



THE UNIVERSITY
OF QUEENSLAND
AUSTRALIA

School of
Biomedical Sciences

HONOURS APPLICATION AND ENROLMENT GUIDE

2018



Bachelor of Science
(Hons) Biomedical
Sciences

Bachelor of Biomedical
Sciences (Hons)

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This handbook is intended to give information on applying and enrolling in the Honours program in the School of Biomedical Sciences. This information is advisory and does not in any way supersede The University of Queensland Calendar & electronic course profile.

ENROLMENT CHECKLIST

1. Check if you meet entry requirements. [BSc graduates](#) can check their eligibility to enrol in honours by reading the program rules and requirements [here](#). Current [BBiomedSc \(Hons\)](#) students can check their eligibility to enrol in honours by reading the program rules and requirements [here](#) for their 4 year degree. [BBiomedSc graduates](#) can check their eligibility to enrol in honours by reading the program rules and requirements [here](#) for the 1 year degree. In some circumstances, and subject to the approval of the Head of School and Executive Dean, BSc and BBiomedSci graduates who do not fulfil the above requirements may be permitted to enter the Honours program if they have a high GPA in other science courses and if their proposed project fits well with their background
2. Choose a research area you would like to work in and discuss potential projects with a range of possible supervisors. Research profiles of our academics can be found on the SBMS web site (<https://biomedical-sciences.uq.edu.au/research/programs>) and UQ websites. You can also find a list of Honours projects at: <https://biomedical-sciences.uq.edu.au/study/honours> and at the end of this booklet.
3. Select supervisor(s) and project and ensure your supervisor has agreed to enrolment.
4. [Return completed application](#) to the SBMS Honours administrator (Email: sbms.hons@uq.edu.au or Room 312, Skerman Building (#65)).

Important: All BSc Honours applicants, BBiomedSc Honours 1 year degree applicants and new to UQ students must also complete the [UQ Online application form](#)

Deadline: 8 December 2017 for commencement in Semester 1 2018
18 June 2018 for commencement in Semester 2 2018

5. We check that you meet the GPA requirements and application details.
 6. You will receive notification advising which courses you need to add in mySI-net. You need to enrol in these courses before the census date (census dates are indicated on the University calendars). If awaiting results, students are not enrolled until the results are released.
 7. Official starting date for Honours (**can vary by a week**):

First week in February for commencement in Semester 1
Third week in July for commencement in Semester 2
 8. The Honours calendar of events and deadlines will be finalised before commencement of your Honours program. It will be emailed to you as well as posted on the SBMS Honours website (<http://www.uq.edu.au/sbms/honours-program>) and the course Blackboard site.
- *Steps 1-3 should be completed well before the proposed commencement date*

GENERAL INFORMATION

After completing your Bachelor of Science or equivalent degree, Honours will be the most intensive – and for many the first - contact with original research. Through Honours you will experience the different facets of research: the excitement of discovering something new, the satisfaction that comes with being an expert in your chosen field as well as frustrations, problem-solving and communication of your findings. You will be part of a research team, learning from more experienced researchers around you, such as your supervisors and other members of the laboratory.

Whether you consider Honours a stepping stone to a Masters or PhD and onto a career as a researcher, or a vital research experience giving you credibility in science and research-associated careers, you will find the course will add significantly to your training as a Science graduate.

Honours with SBMS

The Honours year with SBMS is a hands-on experience in research and associated skills. This includes the development of technical skills in scientific methodology as well as intellectual skills in experimental design, critical appraisal of scientific literature and assessment of the impact of your original data on current knowledge. Research projects are selected by negotiation between you and supervisor(s) and are reviewed by the SBMS Honours Committee. We encourage you to seek contact with staff members to discuss likely research projects early in your Level 3 studies.

In order to find a supervisor and suitable project we advise you identify research areas you are interested in and approach staff working in these areas. Our staff at the School of Biomedical Sciences research and teach in a wide range of areas from the genomic level through to the structure and function of intact humans and other organisms. We have a strong focus on molecular, cellular and structural biology. Students who want to study physiology will focus their research on how organ systems, tissues, cells and molecules function together; those who concentrate on anatomical studies will investigate how structures are created and how they function whilst pharmacology/toxicology students will research how drugs and toxins modify or affect biological functions.

The School and its associated centres and companies are heavily involved in cutting edge biomedical research and most of our academics have an active research program with projects available for Honours students. More details can be found at <http://www.uq.edu.au/sbms/programs/all>. The research areas of SBMS staff members are grouped under the following programs:

- Therapeutic Development and Translation
- Functional Morphology
- Cellular Signalling and Function
- Innovation in Biomedical Education
- Tissue Injury and Repair
- Brain Development and Function

Collaborative projects may also be available with several University Institutes such as the Queensland Brain Institute (QBI), the Institute for Molecular Bioscience (IMB), The Australian Institute for Bioengineering and Nanotechnology (AIBN), the Diamantina Institute and the National Research Centre for Environmental Toxicology (EnTox). We also participate in projects with the Departments of Medicine and Obstetrics & Gynaecology and the School of Pharmacy. More information about these institutes and centres can be found on their respective UQ websites.

Bachelor of Biotechnology (Drug Design and Development)

Laboratories within SBMS frequently host students who are engaged in the Biotechnology degree program. Details regarding this program and its requirements can be obtained from the following website: <http://scmb.uq.edu.au/biotech>

Information for Students of other Faculties

The School is within the Faculty of Medicine and most of our Honours students are enrolled in either Bachelor of Science or Bachelor of Biomedical Science. However, there are avenues for students enrolled in Medicine, Veterinary Science, Dentistry and other professional courses to undertake research studies with us. Students enrolled in professional courses may obtain more detailed information from their relevant faculty and discuss their interest with the Chair of the Honours committee.

The main focus of this handbook is for Honours in Biomedical Science. Students wishing to pursue similar degrees with us should also contact the faculty in which they are enrolled.

SBMS-Oxford Honours Scholarships

We have established a program with Oxford University (UK), designed to promote learning in the form of special lectures and Honours scholarships for students in the biomedical sciences. For details on applying for one of these competitive fellowships please see the Honours website: (<https://biomedical-sciences.uq.edu.au/study/honours>)

Careers

An Honours degree is the qualification most often required for employment in research positions and industry. Numerous career opportunities await students with backgrounds in biomedical science, where universities and research institutions are the major employers. Many students have opted to study biomedical sciences as a prelude to careers in professional disciplines such as medicine, dentistry and speech therapy. Increasingly an Honours degree is a minimum requirement for entry-level employment in industry.

Candidates who obtain Honours I or Honours IIA may proceed directly to studies for the degree of Doctor of Philosophy (PhD). An Honours IIB is the minimum requirement for entry to the degree of Master of Science (MSc). The path for students aspiring to careers as academics or research scientists is usually the PhD.

HONOURS ENROLMENT REQUIREMENTS

Entry Criteria

For entry into Honours, SBMS requires a satisfactory background in Level 2 and 3 relevant courses. For BSc and BBiomedSc graduates, the minimum requirement is a GPA of at least 4.5 in the “most relevant 8 units of third level (or advanced) study”. In addition, an overall GPA of 4 (minimum) for the BSc degree (or for the first three years of the BBiomedSc 4 year degree) is required. In some circumstances, and subject to the approval of the Head of School and Executive Dean, BSc graduates and BBiomedSc students who do not fulfil the above requirements may be permitted to enter the Honours program if they have a high GPA in other science courses and if their proposed project fits well with their background.

