

New Chemistry of Organometallic Rhenium Complexes for Drug Development

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Today, there are numerous examples for medicinal application of metal complexes especially of the heavier transition metals. Following the success of the Pt-derived metallodrugs (e.g. Cisplatin) and Au complexes (e.g. Auranofin), other elements moved into the spotlight, such as Ru and Ir for antitumor-active compounds and imaging purposes, respectively. In an attempt to further broaden the range of useful metals for biomedical purposes, our group has explored applications of Re compounds in cell biology and biomedical research.

Re in the oxidation state +I is a d⁶ metal center. As such, we expected favourable imaging parameters. Indeed, complexes with a suitable N₃ ligand set derived from bis(picoly)amine and a Re(CO)₃ core proved to have very favourable properties as cellular imaging agents. By tethering the ligand to suitable targeting peptides, we were able to demonstrate good cellular uptake and intracellular localization by fluorescence microscopy.¹ The imaging properties (phosphorescence lifetime and quantum yield) could be further optimized by modifying the ligand set. Most importantly, the best compounds were obtained with an unsymmetrical ligand set containing quinoline and phenanthridine rings on the chelating tridentate ligand. Upon excitation at 350 nm, the complexes commonly emit in the orange range ($\lambda_{\text{max}} > 560$ nm) of the visible spectrum, with large Stokes shifts > 20 nm. By colocalization imaging with commercial dyes, a predominant localization in the endoplasmatic reticulum (ER) was shown.²

Interestingly, some of these complexes also displayed high cytotoxicity against a range of mammalian cells. The mechanism of cell death was elucidated by resistance breaking profiling and gene expression analysis, with activation of both, the extrinsic and the intrinsic apoptotic pathway.³ Finally, modifications of the ligand set around the Re center revealed some very interesting new bioactive Re complexes with N-heterocyclic carbene (NHC) ligands.⁴ In total, these complexes should well add to the growing toolbox of organometallic complexes for biomedical applications.⁵

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