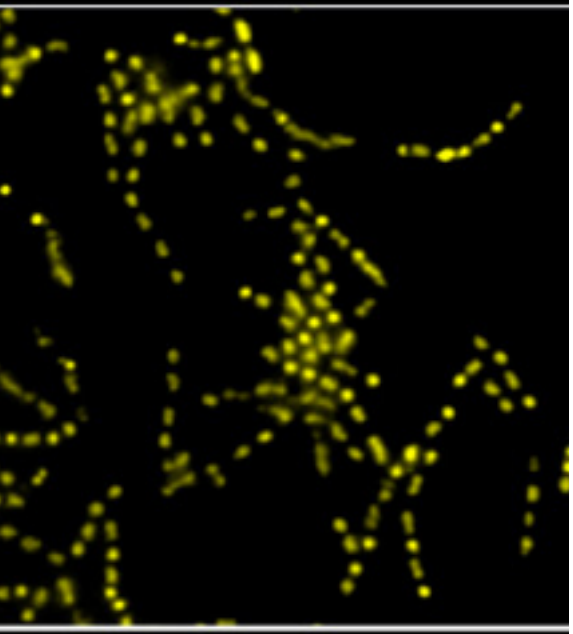
PRIORITY RESEARCH CENTRE FOR CHEMICAL BIOLOGY



THE UNIVERSITY OF NEWCASTLE AUSTRALIA

OVERVIEW

Chemical biology is an emerging area recognising the need to synergistically integrate chemistry, biology and medicine to accelerate drug development. All major therapeutic breakthroughs are underpinned by advances in our understanding of the **chemistry** and **biology** of basic cellular and molecular mechanisms of biological processes.

Currently, Medical Research Institutes and the NHMRC rely heavily on molecular biology techniques to identify biological targets and build understanding of the biological systems responsible for a particular disease. These methods (knock outs, mutations, etc) are powerful in model organisms such as *Escherichia coli*, *Saccharomyces cerevisiae* and *Drosophila melanogaster*. However, mammals represent a significant experimental challenge to molecular biology approaches with slower rates of reproduction, large sizes and large genomes. The chemical biology approach avoids these problems by studying the effect of small molecules on the proteome rather than the genome.

Chemical biology uses a molecular toolkit to interrogate biological systems; its goal is to use small-molecule probes to discover specific biomolecular targets and pathways that are modulated by the particular compound. Small molecules, in contrast to classical genetics where manipulation occurs at the DNA level, typically modulate protein function by inducing conformational changes or by competing for endogenous protein-ligand, protein-nucleic acid or protein-protein interaction sites, resulting in altered activity.

This allows temporal study of signalling pathways and the ability to wash-out probes to study reversible inhibition.

Access to focused, diverse and biologically relevant **small-molecule compound libraries** is essential to the advancement of knowledge in the post-genomic era for interrogation of biological systems (chemical biology). The **chemical optimisation (CO)** of promising small-molecule probes will be starting points (chemical biology and lead identification) for early phase drug discovery (medicinal chemistry). This has obvious commercial implications and we are well placed to exploit these through our collaborators and industry partners.

OBJECTIVES

The Centre for Chemical Biology (CCB) is committed to providing *innovative* therapeutics for the treatment of human disease. By bringing together research teams of international *excellence* from chemistry, biology and medicine we will *unravel* the causes of disease, *identify* crucial biological targets and *pioneer* the rapid development of novel drugs for the fight against disease.

The CCB will be the *central facilitator* of drug development at UoN and our collaborators displaying *leadership* and *research excellence*.

The CCB will:

- provide a supportive forum for career development and enhancement of junior staff across chemistry, biology and biomedical sciences

Provide biomedical researchers with:

- a molecular 'toolkit' to unravel the intricacies of biological processes;
- a 'lab to clinic' drug development pipeline to clinical setting.

EXTERNAL COLLABORATORS

Prof David Jans, Head Nuclear Signalling, Biochemistry Dept, Monash University

Dr Gary Hime & Prof Minx Fuller, Dept of Anatomy and Cell Biology, The University of Melbourne & Stanford University, USA

Prof Phillip J Robinson, The Children's Medical Institute and University of Sydney

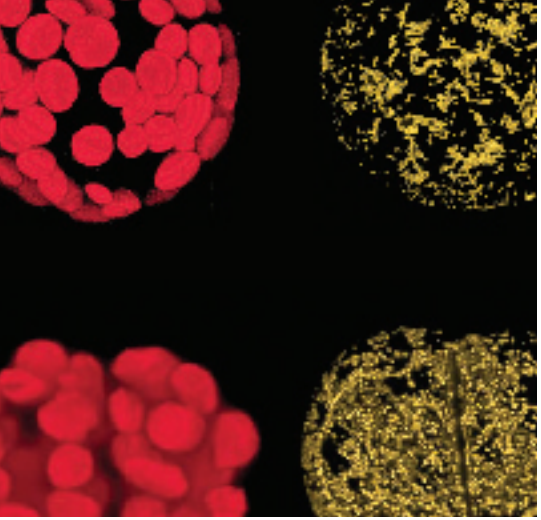
Prof Wah Chiu, Director National Centre for Macromolecular Imaging, Baylor College of Medicine, Houston, TX, USA

