Overview

The Centre for Medicinal Chemistry (CMC), established in November 2006, comprises 14 academic staff, 5 postdoctoral fellows and more than 30 PhD and Masters students with expertise and research strengths in:

- Organic and Inorganic chemical synthesis
- Drug design and development
- Lipid structure and function
- Mass spectrometry
- Nuclear Magnetic resonance (NMR)
- Natural Products Chemistry
- Traditional medicines
- Bioactivity and Toxicology
- Preclinical development of anti-cancer drugs and formulations
- Reaction mechanisms and new reagents and catalysts
- Analytical chemistry
- Synchrotron radiation spectroscopic analysis

The CMC is concerned with the fundamental structure and function of molecules in living systems. A key component of this research is focussed on the discovery of bioactive molecules from Nature such as plant and marine metabolites and even traditional medicines. The discovery of new molecular scaffolds and the elucidation of the mechanism of action provide unique starting points for rational drug design that can then be augmented by powerful computational models. CMC researchers have strong track records of developing new compounds that through partnership with industry have been further developed and tested in the fight against diseases, including pathological bacterial infections and cancer. CMC staff members are also developing new chemical reagents and catalysts as fundamental tools for new drug discovery and development.

CMC is affiliated with the School of Chemistry and also includes members from allied disciplines including Health and Medical sciences. The School of Chemistry supports state-of-the-art mass spectrometry and nuclear magnetic resonance facilities that, along with excellent protein crystallography and molecular modelling facilities, underpin the elucidation of the structure and function of molecules. The School also has well equipped synthetic chemistry laboratories. CMC supports an extensive network of collaborations with other academic researchers both nationally and internationally and has a proven track record of working effectively with industry partners.

In the recent Australian Government Research Quality exercise, CMC rated at and above world standard in the areas of Medicinal Chemistry, Organic Chemistry, Analytical Chemistry and Physical Chemistry, ensuring the continuing reputation of the School of Chemistry at Wollongong as being one of the best chemistry research units in the country with outstanding national and international success at producing quality and significant research.

Key people

The Director of CMC, Prof. Stephen Pyne, has more than 20 years experience in working with the pharmaceutical drug company, Johnson & Johnson (Research) in new drug discovery and development.

Prof. S. Pyne, A/Prof. P. Keller, and Emer. Prof. J. Bremner have more than 12 years experience working with the Australian drug discovery company, Avexa, in the development of new antibacterial drugs against resistant strains of pathological bacteria, including methicillin resistant Staphylococcus aureus (MRSA) or drug resistant “Golden Staph”. This work resulted in the licensing of some of these UOW discovered compounds to the Swiss pharmaceutical development company Valevia, to take these compounds to clinical trials for topical applications for nasal bacterial infections, wounds (burns) and catheter-related infections.

Other approaches for identifying drugs against resistant strains of pathological bacteria are being developed by Dr. Kelso, including those to combat biofilm infections (e.g. P. aeruginosa lung infections). Dr. Hyland is working on porphyrin dimers with the Menzies Research Institute to investigate the mechanism of bacterial uptake of iron to provide information for the synthesis of novel antibiotics. These ongoing projects have been supported by the CMC, Avexa, the NHMRC and the NIH (USA).

Prof. S. Blanksby and Dr. T. Mitchell have been at the forefront of lipidomic research within Australia over the last 10 years. Together this team has published over 30 papers and been awarded over $1,400,000 in competitively awarded funding in the field of lipid
analysis, structure and function. Their work has led to two patents on a novel lipid analytical technology known as Ozone-Induced Dissociation, which is now licensed to the international mass spectrometry company AB Sciex (Toronto, Canada). Research undertaken by Blanksby and Mitchell has provided significant insights into the composition and molecular structure of lipids in the human ocular lens. Critical molecular-level changes associated with age have been identified providing new clues as to the causes of age-related conditions such as cataract and presbyopia.

