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# Abstract

*This thesis details chemistry and cell biology based interdisciplinary studies on a series of ruthenium based biomolecular probes that were synthesised and investigated for their anti-cancer properties.*

*The previously reported mononuclear ruthenium-based [(phen)2Ru(tpphz)]2+ and three related new complexes were synthesised as a series to explore DNA binding. Binding to genomic DNA in vitro was confirmed for all complexes utilising their luminescence properties – specifically the DNA light switch effect via aqueous luminescence titrations.*

*Cellular activity in the model of cisplatin sensitive/resistant A2780/A2780cis human ovarian carcinoma was then studied, with IC50 concentrations determined for each complex in each cell line and adequately repeated. This revealed a clear series of toxicities comparable to the level of cisplatin, furthermore a variety of positive and negative cross resistance profiles were observed. Time lapse microscopy data was then obtained for each complex and cell line permutation to visualize the mode of cell death, and a proteomic study was conducted with the aim of gathering more mechanistic detail behind the cell death pathway.*

*After optimisation of a consistent workable protocol, photocytotoxicty was also investigated. Although this work was primarily with the ruthenium-rhenium and ruthenium-platinum binuclear complexes of the original series, further systems incorporating ruthenium-rhenium molecules were also investigated. Interestingly, these studies revealed contrasting phototoxic activity and a particularly impressive phototoxic index score for a Ru2Re2 macrocyclic cation.*

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# Declaration

All work contained herein is an original work of the author, unless specifically referenced otherwise. Some results have already been submitted to peer-reviewed journals and will be published subject to acceptance.

Paul James Jarman

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# Abbreviations

bipy - bipyridine

BSA - bovine serum albumin

cisplatin - diamminedichloroplatinum

DNA - deoxyribonucleic acid

DPQ - 1,10-phenanthroline-5,6-dione

FBS - fetal bovine serum

HCl - hydrochloric acid

IC50 - half maximal inhibitory concentration

ICP-MS - Inductively coupled plasma mass spectrometry

K2[PtCl4] - potassium tetrachloroplatinate

LISA - light irradiation source apparatus

MLCT - metal-to-ligand-charge-transfer

MQ H2O - milli-Q ultrapure water filtration/deionization

MS - mass spectrometry

MTT - 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide

N2 - nitrogen

NH4PF6 - ammonium hexafluorophosphate

NMR - nuclear magnetic resonance spectroscopy

PBS - phosphate buffered saline

Pd/C - palladium on carbon

phen - phenanthroline

phen-diamine - 1,10-phenanthroline-5,6-diamine

phen-dioxime - 1,10-phenanthroline-5,6-dioxime

PI - phototoxic index

Re(CO)5Cl - pentacarbonyl rhenium chloride

RNA - ribonucleic acid

RPMI medium - Roswell park memorial institute medium

SDS-PAGE - sodium dodecyl sulfate polyacrylamide gel electrophoresis

SILAC - stable isotope labelling by amino acids in cell culture

taptp - 4,5,9,18-tetraazaphenanthreno[9,10-b] triphenylene

tpphz - tetrapyridophenazine

λmax - maximum emission wavelength

φ(1O2) - singlet oxygen quantum yield