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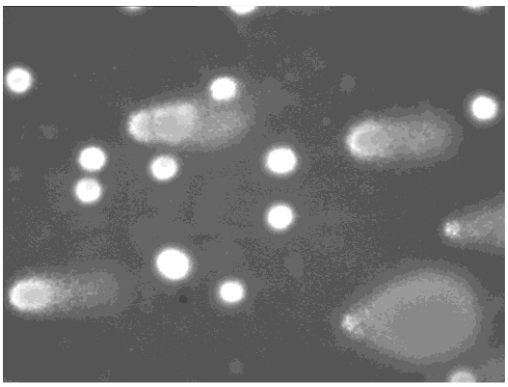
This proposal is representative of the projects currently on offer in our group. For more details of active research projects, please visit our webpage at: http://www.chem.leeds.ac.uk/People/McGowan.html

The use of organometallic compounds as anticancer drugs

Metal-based drugs are known for their potent cytotoxic activity and clinical efficacy. Cisplatin exemplifies the fact that metal-containing drugs can be effective anticancer drugs but their activity is however compromised by the emergence of resistance and toxicity to normal tissues. We have invented a new library of compounds which have shown extremely promising activity against a number of different cell lines including ovarian (A2780), breast (MCF7), and colon (HT-29, LS174T, LoVo) cancers.[1-5] The reagents have also shown high activity towards cisplatin (conventional anti-tumour drug) resistant cell lines.[2-4]



There is a need for novel metal-containing drugs that are effective against cisplatin-resistant tumour cells and have greater selectivity for tumour tissue. Drug candidates based on titanium,[2] zirconium,[2] , hafnium,[2] rhodium,[3] iridium,[2,5] iron,[4] and ruthenium[1,2,5] have been synthesised and the aim of this project is to characterise the pre-clinical activity of these compounds. Selectivity for hypoxic tumour cells (see above) and drug resistant cell lines will be evaluated and the results of preclinical testing will inform subsequent rounds of synthetic chemistry. The student will gain skills in all aspects of lead compound identification and optimisation.

Project work will involve *organic synthesis* of ligands; *synthetic coordination chemistry*; investigations of the *anticancer behaviour* of using a range of different cancer cell lines and NMR; all aspects of *single crystal X-Ray structure determination*;

References

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