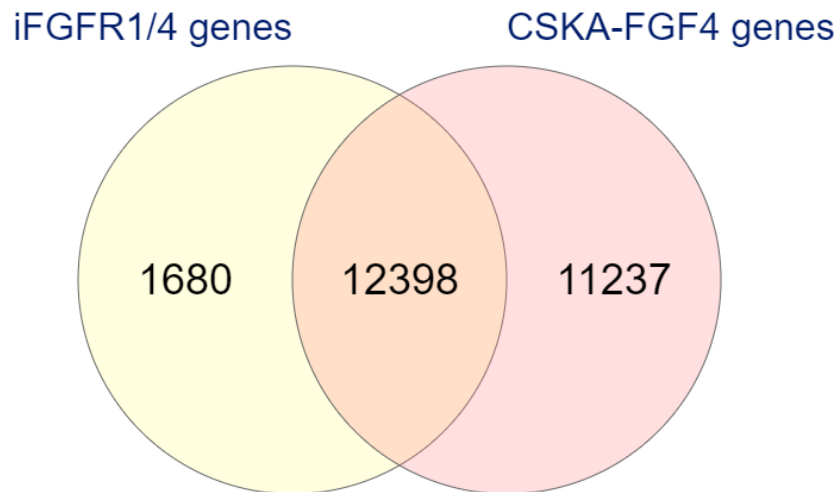
Figure S7: Number of genes present in both CSKA-FGF4 and iFGFR1/4 RNA-Seq data sets. Lists of gene names were compared and genes were counted once regardless of the number of transcripts identified. List analysis was performed using Multiple List Comparator (http://www.molbiotools.com/listcompare.html).

Figure S8: Expected size of overlaps modelling CSKA-FGF4 and iFGFR1/4 RNA-Seq data using Python. (A) Up regulated genes by CSKA-FGF4 and iFGFR1: 53 and 137 genes satisfied high stringency filtering by CSKA-FGF4 and iFGFR1 respectively, with an overlap of 6. Histogram shows size of overlaps generated by random sampling of sets of 53 and 137 numbers between 1 and 12,398 (number of genes present in both RNA-Seqs) in 10,000 iterations. **(B)** Up regulated genes by CSKA-FGF4 and iFGFR4: 53 and 250 genes satisfied high stringency filtering by CSKA-FGF4 and iFGFR4 respectively, with an overlap of 3. Histogram shows size of overlaps generated by random sampling of sets of 53 and 250 numbers between 1 and 12,398 (number of genes present in both RNA-Seqs) in 10,000 iterations. **(C)** Genes up regulated by CSKA-FGF4 and down regulated by iFGFR4: 53 and 117 genes satisfied high stringency filtering by CSKA-FGF4 and iFGFR4 respectively, with an overlap of 1.

Histogram shows size of overlaps generated by random sampling of sets of 53 and 117 numbers between 1 and 12,398 (number of genes present in both RNA-Seqs) in 10,000 iterations. **(D)** Genes down regulated by CSKA-FGF4 and up regulated by iFGFR1: 57 and 137 genes satisfied high stringency filtering by CSKA-FGF4 and iFGFR1 respectively, with an overlap of 1. Histogram shows size of overlaps generated by random sampling of sets of 57 and 137 numbers between 1 and 12,398 (number of genes present in both RNA-Seqs) in 10,000 iterations. **(E)** Down regulated genes by CSKA-FGF4 and iFGFR1: 57 and 68 genes satisfied high stringency filtering by CSKA-FGF4 and iFGFR1 respectively, with an overlap of 1. Histogram shows size of overlaps generated by random sampling of sets of 57 and 68 numbers between 1 and 12,398 (number of genes present in both RNA-Seqs) in 10,000 iterations. **(F)** Down regulated genes by CSKA-FGF4 and iFGFR4: 57 and 117 genes satisfied high stringency filtering by CSKA-FGF4 and iFGFR4 respectively, with an overlap of 4. Histogram shows size of overlaps generated by random sampling of sets of 57 and 117 numbers between 1 and 12,398 (number of genes present in both RNA-Seqs) in 10,000 iterations.