Commencement of Study

Studies may commence on the following dates: (slight variations are possible if there is any change in the UQ Academic Year).

1st Semester enrolments (can vary by a week)

Application Due: Friday 8th December 2017

Start Date: First week in February 2018 (check the eCP for confirmed date)

2nd Semester enrolments (can vary by a week)

Application Due: Monday 18th June 2018

Start Date: Third week in July 2018 (check the eCP for confirmed date)

PROGRAM DESCRIPTION

General Information

- The Honours program consists of a research project with associated research proposal, research report, seminars, journal clubs and evaluation of laboratory performance.
- It is very important for students and supervisors to be aware that the research report represents the bulk of the year's work and is therefore the primary indicator of the level of the student's research and communication skills.
- On receiving the application, the Honours committee will evaluate the candidate and the project descriptions. Any questions or concerns will be discussed with the supervisor or candidate before approval is given. Any subsequent major changes to the research project throughout the Honours year will require approval from the SBMS Honours Committee chairperson.

Assessment Items

- **Journal Club:** This component involves the presentation and contribution to discussion of a research paper amongst your peers.
- **Research Proposal:** Submitted as a document of 4000 words (maximum) outlining and justifying the proposed project and introducing the background literature.
- **Proposal Seminar:** Students will give a 10 minute oral presentation (with 5 minutes of questions) on the background and rationale for their study. This will include a statement of aims and hypotheses along with research methods to be used.
- **Research Report:** Submitted as a document of 8000 words (maximum) describing and critically appraising the research work undertaken during the Honours year.
- **Seminar Diary:** Students will attend at least 12 seminars (these can be external to SBMS) given by academic/research staff, invited speakers or PhD students (M1 confirmation only).
- **Supervisor's Report:** Supervisors will provide a report based on the student's performance over the course of the Honours year.
- **Final Research Seminar:** This component includes the final seminar presented at the end of the year (15 minute talk & 10 minutes for questions).

Assessment Marking

- Two examiners are invited by the SBMS Honours Committee to assess the research proposal and research report. Their feedback will be made available to the students, although examiners have the option of remaining anonymous. If appropriate, examiners may be from another department or institution.

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- Seminars are examined by two members of the SBMS Honours Committee or appropriate proxies.
- Templates of marking sheets used by examiners for the assessment of items of work can be found in the learning resources section of the Blackboard site.
- Students will be informed of the grading of any item's assessment at the end of each semester. Students should direct any queries in relation to marks to the Honours Coordinators or Committee.
- Final results are recommended by the SBMS Honours Committee to the Head of School, who advises the Executive Dean. The award of various classes of Honours is also made by the Head of School and relevant Executive Dean.
- Criteria marking sheets for all Honours assessment items will be posted on Blackboard sites for the courses.

Assessment Summary BSc and BBiomedSc Honours

Subject Code	Subject Title	Credit Unit
BIOM6191 or BIOM6192	Research Project in Biomedical Sciences	16
BIOM6501 or BIOM6502	Research Project in Biomedical Sciences	16

Assessment Task	Weighting
<i>Journal</i> Journal Club Presentation and Participation	5%
<i>Seminar</i> Research Proposal Seminar	5%
<i>Report</i> Research Proposal	10%*
<i>Diary</i> Seminar Diary	Mandatory
<i>Report</i> Research Report	55%*
<i>Report</i> Supervisor's Report	5%
<i>Seminar</i> Final Research Seminar	20%

* *submission of final version via Turnitin*

HOW TO FIND AN HONOURS SUPERVISOR/PROJECT

- Decide what broad research field you are interested in
 - Also consider what techniques you would like to learn
- Find a supervisor in that field
 - Lecturer or Researcher
 - Are they actively publishing?
 - Do they have other students/staff (to provide you with extra support)?
- Contact your potential supervisor
 - Do not send a generic email
 - Be familiar with the Supervisor's work
 - Tell them why you want to do an Honours project in **their** lab
 - Contact them early – i.e. NOW!!
 - Meet with them in person – will they be supervising you day-to-day or will it be a post-doc? If it is the latter then ask to meet the post-doc.

WHERE DO I LOOK FOR A SUPERVISOR/PROJECT?

The following pages have information for specific Honours projects that have been submitted by potential supervisors. This is not an exhaustive list and you might also be able to find a project by contacting a researcher directly. Information and contact details for researchers can typically be found on School and Institute web sites, some of which are listed below:

School of Biomedical Science - <https://biomedical-sciences.uq.edu.au/research/programs>

School of Clinical Medicine - <https://medicine-program.uq.edu.au/school-of-clinical-medicine/research>

Diamantina Institute - <http://www.di.uq.edu.au/honours>

Mater Research Institute – <http://www.materresearch.org.au/students.aspx>

UQ Centre for Clinical Research - <https://clinical-research.centre.uq.edu.au/honours>

UQ Child Health Research Centre - <https://child-health-research.centre.uq.edu.au/study-chrc>

Queensland Brain Institute - <https://qbi.uq.edu.au/study/honours>

Institute for Molecular Biosciences - <http://postgraduate.imb.uq.edu.au>

QIMR-Berghofer Medical Research Institute - http://www.qimrberghofer.edu.au/student_projects/

The Critical Care Research Group - Prince Charles Hospital - <http://ccrg.org.au/>



Professor Elizabeth Coulson

School of Biomedical Sciences
Neuroscience

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Neurotrophin Biology Lab

My lab is currently focusing on the reasons why cholinergic neurons of the basal forebrain die in Alzheimer's disease, what contribution their loss makes to cognitive decline and whether manipulating neurotrophic signalling (NGF, BDNF, TrkA/B, p75) can protect or restore cognitive function, and what role the neurotrophins play in the normal function of these neurons. Possible projects include:

- Project 1: The role of cleavage of p75 neurotrophin receptor in neurodegeneration (cell biology and/or mouse studies)
- Project 2: The role of neurotrophins in regulating the synaptic function of cholinergic basal forebrain neurons (mouse studies:, mouse surgery for in vivo genetic manipulation, mouse behaviour, and potentially mouse MRI, or slice electrophysiology)
- Project 3: Studying basal forebrain function in Alzheimer's disease and sleep apnea (cell signalling pathways OR human MRI and PET image analysis)
- Project 4: Developing optimised peptides for treating neurotrophic dysfunction in neurodegenerative disease (biochemistry)

Techniques you will learn in our group may include: histology, microscopy, cell biology, biochemistry and potentially, advanced imaging analysis methods.



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Neuroscience

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Millard Lab – Molecular mechanisms for wiring the brain

The overall goal of the Millard lab is to understand how specificity is generated in the brain. This problem is best exemplified by considering that 100 trillion synapses are generated and maintained in the human brain using a toolkit of only 20,000 genes. We have been approaching this problem using molecular genetics in the fruit fly, *Drosophila melanogaster*. Most projects in the lab revolve around how a broadly expressed cell surface protein, called Down syndrome cell adhesion molecule 2 (Dscam2), is able to perform specific functions in different neurons. We are also interested in mechanisms of neurological disease, particularly those that involve changes in synaptic function.

