

Faculty of Science - School of Molecular Sciences

Main Supervisor : Prof Murray Baker

Co-supervisor (s) : Prof George Yeoh and PhD student Weihao Zhao

Project title: **Finding a golden solution to cancer**

Group: Mylne Lab - www.mylne.org

Project description:

The projects available are part of a broad research program exploring applications of metal complexes as anti-cancer agents.

Project 1

Project 1 is about using gold complexes as anti-cancer agents. We know that gold in the 1+ oxidation state is "soft" and so it binds strongly to other "soft" atoms, such as selenium. We also know that when cells are treated with certain cationic gold complexes, gold accumulates in the mitochondria within the cells. Moreover, the gold tends to accumulate preferentially in the mitochondria within cancer cells rather than within normal cells. In the mitochondria, the gold is believed to bind to selenium in a critical enzyme called thioredoxin reductase. This binding poisons the enzyme and triggers the process of apoptosis, a type of cell death. Because the gold tends to target mitochondria in cancer cells, the gold compounds have the potential to act as anti-cancer agents.

This project is suitable for students interested in organic chemistry and coordination chemistry. Chemically-inclined students will be synthesizing interesting new gold complexes, to help us learn about the relationships between the structure of the complexes and their biological properties.

This project is also suitable for students interested in cell biology. Biochemically-inclined students can use cell-culture techniques and fluorescence microscopy to study the effects of gold complexes on normal and cancer cell lines. This work will help us understand the fate of these sorts of compounds in cells and learn about their mode of action.

For more information about this project, see: Mageed, Skelton and Baker, Dalton Trans 2017, 46, 7844; Mageed, Baker, et al. Eur J Inorg Chem 2018, 109; Wedlock, Baker, et al., Dalton Trans 2016, 45, 12221; Hickey, Baker, et al., J Am Chem Soc 2008, 130, 12570; Barnard, Baker, et al., Angew Chem Int Ed 2006, 45, 5966; Barnard, Baker, et al., Dalton Trans 2004, 1038; Baker, Williams, et al., Dalton Trans 2001, 111.

Project 2

Project 2 is about using triazacyclohexane complexes as anticancer agents. Triazacyclohexanes are a family of ligands that can easily be synthesized from primary amines and formaldehyde. Metal complexes of triazacyclohexanes are also remarkably easy to synthesize. These complexes have interesting prospects as anti-cancer agents, because they can act as devices to deliver the cytotoxic agent formaldehyde to cancer cells. For example, consider the iron(III) chloride adduct of 1,3,5-trimethyltriazacyclohexane. In this complex, the iron(III) chloride acts as a protecting group for the 1,3,5-trimethyltriazacyclohexane molecule. In biological media at around pH 7, the complex should be stable, but at lower pH (as found in certain types of cancer cells or tumours) the iron(III) chloride group will be cleaved off. The free 1,3,5-trimethyltriazacyclohexane molecule will then decompose, to release formaldehyde, which should kill the cancer cell.

This project is suitable for students interested in organic chemistry and coordination chemistry. Chemically-inclined students will be synthesizing interesting new triazacyclohexane complexes, to help us learn about the relationships between their structures and their biological properties.

This project is also suitable for students interested in cell biology. Biochemically-inclined students can use cell-culture techniques and fluorescence microscopy to study the effects of triazacyclohexane complexes on cells. This will be the first investigation of the biological activity of triazacyclohexane complexes.

For more information about this project, see: Armanasco, Baker, et al. Dalton Trans 1998, 1145; D H Brown, PhD Thesis, The University of Western Australia, 2001; A J Barnes, PhD Thesis, The University of Western Australia, 2011; Baker et al. Inorg. Chem 1999, 38, 4515. /

Required skills, knowledge or experience:

Either: (1) Experience in laboratory organic chemistry, interpretation of infrared and NMR spectra, mass spectra (for a project that is primarily about synthesis of ligands and metal complexes); or (2) Experience at cell culture techniques and microscopy of cells (for a project about evaluating the effects of metal complexes on cells).

Keywords: organic chemistry, cancer, organometallic chemistry, medicinal chemistry

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Project done on Crawley campus: Yes

Total number of project(s)
offered by supervisor: 2

Total number of place(s)
available with supervisor: 4