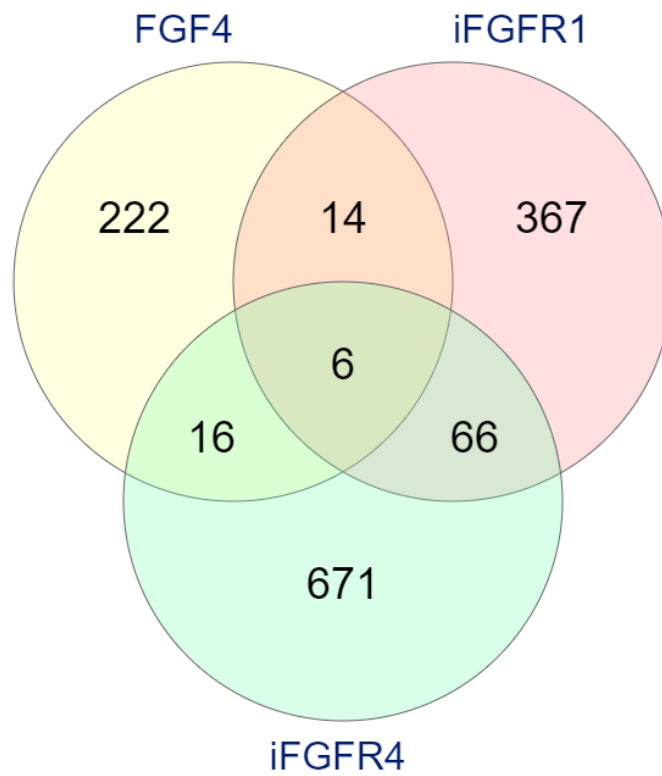
Figure S9: Overlap of differentially expressed genes in embryos subject to increased FGF signalling by CSKA-FGF4, iFGFR1 or iFGFR4, from low stringency filtering. Up and down regulated gene lists were compiled to produce differentially expressed gene lists, containing 258, 453 and 759 for FGF4, iFGFR1 and iFGFR4 respectively. List analysis was performed using Multiple List Comparator (http://www.molbiotools.com/listcompare.html).
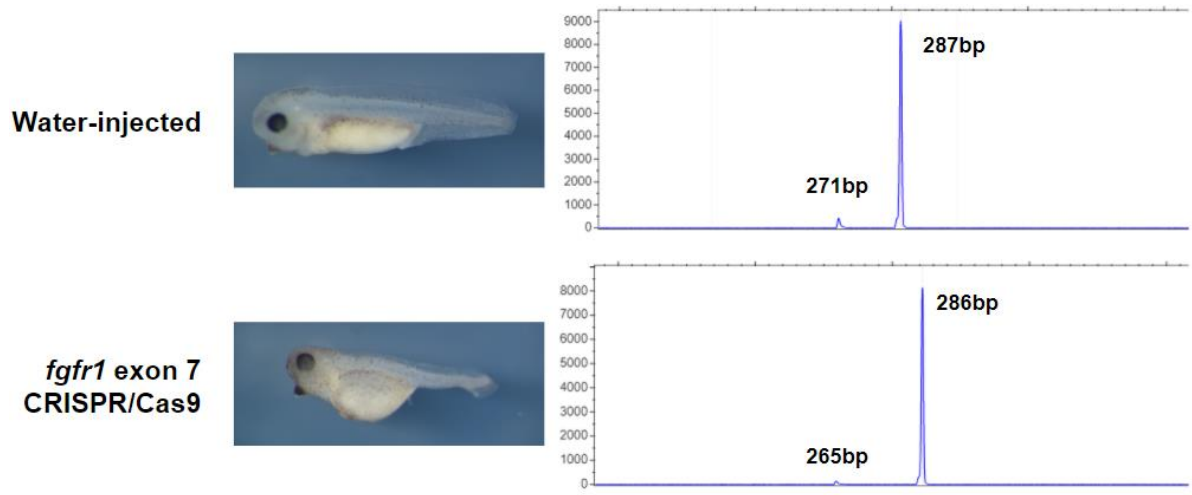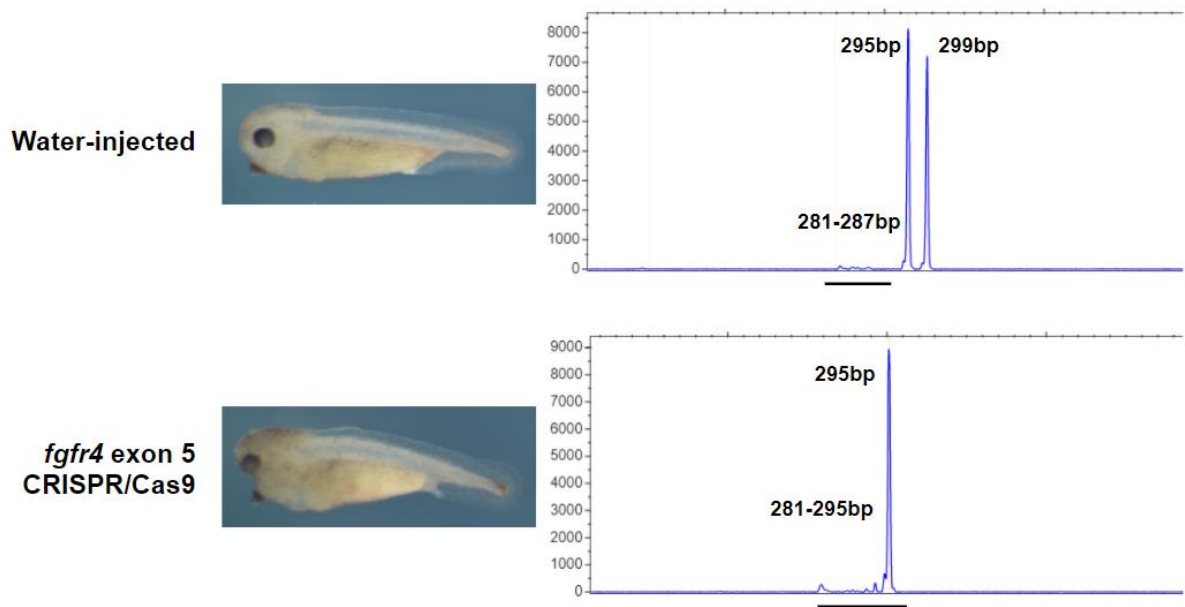