Project 1 - Motor Neuron Disease: Insights from *Drosophila*

Through a collaboration with Prof Naomi Wray's Centre at the IMB, we are using *Drosophila* to validate and characterise candidate genes for sporadic motor neuron disease. We are screening a list of genes generated through human GWAS studies for phenotypes in flies and have already validated several genes. Once candidates are validated, we can use CRISPR to modify these genes in order to assess how they function. Several projects are available.

Project 2 - Dscam2 synaptic functions

We have identified a synaptic role for Dscam2 at the fly neuromuscular junction and several projects centred around the molecular mechanisms involved are available.

Project 3 - Dscam2 localisation

Dscam2 gets trafficked exclusively to dendrites in some cells. We are trying to understand how this happens and one project in the lab is testing whether one of the four distinct juxtamembrane isoforms is responsible. Projects would involve analysing the localisation of transgenes expressing these different isoforms and using qRT-PCR to determine whether they are expressed in a cell-specific manner.

Techniques: Molecular biology, genetics, immunohistochemistry, microscopy



Associate Professor Michael Piper

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Neuroscience

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Neural Stem Cells in Development and Disease

We use the cortex, cerebellum and spinal cord of the developing and adult mouse as model systems to elucidate the biology of neural stem cells within the brain. Ultimately, we hope to define the genes that drive the differentiation of neural progenitor cells into either neurons or glia, work that will provide insights into neurodevelopmental disorders, ageing and cancer. Dr. Piper currently has funding from the ARC (Discovery Project grant; 2016-2018) to investigate how neural stem cell quiescence in the adult brain is coordinated. This work will provide pivotal insights into how ongoing neurogenesis in the adult brain is regulated, and the behavioural consequences of deficits to this process. Dr. Piper is funded also by the Cancer Council Queensland (2016-2017) to investigate the transcriptional regulation of stem cell biology within the developing cerebellum and in medulloblastoma, a cerebellar tumour that is the most common malignant paediatric brain cancer. We envisage that this research will provide important insights into the control of neural stem cell differentiation within the cerebellum, as well as providing avenues that will lead to improved treatment for this devastating disorder.

Project 1

We are currently investigating the role of transcription factors in cerebellar development and disease. We have an Honours Project available for 2018 that will investigate how NFIX mediates stem cell differentiation within the postnatal cerebellum.

Techniques you will learn in our group may include:

Immunohistochemistry

Microscopy

qPCR

In situ hybridisation

Histology



Associate Professor Trent Woodruff

School of Biomedical Sciences
Pharmacology, Neuroscience

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Neuroinflammation Laboratory

Our laboratory focuses on the role of inflammation and the immune system in neurodegeneration, and the identification of novel drug targets to slow progressive brain disease in humans. Our projects encompass the identification and development of novel drugs, to the testing of novel drugs in animal models of neurodegenerative disease, and the exploration of novel inflammatory pathways in diseased patients. In doing so, we hope to accelerate the clinical translation of our findings and novel drugs candidates to clinical trials.

Project 1

Identification of new immune system contributors to neurodegenerative disease progression

Project 2

Novel therapeutic strategies to treat motor neuron disease

Project 3

Pharmacological characterisation of novel anti-inflammatory compounds in cell-based models

Techniques you will learn in our group may include: pharmacological profiling (cellular signalling assays), animal behaviour and drug testing (cognitive and motor testing), immune cell profiling (flow cytometry), neuropathology (immunohistochemistry) and molecular analysis (qPCR, western blotting).



Dr John Lee

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Pharmacology, Neuroscience

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Our laboratory focuses on the role of inflammation and the immune system and its involvement in stress and metabolism in motor neuron disease (MND). Our projects encompass the utilisation of genetically modified mice and identification and development of novel drugs to investigate the role of inflammation and its modulation of stress and metabolism in disease progression of MND. In doing so, we hope to have better understanding of underlying disease mechanism of MND and accelerate the clinical translation of our findings and novel drugs candidates to clinical trials.

Project 1

Understanding the role of immune system in stress response and how this contributes to disease progression of motor neuron disease

Project 2

Understanding the role of immune system in metabolism and how this contributes to disease progression of motor neuron disease

Techniques you will learn in our group may include: animal behaviour and drug testing (cognitive and motor testing), immune cell profiling (flow cytometry), neuropathology (immunohistochemistry) and molecular analysis (ELISA, qPCR, western blotting).



Dr Richard Clark

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Pharmacology

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Peptide Chemical Biology Lab

We are interested in studying the role of naturally occurring bioactive peptides in a broad range of human diseases. Peptides have a diverse range of functions in human biology including acting as hormones, neuro-regulators and in the protection against pathogens. Our work in this area is focused on understanding the molecular mechanism that these peptide use to elicit a biological response with the hope of using this knowledge to develop new drug leads.

Project 1: A new GPCR target for conotoxins

This project aims to characterise the interaction between conotoxins and the GABA(B) receptor, discover new conotoxins that target this receptor and design new ligands for related receptors that are also involved in nerve signalling. This involves undertaking structure/activity studies, screening venom extracts, mechanistic studies using receptor constructs and assays and functional studies in cell-based systems and native tissue. This will provide us with an intimate understanding of the effect of conotoxins on this novel receptor that will underpin the future development of new drug leads for treating neurological diseases including pain, anxiety, depression, epilepsy and drug addiction.

Project 2: Discovery and development of peptides for the treatment of inflammation and infection

This project involves the discovery of novel peptides from nature that modulate the immune response to prevent inflammation or infection by pathogens. Using peptide engineering we can modify these leads to understand how they mechanism of action, improve their drug-like properties, and develop therapies that are targeted to one location in the body.

Project 3: Discovery, synthesis and characterization of novel antimicrobial peptides from insects

Increasing pathogen resistance against commonly used antibacterial drugs is an escalating health threat and there is an urgent need for novel lead molecules to target these organisms. Insects, making up ~80% of all living organisms, are populating a diverse range of ecological spaces and thus have evolved a complex immune system involving numerous antimicrobial peptides. The project seeks to discover novel bioactive peptides from ant species using state-of-the-art techniques such as transcriptome mining combined with mass spectrometry based peptidomics. Solid phase peptide synthesis will be used to generate sufficient amounts of peptides for bioactivity studies and structural characterization. This project is led by Dr Johannes Koehbach

Techniques you will learn in our group may include: Solid phase peptide synthesis, High Performance Liquid Chromatography (HPLC), NMR Spectroscopy, Mass Spectrometry, Cell culture and cell-based assays, Compound stability assays.



Dr Lisa Kaminskas

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Targeted Drug Delivery Lab/Pharmaceutical characterisation of nanoparticles as novel drug delivery systems

Nanoparticles are increasingly being used as drug delivery systems to improve the pharmaceutical behaviour of small molecule drugs, particularly toxic anticancer drugs. They are being explored as delivery systems that can either be given as intravenous or subcutaneous injections, or via inhalation into the lungs to improve the treatment of local lung-resident diseases. This project (several available) will aim to characterise the pharmacokinetics of novel nanoparticle based drug delivery systems in rodent models.