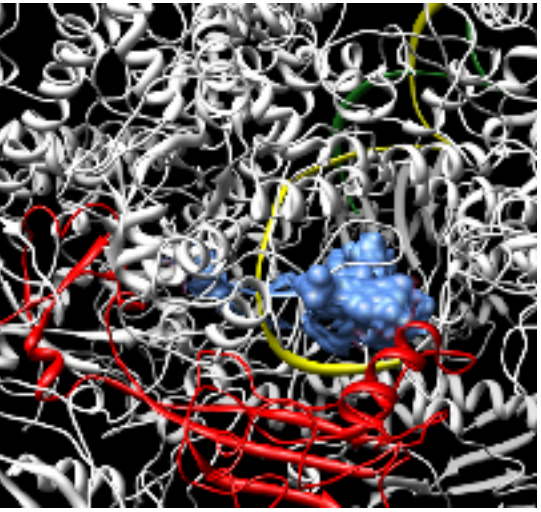
Prof Jan Lowe FRS, Head of Structural Studies Division, MRC-LMB, University of Cambridge, UK

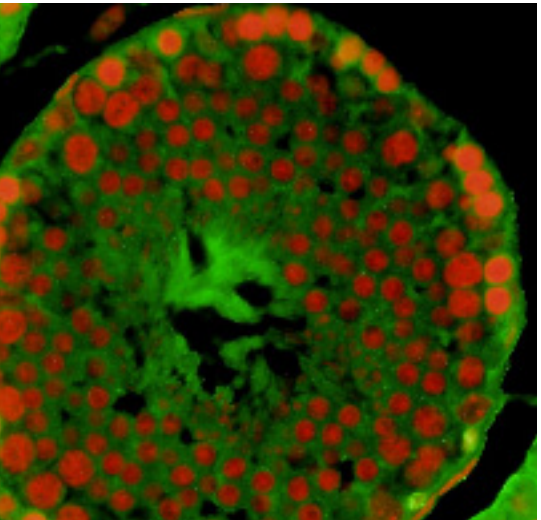
Prof Rick Lewis, Professor of Structural Biology, ICAMB, University of Newcastle, UK

Prof Volker Hauke, Professor of Biochemistry, Freie Universitaet, Berlin

BaSysBio European Union 6th framework consortium







FACULTY OF SCIENCE AND INFORMATION TECHNOLOGY

THE UNIVERSITY OF NEWCASTLE AUSTRALIA

RESEARCH SUPPORT

The CCB has attracted considerable external support from the:

- Australian Research Council (Discovery Project, Linkage Project, Infrastructure, Special Research Centre and International schemes)
- National Health and Medical Research Council (Project, Development and Equipment schemes)
- Cancer Council NSW
- Ramaciotti Foundation
- Australian Cancer Research Foundation
- European Union 6th Framework
- Department of Education and Science Training (DEST: International Science Linkage Program)

EXAMPLES OF CURRENT PROJECTS

Prof Adam McCluskey: ***The dynamin modulators platform*** which has multiple disease indications with epilepsy and cancer of particular note.

Prof Eileen McLaughlin: Fertility control through development of one-shot sterilants for use in domesticated pets, livestock and feral animals.

A/Prof Peter Lewis: Exploitation of bacterial transcription initiation as a target for new antimicrobials.

RESEARCH OUTCOMES

Members of the CCB have been successful in obtaining research funding from national and international sources. Their research is acknowledged as world leading. Key figures are involved in major world initiatives in the areas of anti-infectives, reproductive science and drug discovery and development. Our outcomes are many, but are exemplified by our interactions with the European Network, ARC Special Research Centres and our commercialisation and reagent sales via Ascent Scientific.

RESEARCH TOPICS

- Synthetic Medicinal Chemistry and Chemical Biology of dynamin GTPase
- Application of flow chemistry technologies to drug discovery and development
- Gametogenesis: molecular and cellular characteristics of germ cell development
- Molecular microbiology of transcription, DNA replication, segregation and cell division

GROUP MEMBERS

Prof Adam McCluskey
Prof Eileen McLaughlin
A/Prof Peter Lewis
Prof Ray Rose
Dr Ian Grainge
Dr Shaun Roman
Dr Brett Nixon
Dr Jennette Sakoff
Dr Warwick Belcher
Prof Chris Grof
Dr Nicole Verrils
Prof Hubert Hondermark
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