Figure S10: Fragment analysis of embryos subject to *fgfr1* exon 7 gene targeting by CRISPR/Cas9 with corresponding phenotypes. Stage 38 embryos are either injected at 1-2 cell stage with water or 600pg *fgfr1* sgRNA and 1.5ng Cas9 in 2nl. Wild type peaks are seen at 271bp and 287bp. Embryos are staged according to Nieuwkoop and Faber (1994) stages of *Xenopus* development.
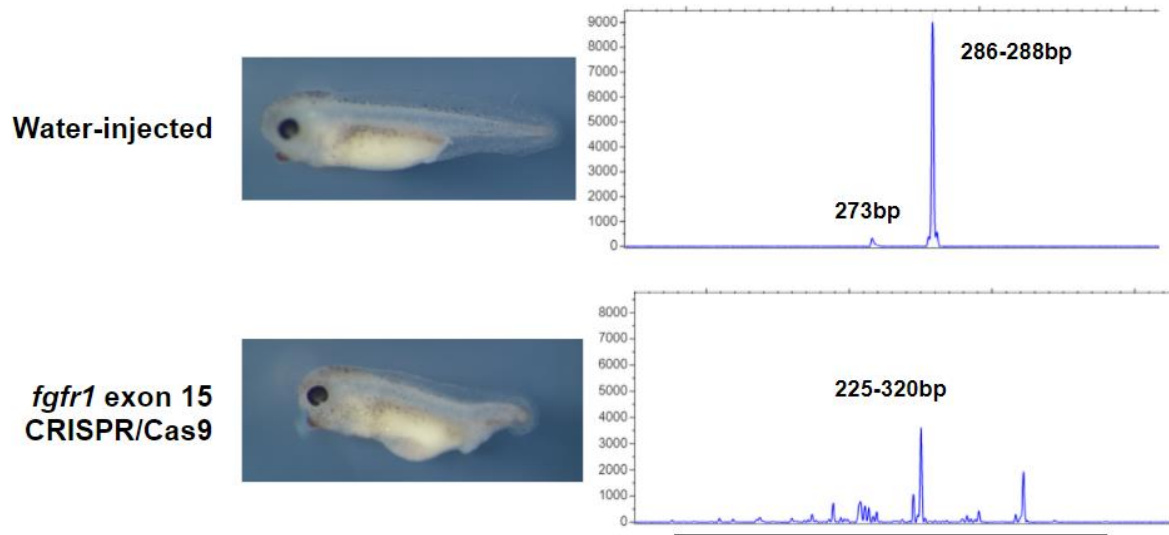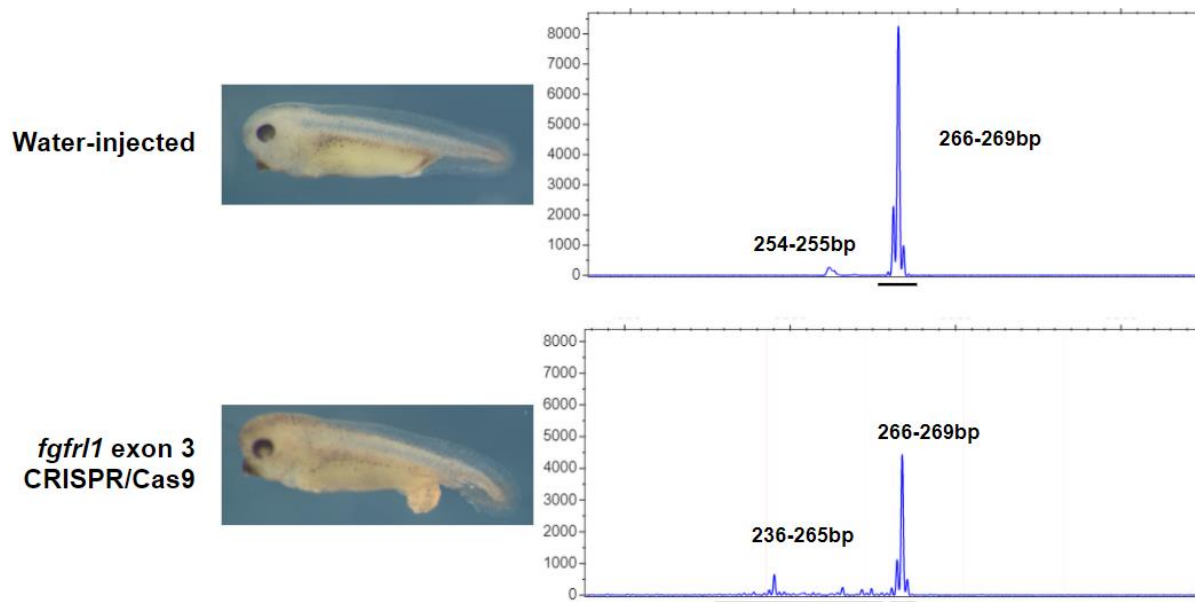
Figure S11: Fragment analysis of embryos subject to *fgfr1* exon 15 gene targeting by CRISPR/Cas9 with corresponding phenotypes. Stage 38 embryos are either injected at 1-2 cell stage with water or 600pg *fgfr1* sgRNA and 1.5ng Cas9 in 2nl. Wild type peaks are seen at 273bp, 286bp, 287bp and 288bp. Embryos are staged according to Nieuwkoop and Faber (1994) stages of *Xenopus* development.
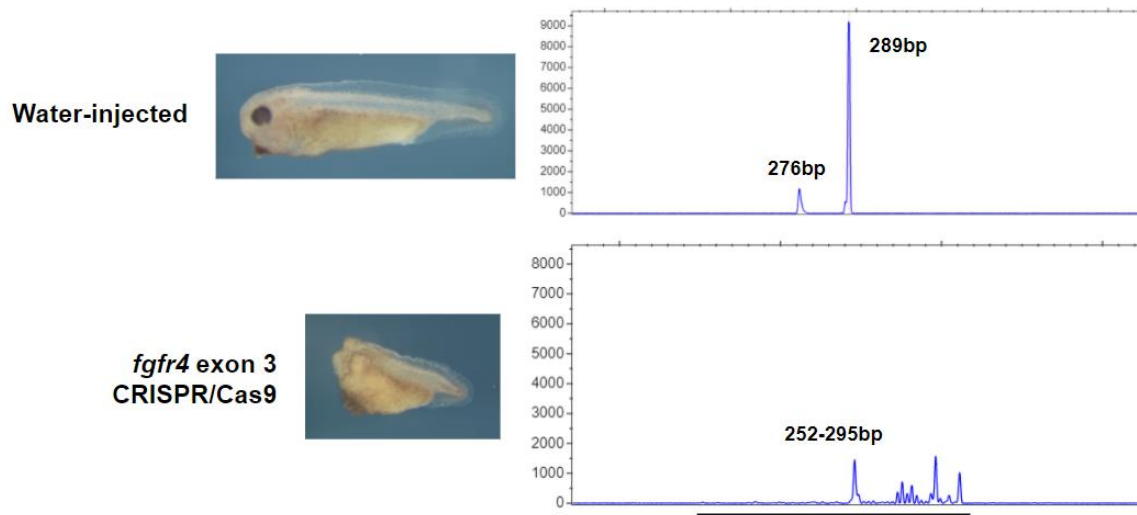
Figure S12: Fragment analysis of embryos subject to *fgfr4* exon 3 gene targeting by CRISPR/Cas9 with corresponding phenotypes. Stage 35 embryos are either injected at 1-2 cell stage with water or 600pg *fgfr1* sgRNA and 1.5ng Cas9 in 2nl. Wild type peaks are seen at 276bp and 289bp. Embryos are staged according to Nieuwkoop and Faber (1994) stages of *Xenopus* development.