Techniques you will learn in our group may include: Surgical microvessel cannulations in rats, pharmacokinetic analysis, cell culture, in vitro and in vivo imaging techniques.



Dr Richard Gordon

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Pharmacology and Translational Neuroscience

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Drug Repurposing & Translational Neuroscience

Our group is focused on identifying and validating novel therapeutic targets to slow progressive neurodegeneration in Parkinson's and other brain diseases. We use a multidisciplinary approach to discover novel targets that are amenable to therapeutic intervention with new and repurposed drugs. We have recently identified promising new therapeutic targets for Parkinson's disease, which can be targeted by repurposing drugs that are currently approved to treat other diseases. We utilise the most relevant preclinical animal and cellular models of neurodegeneration, as well as *ex vivo* patient studies to evaluate the effectiveness of our prioritised therapeutics. These preclinical efficacy studies will provide key mechanistic and therapeutic evidence to support the rapid clinical translation of these drugs as novel disease-modifying treatments for progressive neurodegeneration.

Project Description 1

Novel targets for therapeutic intervention in Parkinson's disease

Project Description 2

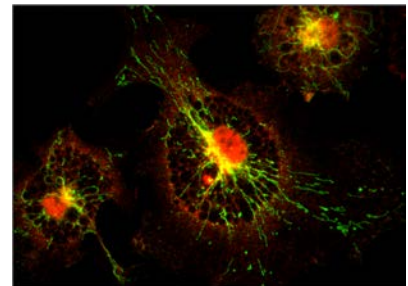
Therapeutic switching of licensed oncology drugs to target progressive neurodegeneration

Project Description 3

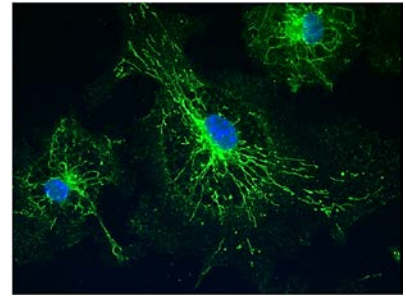
Targeting chronic immune activation and neuroinflammation in Parkinson's disease

Techniques you will learn in our group may include:

- Primary mammalian cell culture of isolated brain cells
- Animal models of neurodegenerative disease
- Drug efficacy testing in CNS models using behavioural phenotyping studies
- Neurochemistry and neurotransmitter analyses



- Pharmacokinetic studies with therapeutic drugs
- Gene and protein expression analyses (qPCR and western blotting)
- Immune activation assays
- Immunocytochemistry and immunohistochemistry
- Confocal microscopy and advanced imaging





Dr Lachlan Rash

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Ion Channel Pharmacology

Given the crucial role of ion channels in normal physiology, many venomous predators (spiders, scorpions, sea anemones, wasps etc.) have evolved libraries of molecules that potently interfere with ion channel function in order to rapidly paralyse prey. The Ion Channel Pharmacology lab uses animal venoms as well as man-made drugs to help understand the function and modulation of various ion channels in health and disease. We have a particular focus on acid-sensing ion channels and voltage-gated sodium channels and their role in pain, inflammation and neurological disorders such as stroke and spinal cord injury. The broad research fields of the group cover pharmacology, physiology, biochemistry and toxinology.

Project 1: Characterisation of novel voltage-gated sodium channel (Nav) modulators from spider venoms and their use to gain structural insights into Nav channels.

Project 2: Venom peptides and herbal medicines as tools to study acid-sensing ion channels structure and molecular function.

Project 3: Biological and pathological roles of acid-sensing ion channel. Pathological conditions of interest can include neurogenic inflammation, ischemia, tumors, neurodegeneration.

Techniques you will learn in our group may include: electrophysiology (*Xenopus* oocytes), high-performance liquid chromatography, mass spectrometry, molecular biology, peptide and protein production & mutagenesis, cell culture/assays, organ bath assays.



Dr Dominic Ng

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Cancer and/or Cell Signalling

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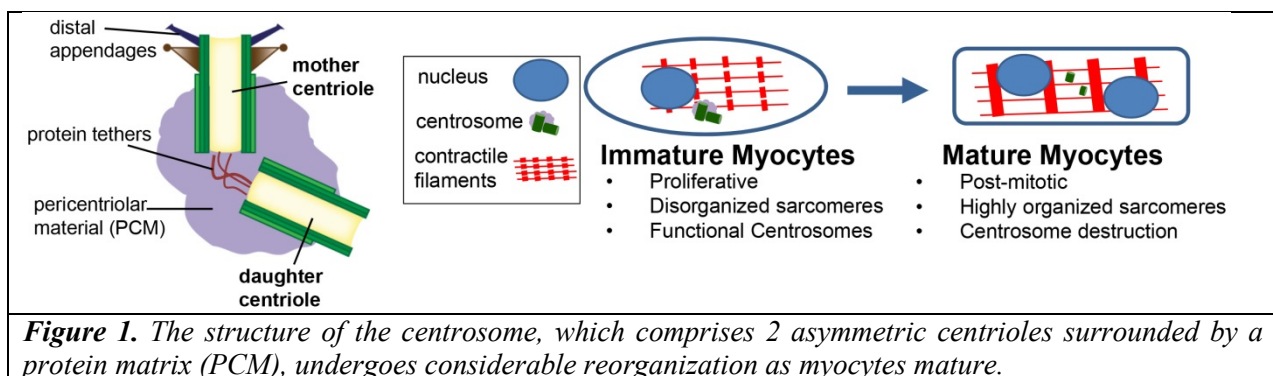
Web: <https://biomedical-sciences.uq.edu.au/research/labs/kinase-biology>

Laboratory for Kinase Biology: Molecular and functional characterization of kinase signalling pathways.

Our research is focused on signal transduction pathways that are required for normal human development and that are dysfunctional in disease states. In particular, we are interested in the regulation and function of protein kinases (enzymes that mediate phosphorylation reactions) that control key cellular process including proliferation, differentiation and cell death. The human genome encodes over 500 kinases and pseudokinases (kinome) but the vast majority of these are poorly characterized. Honours projects in the Ng lab will contribute to fundamental research to understand how the substrate selectivity, subcellular distribution and functional pleiotrophy of kinases are determined and the effect of targeting kinases for therapy in animal and cellular models of human disease including cardiovascular, neurological and oncological conditions.

Project 1: Are centrosomes involved in making mature myocytes?

Centrosomes are small organelles that co-ordinate kinase signalling and cytoskeletal organization in mammalian cells. There is increasing appreciation for the contribution of centrosomes in cell fate specification and the structural reorganization of the centrosome in many somatic cell types including myocytes co-incide with their differentiation (Figure 1). In this project, you will investigate the role of dynamic centrosome reorganization in myocyte differentiation, maturation and terminal differentiation. A secondary objective would be to define the contribution of centrosomal-associated kinases in myocyte differentiation. This study will provide insights into the molecular control of the postmitotic state of myocytes and address a long-standing question of whether these processes can be manipulated for cellular regeneration and tissue engineering purposes. The work will utilize immortalized cell lines, primary myocyte cultures and human stem-cell derived myocytes as experimental models and is performed in collaboration with James Hudson's Laboratory for Cardiac Regeneration at SBMS, UQ.