Dr. D. Jolley and Dr. C. Dillon are unravelling the cellular mechanisms of toxicity through the development of new analytical approaches, bioactivity assays, biomarker discovery, and state-of-the-art synchrotron metal speciation and molecular imaging. A/Prof. S. Ralph and Dr C. Dillon are designing and studying metal containing anti-cancer drugs (arsenic anti-leukemia drugs and platinum intercalators) and anti-inflammatory drugs (bismuth and gold complexes). Approaches include mass spectrometry studies of interactions with key proteins, X-ray absorption spectroscopic analysis of intracellular interactions, and X-ray fluorescence imaging to confirm interactions with targets, such as DNA.

The discovery of new chemical entities for new drug discovery from traditional medical plants is actively being pursued by Prof. S. Pyne, A/Prof. P. Keller, Dr. D. Skropeta and Dr. C. Hyland.

In addition Prof. Pyne, A/Prof P. Keller, Dr M. Kelso, Dr. C. Richardson, Dr. D. Skropeta and Dr. C. Hyland are pioneering methods for the chemical synthesis of new drugs and novel chemical scaffolds for new drug discovery.

**Research Themes**

The basic research and discovery projects of CMC can be categorised into:

1. Molecular Discovery: from traditional medicines, natural products and lipids and metabolites;
2. Molecular Design: drug design, molecular synthesis, inorganic frameworks and catalysis and reaction mechanisms and reagents;

The results of these discoveries and innovations can, and in some cases already have, lead to:

- International and Industry partnerships;
- Drug and therapeutic discovery; and
- Development of Advanced Analytic technologies and contract research.

**Key Projects**

- Development of new anti-microbial agents, specifically against drug resistant pathological bacteria and viruses.
- The discovery of new chemical entities (small molecules) from traditional medicines for new drug development.
- Development of new methods and catalysts for the chemical synthesis of bioactive molecules.
- The discovery of novel chemical scaffolds for new drug development.
- New laser and mass spectrometry-based tools for comprehensive structural elucidation of lipids and their biomolecular interactions.
- The development of ozone induced dissociation for lipidomic workflows.
- Microbial infestation of pre-painted steel building materials: chemical & microbial characterization, model development and control strategies.
- Synthesis of novel porphyrins for the investigation of iron uptake by bacteria.
- Development of new antiviral agents.
- Design of metal complexes that selectively bind to DNA.
- Development of new formulations and medicinal agents for cancer treatment.
- Development of selective arsenic anti-leukaemia drugs.
- Investigating the reactivity of metallo drugs towards biomolecules.
- New approaches to identify the toxicity of environmental pollution.
- Unravelling the molecular mechanisms of metal toxicity.
- Identifying tear lipids, their deposition onto contact lenses and their role in the development of dry eye.
- Understanding lipid alterations in the ageing human lens and their role in the development of cataract and presbyopia.
- Identify alterations in lipid-protein interactions in the ageing brain.
- Design, synthesis and investigation of metal complexes as radiotherapeutics and imaging agents.
- Design and synthesis of multi-action antimicrobial and anti-cancer hybrid drugs and prodrugs.

**Key Partnerships**

CMC have national and international collaborations with scientists in antibacterial discovery (Avexa, Harvard Medical School, Northeastern University, Monash University, University of NSW, University of WA, Menzies Research Institute, University of Southampton), natural product chemistry discovery (Universities in Australia, Thailand, Indonesia and Malaysia), organic synthesis (University of Tasmania, California State University), anti-viral discovery (University of NSW, Emerging Viruses and Inflammation Research Group, Institute for Glycomics, Griffith University and University of Erlangen). Partnerships with AB Sciex (Toronto, Canada) an international mass spectrometry company who have licensed the Ozone Induced Dissociation patent and currently support an ARC Linkage Grant.

Investigation of lipids on contact lenses has led to partnerships with Allergan (Irvine, California), a multi-national health care company who manufacture lens care and dry eye solutions. In the analytical chemistry and environmental toxicology area we have collaborations with CSIRO, Institut national de la recherché scientifique (INRS) Quebec, Le Centre national de la recherché scientifique (CNRS) France and the University of Lancaster, UK. In the area of synchrotron research, collaborations are ongoing with research staff at the Australian Synchrotron, Advanced Photon Source (APS), Chicago; the Australian National Beamline Facility (ANBF), Tsukuba, Japan; Monash University and the University of Adelaide.
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