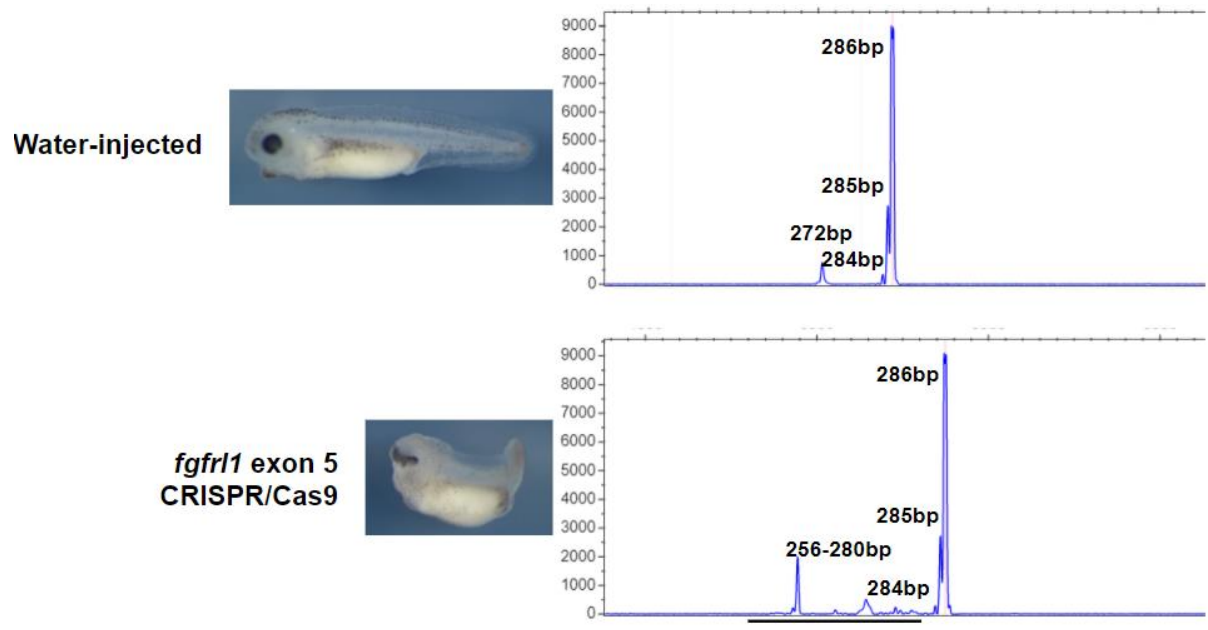
Figure S13: Fragment analysis of embryos subject to *fgfr4* exon 5 gene targeting by CRISPR/Cas9 with corresponding phenotypes. Stage 36 embryos are either injected at 1-2 cell stage with water or 600pg *fgfr1* sgRNA and 1.5ng Cas9 in 2nl. Wild type peaks are seen at 281bp, 284bp, 285bp, 287bp, 294bp, 295bp, 298bp and 299bp. Embryos are staged according to Nieuwkoop and Faber (1994) stages of *Xenopus* development.

Figure S14: Fragment analysis of embryos subject to *fgfrl1* exon 3 gene targeting by CRISPR/Cas9 with corresponding phenotypes. Stage 36 embryos are either injected at 1-2 cell stage with water or 600pg *fgfr1* sgRNA and 1.5ng Cas9 in 2nl. Wild type peaks are seen at 281bp, 284bp, 285bp, 287bp, 294bp, 295bp, 298bp and 299bp. Embryos are staged according to Nieuwkoop and Faber (1994) stages of *Xenopus* development.

Figure S15: Fragment analysis of embryos subject to *fgfrl1* exon 5 gene targeting by CRISPR/Cas9 with corresponding phenotypes. Stage 36 embryos are either injected at 1-2 cell stage with water or 600pg *fgfr1* sgRNA and 1.5ng Cas9 in 2nl. Wild type peaks are seen at 272bp, 284bp, 285bp and 286bp. Embryos are staged according to Nieuwkoop and Faber (1994) stages of *Xenopus* development.