Project 2: Exploring a new way to target mitotic kinases in cancer cells.

Mitotic kinases promote cell division and proliferation and are upregulated in expression and activity in many tumour types. The targeting of mitotic kinases such as mitogen-activated and cyclin-dependent protein kinases are under intense investigation as novel drug targets for cancer treatment. However, emerging evidence also highlights roles for mitotic kinases in non-mitotic functions. In this project we will investigate the alternative approach of targeting protein kinase signalling complexes by disrupting the interface between mitotic kinases and signalling scaffolds that are required for the spatio-temporal co-ordination of kinase activity for specific mitotic functions (Figure 2). This honours work will contribute towards a multi-lab project that involves collaboration with researchers at the Department of Cancer Biology and Therapeutics at ANU (Dr Leonie Quinn) and the Department of Biochemistry and Molecular Biology at the University of Melbourne (A/Prof. Marie Bogoyevitch).

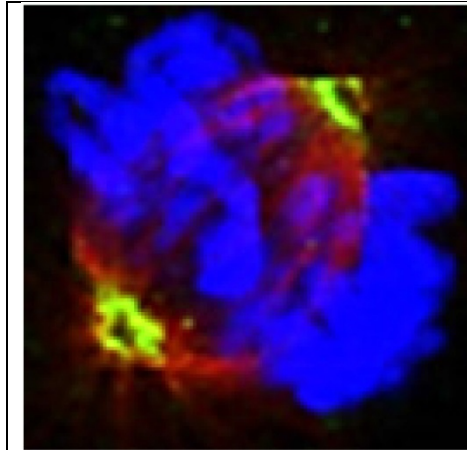


Figure 2. Mitotic spindle assembly labelled for tubulin (red), chromatin (blue) and a kinase scaffold (green) that co-ordinates MAPK and Aurora activity at the spindle pole.

Project 3: How do microcephaly genes govern brain growth?



Figure 3. *Drosophila* larval brains are an established model system to study molecular regulation of neural stem cell proliferation and fate decisions.

Microcephaly is a serious neuropathological condition that encompasses a spectrum of reduced brain size and cortical malformations that significantly impact learning, memory and behaviour. A number of genetic mutations have been identified as causative of heritable or primary microcephaly (MCPH). Although these mutations are rare, they provide novel insights into non-redundant molecular processes in neural stem and progenitor cells that are required for growth and normal development of the human brain. This project is focused on *MCPH2* which encodes a WD40-repeat protein that interacts with multiple kinases including c-Jun N-terminal kinase (JNK) and Aurora family kinases. Our goals are to define the signal transduction mechanisms and cellular processes regulated by MCPH genes that are essential for neural stem cell proliferation, fate commitment and brain growth. This project is conducted using *Drosophila* and mouse models of neurodevelopment in collaboration with Dr Sean Millard and A/Prof Michael Piper respectively.

Techniques you will learn in our group may include:

- dynamic live cell fluorescence imaging:
 - o quantitative confocal laser scanning microscopy
 - o fluorescence recovery after photobleaching (FRAP)
 - o Förster resonance energy transfer/fluorescence-lifetime imaging microscopy (FRET/FLIM)
 - o bimolecular fluorescence complementation
- super-resolution light microscopy
- proximity-tagging and ligation
- quantitative proteomics with stable isotope labelling and mass spectrometry.

- mammalian cell culture including primary isolation of cardiac myocytes and cortical neurons
 - viral transduction of mammalian cells
 - recombinant protein expression/purification
 - flow cytometry
 - siRNA/shRNA knockdown
 - transmission electron microscopy
 - sgRNA-guided gene editing with CRISPR/Cas9
 - sub-cellular and cytoskeletal purification
 - in vitro enzymatic assays
 - in vivo disease models
 - antibody-based detection of post-translational protein modifications
-



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Protein Trafficking in Disease

Protein trafficking controls the spatial organisation of individual proteins within cells. This highly co-ordinated movement of the thousands of distinct membrane proteins within cells is essential for the regulated localisation of proteins to the plasma membrane which in turn controls the organisation of cells within tissues and coordinates their communication with the environment. The success of this process depends on the regulated sorting and trafficking of proteins within the highly dynamic endosomal compartments of the cell in processes that are also emerging as important drivers of neurodegenerative disease, cancer and metabolic pathologies. An understanding of how endosomal traffic is regulated, and how lysosomal traffic and degradation are modulated, is critical for providing insights into the physiological processes associated with proteins that traffick through these intracellular organelles.

Project 1 - Retromer's role in neurodegeneration. Multiple neurodegenerative diseases are caused by defects in the degradation of biological materials. This degradation is dependent on a network of intracellular compartments that form the mammalian endosome/lysosome system within cells. Recently, we have defined the underlying molecular causes of Parkinson's disease for familial mutations identified in *Retromer*, a central endosome protein machine responsible for the sorting of membrane cargo to a range of destinations. We have projects focused on determining the rigorous mechanistic understanding that result in the changes in cellular homeostasis that occur during disease induction and progression that impair the cell's ability to degrade protein aggregates like that associated with Parkinson's disease.

Project 2 - Retromer – A master regulator of endosome protein trafficking. Fidelity of transport through the endosomal system thus requires mechanisms that precisely sort cargoes for delivery to a range of different destinations. This is achieved by cargo engaging specific sorting machinery that is responsible for their accumulation into tubules that then undergo scission to generate endosome-transport carriers (ETCs). Once formed, these carrier vesicles engage the machinery at the target membrane, resulting in cargo delivery to the specific membrane, e.g. plasma membrane. Retromer has a central role in this process through interaction with associated proteins that determines the properties of the individual ETCs formed. We have projects available to investigate the contribution each of the variant Retromer complexes has on the formation of the distinct ETCs types and defining the cargo transported by these vesicles.

Techniques you will learn in our group may include: Cell Biology, Tissue Culture, Microscopy (super-resolution; live cell imaging, confocal etc), Cell based trafficking assays, Molecular Biology and Biochemical techniques.



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Neuromuscular Biomechanics Research Laboratory

Our research aims to understand the neural and musculoskeletal mechanisms that underlie healthy and impaired locomotor performance. We use a highly integrative approach that combines novel experimental and computer simulation tools to improve our understanding of the interactions between muscles and tendons; how neuromuscular properties are altered with age or disease; and how disruptions affect muscle force production and movement.

Project Description

Tendinopathy is a highly prevalent condition that is commonly used to describe the clinical presentation of localised tendon pain with loading. Achilles tendinopathy is extremely common in runners, with an annual incidence of 9% (Lysholm et al., 1987), and is typically characterised by morphological changes (Mafulli et al., 2004) as well as altered mechanical properties (Sconfienza et al., 2010; Child et al., 2010). Once developed, tendinopathy symptoms may last for years and limit ones' ability to engage in regular physical activity. The Achilles tendon is the largest and strongest tendon within the human body, connecting the triceps surae muscle group (calf muscles: medial gastrocnemius, lateral gastrocnemius, and soleus) to the ankle. These muscles and the Achilles tendon are essential for normal walking and running as they generate 70-80% of the mechanical power needed for forward propulsion. The potential for disrupted force sharing between the triceps surae muscles which leads to altered foot and ankle kinematics and suboptimal loading of the Achilles tendon may contribute to the development and persistence of pain in those with Achilles tendinopathy. In this project we will determine if runners with Achilles tendinopathy display altered neural and mechanical force-sharing strategies between the triceps surae muscles in comparison to runners without Achilles tendinopathy. A better understanding of the mechanisms underlying Achilles tendinopathy will aid in the development of both preventative and rehabilitation strategies.

Techniques you will learn in our group may include: Electromyography (neural drive), Ultrasound (muscle and tendon length changes and stiffness), Force Plate (centre of pressure and ground reaction forces), and Kinematics (body segment motions and joint angles).

Collaborators: This project will be a collaboration with co-advisor Dr Kylie Tucker, who is a Senior Lecturer with expertise in motor control and pain within the School of Biomedical Sciences <http://researchers.uq.edu.au/researcher/1745> and Dr Brooke Coombes, who is a physiotherapist and researcher within the School of Biomedical Sciences specializing in the assessment and treatment of tendinopathy <http://researchers.uq.edu.au/researcher/1977>



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Laboratory of Motor Control and Pain research

We aim to gain insight into the development of movement and postural control in children and adolescents, and determine the affect of acute pain and chronic injury on motor control parameters in children and adults. We use innovative methodologies to improve knowledge about muscle mechanical properties and the way we drive our muscles to produce force and movement.

Project Description

Idiopathic patellofemoral (PF) pain is the most common cause of knee pain in female adolescents, affecting 14-21% of this population. Despite being prescribed evidence-based treatments, less than half of adolescents recover after 12 months, and 1 in 3 still have pain at 5 year follow up. A leading model for the genesis and persistence of PF pain in adults is that altered muscle coordination of the vastus lateralis and vastus medialis (the two largest knee extensor muscles), fosters altered PF kinematics, which leads to suboptimal PF joint loading. In contrast, for adolescents, overuse (i.e. excessive loading of the PF joint structures) is thought to underpin pain development.

The potential for a force imbalance between vastus muscles to underlie altered PF kinematics and contribute to the development and persistence of PF pain, needs to be thoroughly tested in the adolescent population. Advances in this field will support the development of treatments that lead to higher recovery rates, and support adolescents progressing through to adulthood without knee pain limiting their physical, emotional, educational, and intellectual development.

Here we will determine if 2 commonly used rehabilitation interventions (a motor control and an orthodic intervention) are associated with an immediate change in the neural drive to the vastus lateralis and vastus medialis in adolescents and young adults with PFP.

Techniques you will learn in our group may include: Electromyography (neural drive), Force Plate (centre of pressure), Kinematics (joint angles), Shear-wave elastography (muscle stiffness).

Collaborators: This project is part of a larger study that involves multiple national and international collaborators. In particular this work will be completed with co-advisor Dr Natalie Collins, who is a physiotherapist and researcher within the School of Health and Rehabilitation Sciences at UQ.
<http://researchers.uq.edu.au/researcher/12040>



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Research into Student Behaviour in University Settings

My research themes aim to better understand the motivating factors that promote student behaviours, which can then impact on learning outcomes. By better understanding the reality of our students, both in and out of the classroom, we can better adjust and adapt our teachings as needed to maintain support that is effective, as informed by the students themselves.

a) Lecture Attendance and Associated Factors amongst Science and Professional Students: This project is the next step in analysing the factors which favourably and unfavourably impact on lecture attendance. In 2014, we assessed science and allied health student lecture attendance with some significant differences observed regarding motivational factors:

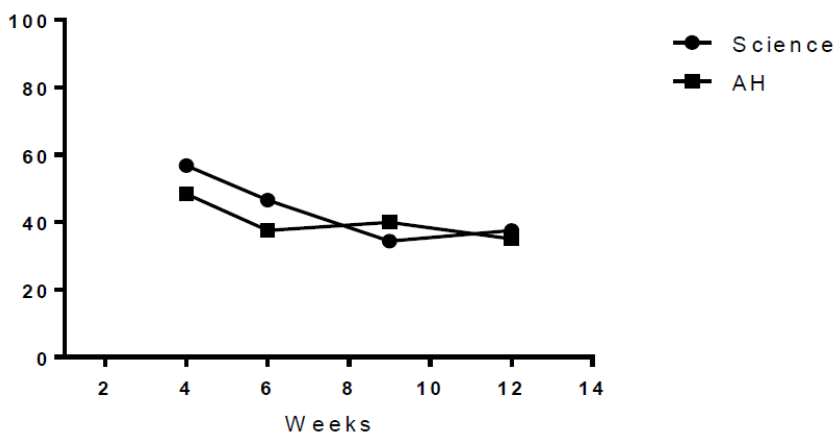


Figure 1. Trends in attendance of all Science and HP students from weeks 4 to week 12 in Semester 2, 2014. Student attendance is percentage of total enrolment as dependent variable plotted against weeks of the semester. Circle and square represent Science and HP respectively. Both disciplines exhibit a negative slope but insignificant correlation with time (Science: $r=-0.8689$, $R^2=0.755$, $p=0.1311$; HP: $r=-0.7927$, $R^2=0.6283$, $p=0.2073$). (Catherine Hsieh, Honours)

This project will assess the reality in 2018, to see if lecture attendance across eight courses in different programs has changed, using a combination of physical counting of students in lectures and meta-learning questions delivered through Bb. Text analysis will be used to look for trends and the results contrasted, where appropriate, with data from 2014.

Such information is crucial as universities consider how to best use their campus spaces. If a course has 400 students registered, but 150 regularly attend, is it strategic to build lecture theatres that cater for 400? If students prefer to listen to lectures on-line, what factors should the lecturers take into account to ensure

that the quality learning experience is reflected in such recordings? What is it that brings students to lectures, particularly in the third year courses where attendance percentages are the lowest? Why are they the lowest? Is there a correlation between grades earned and lecture attendance?

b) Do university outreach programs actually motivate and impact on student choices? Each semester break, students are invited to UQ to attend a variety of programs to expose them to the university experience. These include week-long experiences in which students stay on campus and visit different Faculties for hands-on sessions, half day tours or talks. A lot of energy and enthusiasm of current staff and students goes into this mechanism of student recruitment to UQ and to specific programs.

This project will critically assess the effectiveness of such efforts. Of those who attend, how many come to UQ? What do they study? Did the program make a difference in their choices? Did they attend any university at all, and if so, where and why?

Working with the Faculty of Science, we will extract such data and design surveys for the mid-year cohort to determine their initial impressions about university attendance. Results will much better inform future programs in an ever-increasingly competitive market place for higher education.

Techniques you will learn in our group may include: critical analysis of education-based literature to inform survey development, scientific writing skills, statistics, text analysis, oral presentation skills.

Do you have an education based question or problem that you have wondered about? This can certainly be discussed, considered, and developed into a research question for research.



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Critical Care Research Group (CCRG)

The CCRG is based at the Australia's largest cardiothoracic hospital, The Prince Charles Hospital, and regularly realises the huge potential of integrating technology and biology in combating cardiovascular disease. The group is a multi-disciplinary team consisting of clinicians, scientists, statisticians, allied health professionals and engineers. The CCRG aims to improve both the understanding and use of technologies to improve the outcomes of patients via organ transplantation and mechanical assist device (MAD) options, used by clinicians in the management and treatment of patients suffering from cardiovascular disease.

Since its establishment by Professor John Fraser in 2004, the CCRG has attracted more than \$28 million in grants and industry funding, published over 300 papers, and was awarded the first NHMRC Centre of Research Excellence for MADs. The CCRG also has active ongoing collaborations with The Alfred Hospital and St Vincent's Hospital, which, combined with the CCRG's base location of The Prince Charles Hospital gives the group a strong network across the three major cardiac hospitals in Australia. In addition, the group belongs to multiple national and international research networks, including ECMOnet, EuroELSO, APELSO, ANZICS amongst others. The group specialises in clinically validated large animal models, within a state of the art research facility. CCRG also has an extensive network of collaborators across UQ, and both within Australia and overseas.

Research Projects are available in a number of areas for honours, masters (research/coursework), and PhD students. Projects can range from animal experiments, to biological characterisation of tissue samples, through to translation of research findings to improve current clinical outcomes. Large animal, pre-clinical studies are a major focus of the CCRG, but through collaborations with other research scientists (at UQ and overseas), the group encourages multidisciplinary projects. Students will be expected to apply for research funding, and the group has a strong track-record in mentoring students to obtain novice grants successfully (up to \$10,000 each). Students will also gain valuable experience working with leading clinician researchers from major hospitals around Australia, as well as cutting edge researchers in medical engineering and biomedical science.

Currently available projects:

1. *The Dead Heart Project – When is a dead heart truly dead?*

Students will be involved in a multi-disciplinary team across the 3 biggest cardiac hospitals in Australia. The project aims to improve the quantity and quality of donor hearts through organ reconditioning and new donor sources, as well as understanding ischemia-induced molecular damage to cardiomyocytes during transplant. The model is clinically relevant with study transplants performed by leading Australian cardiothoracic surgeons.

2. *Treating Acute Respiratory Distress Syndrome (ARDS) with mesenchymal stem cells*

ARDS is a critical illness with unacceptably high mortality rate (up to 45%). Currently, there is no effective treatment, partly due to its heterogeneity nature. CCRG is exploring the possibilities in treating ARDS via mesenchymal stem cells. Students will have the opportunity to work with commercial-grade stem cells provided by an industry partner. There is also an opportunity for a short-term visit to our collaborator in the UK.

3. *Impact of Extra-Corporeal Membrane Oxygenation (ECMO) on leukocytes*

ECMO is a life saving device for patients with severe cardiac and/or respiratory dysfunction. It allows patients to rest in otherwise life-threatening situations. However, mortality remains high. This undesirable outcome is often associated with immune perturbation mediated by the contact of patient blood cells with the foreign surface of ECMO. This project aims to better understand the impact of ECMO on leukocyte fate.

4. *Gastrointestinal bleeding caused by ventricular assist device (VAD)*

Gastrointestinal bleeding is one of the most common complications in patients with continuous flow VAD (Ventricular Assist Devices - artificial mechanical hearts), but the exact cause is unknown. This project involves testing whole blood and endothelial responses to different flow conditions by connecting vascular models to commercially-available VADs (some of these may have been removed from patients.). Students will develop skills in cell culture, blood circuit assembly, flow cytometry and fluorescent microscopy

For more information of the group and available projects, please contact Dr. Jacky Suen (j.suen1@uq.edu.au).

Techniques/Knowledge you will learn in our group may include:

General: experimental design, good laboratory practise, ethics application, site specific approval application, good record keeping, pipetting and dilution technique

In vitro/ex vivo: SDS-PAGE, Western Blot, ELISA, RT-PCR, RNAseq, ddPCR, single cell PCR, immunofluorescence, flow cytometry, confocal microscopy, electronic microscopy (SEM, TEM), mitochondria profiling, oxygraph, organ bath.

In vivo: animal ethics application, animal handling, dissection, tissue/blood handling, blood differential, histology

Clinical/Human: electrocardiogram, extra-corporeal membrane oxygenation, echocardiogram, cardiopulmonary bypass, mechanical ventilation, rotational thromboelastometry (ROTEM), multiplate analysis, electrophysiology, arterial blood gas, ex vivo lung perfusion, patient recruitment process



Dr Felicity Han

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CIPDD

Project:

Biodegradable polymeric micro/nanoparticles to increase the half-life of a C5aR antagonist for the treatment of cancer and cancer-related chronic pain.



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Laboratory of Functional and Molecular Neuroimaging

Neuroimaging, such as functional magnetic resonance imaging (fMRI), is a powerful tool that can map structural, functional and connectomic changes of the brain noninvasively. As the same technique can be applied in both humans and animals, it allows direct translation of findings in animal models to humans, or vice versa. The laboratory aims to identify imaging-based neuro-endophenotype of brain functions and disorders to improve our understanding of cognitive functions, and to facilitate early diagnosis and evaluation of treatment.

Project 1: Imaging brain connectome of mouse models of neurodegenerative diseases

Neurodegenerative diseases, such as dementia, are irreversible and generally incurable and hence early detection is essential so that interventions can be applied to slow down its progression. We focused on characterising the change of brain connectome using MRI techniques for mapping structural and functional connectivity in mouse models and humans in vivo. This project will evaluate the effects of disease-associated risk genes or treatments on the brain connectome in transgenic mouse models of neurodegenerative diseases, such as Huntington disease, frontotemporal dementia and amyotrophic lateral sclerosis, to improve our understanding of the genetic effects on the pathogenesis in human.

Project 2: Imaging brain disorders and treatment response

This project will evaluate the effects of peripheral inflammation on brain function in a cohort of subjects suffering from depression due to the inflammatory bowel disease. In particular, a mindfulness training will be conducted to alleviate their symptom. The structural and functional connectivity before and after the intervention will be assessed and correlated with blood biomarkers and behaviour to understand the effects of inflammation on the brain connectivity and the efficacy of intervention.

Project 3: Understand neural basis of resting-state network

An interesting phenomenon of the brain is that certain brain areas form synchronous low frequency oscillation during the resting state. These resting-state networks can be detected by functional MRI (fMRI) noninvasively and their changes have been associated with attention, learning, memory and disorders. While widely applied, the neural basis of resting-state fMRI is largely unknown. We aim to understand the neural basis underlies the resting-state networks, the axonal connectivity that supports the network topology and their relevance to behaviour, such as learning and memory. We will apply fMRI in rodent under pharmacological and behaviour manipulations and validated by electrophysiology, neuronal tract tracing, lesion and optogenetics to determine the neural underpinning of the fMRI signal oscillation and its relationship with particular neural pathway and transmission system.

Techniques you will learn in our group may include: functional MRI, diffusion tensor imaging (DTI), image processing, neuroanatomy, brain function



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Neuroscience

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Neurula Lab

Since 2008, Dr Medeiros has led the effort to identify the underlying mechanisms related with the development and progression of neurodegenerative diseases. His long-term goal is to advance knowledge of healthy, and diseased, brain function to a point where rational strategies can be developed for the prevention and cure of age-related neurological disorders. To pursue his research goals, Dr Medeiros maintains a research environment in which creative and innovative ideas can be nurtured and brought to fruition using a base of established as well as state-of-the-art approaches. His belief is that this environment will facilitate conceptual leaps in our understanding of the diseases that impact the human brain.

Project 1: Role of the immune system in neurodegeneration

Dr Medeiros discovered that Alzheimer's disease promotes defects in fundamental molecular events that limit and resolve inflammation, and demonstrated that such changes account for a substantial portion of the disease pathogenesis. Currently, the Neurula lab is undertaking the challenge of using and developing novel laboratory models in parallel with studies on affected human subjects to elucidate the underlying molecular mechanisms linking inflammation to β -amyloid, tau pathology and cognitive decline. Understanding these mechanisms will allow definition of the biological pathways involved in the onset and progression of Alzheimer's disease, and identify potential therapeutic targets for the management of this devastating disorder.

Project 2: Impact of comorbidities in brain ageing and disease

The Neurula Lab also studies the impact of comorbidities in neurodegeneration and Alzheimer's disease. We seek to understand how concurrent diseases that commonly occur in the elderly may modulate neurodegeneration and age-related changes in the brain. We have been particularly interested in infections, diabetes and traumatic brain injury as major regulators of biological processes, and are developing genetic and pharmacological agents to manipulate these pathways in Alzheimer's disease.

Techniques you will learn in our group may include: Primary glial and neuronal cell cultures, intracranial delivery of viral vectors, western blot, immunohistochemistry (IHC), immunocytochemistry (ICC) and immunofluorescence (IF).



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Human agenesis of the corpus callosum, autism spectrum disorder and brain wiring

Agenesis of the corpus callosum is a brain wiring alteration that occurs during brain development. Many people have some characteristics that are similar to those with autism spectrum disorder. We are investigating brain wiring connectivity using high-field magnetic resonance imaging and neuropsychological testing to understand how brain connectivity underpins the function of the brain. We also want to understand the underlying causes of agenesis of the corpus callosum by performing genetic analyses of DNA from people with these disorders compared to controls. The work will have a significant impact on our understanding of how changes in brain wiring impact brain function.

Opportunities exist for students with a background or interest in:

Neuroscience, genetics, magnetic resonance imaging and physics, neuropsychology, medicine, computer science (data analysis and software development).

Function of genes and molecules in agenesis of the corpus callosum and brain developmental disorders

Identifying a causal genetic mutation in a person requires functional studies to determine if the mutation causes a change in the function of the gene. This work requires in-depth analysis in animal models to examine gene function in cellular proliferation, differentiation, migration and cortical wiring. We are interested to understand the basic mechanisms regulating these developmental events and how they are altered in human brain disorders including agenesis of the corpus callosum, ventriculomegaly, hydrocephalus and cortical malformations. This work has a significant translational impact on understanding the causes of brain developmental disorders.

Opportunities exist for students with a background or interest in:

Neuroscience, genetics, cell biology, developmental biology, glial development, animal behaviour, medicine.

The function of early neuronal activity on the formation of neocortical circuits

How does the brain acquire its connectivity pattern during development? This project aims at elucidating the main roles of early sensory and spontaneous activity in the formation of neocortical circuits. By combining molecular, electrical and developmental manipulations in developing mammalian embryos and pups, this project will study how early events affect the precise formation of cortical features required for normal cognitive development. The work will have a significant impact on our understanding of how the brain is wired for function.

Opportunities exist for students with a background or interest in:

Neuroscience, developmental neurobiology, neurophysiology, electrophysiological signal analysis and/or computational sciences, mathematical modelling, medicine.

Principles of neural development applied to understanding brain cancer

Brain cancer is a significant health problem in Australia. One of the most aggressive forms of brain cancer is glioblastoma (GBM) and the prognosis for these patients is extremely poor. What is needed is a deeper understanding of the cause of brain cancer. We are approaching this challenge by utilising the principles of neural development to understand how tumours first arise in the brain and how they are able to continue to grow and metastasize in order to find the causes and treatments for adult and pediatric brain cancers that

Biomedical Sciences Honours Projects 2018

originate from glia. Nuclear factor one (NFI) genes have been implicated in brain cancer and in glial development. We have generated a number of animal models of Nfi gene mis-expression to determine the function of NFI genes in brain cancer. This work will have a significant impact on our understanding of the cause and progression of brain cancer.

Opportunities exist for students with a background or interest in:

Neuroscience, genetics, cell biology, developmental biology, glial development, animal behaviour, medicine.



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Visualization of neuronal protein sorting events by high-resolution structural biology methods.

We are focused on understanding the fundamental cellular process of intracellular protein sorting in human neuronal cells. Specifically, we study protein machineries that operate as cargo vans within the cell. These protein complexes direct the cargo (cell surface receptors) either to recycling or degradative sorting routes thereby maintaining the overall cellular homeostasis. Defects in these protein machineries result in abnormal trafficking of cell surface receptors that has implications in several neurodegenerative diseases including Parkinson's, amyotrophic lateral sclerosis.

We take advantage of hybrid structural biology approaches to obtain an overall three-dimensional map of these trafficking protein complexes. We also employ biophysical, biochemical and molecular biology methods to decipher how these protein assemblies (cargo vans) engage their cargo (cell surface receptors). We adopt multidisciplinary approach and together with our cell biology collaborators we aim to construct atomic resolution maps of cellular sorting events.

Project 1: Structural and functional characterization of commander complex.

Project 2: Molecular understanding of the role of retriever complex in intracellular trafficking of cell surface receptors.

Project 3: Towards understanding the assembly of SMCR8-C9orf72-WDR41 holo complex and its implications in amyotrophic lateral sclerosis and frontotemporal dementia.

Techniques you will learn in our group may include: Students will get hands on training in molecular cloning, recombinant protein expression and purification. They will also be able to learn protein characterisation techniques such as size exclusion chromatography, multi angle laser light scattering. Projects also involve characterisation of protein-protein, protein-lipid and protein-ligand interactions using pull-down assays, Isothermal titration calorimetry and optical interferometry. A major aim of all the above-mentioned projects is to solve the atomic structure of apo proteins, protein-ligand complexes as well as holo structures of large multiprotein complexes using X-ray crystallography and electron microscopy. Therefore, training will be given to grow protein crystals for protein atomic structure determination.



Dr Karl Hansford

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Infection and Immunity

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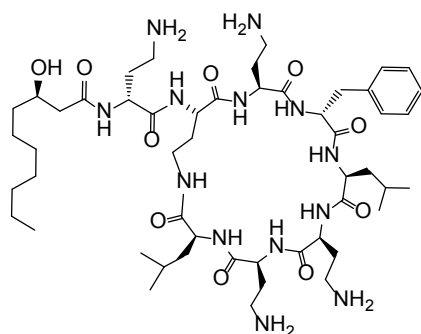
Email: <mailto:k.hansford@imb.uq.edu>

Web: <http://cooper.imb.uq.edu.au/>

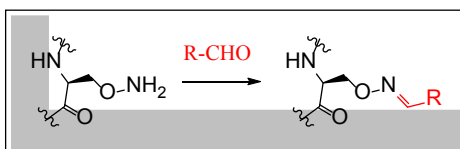
The Cooper group at the Institute for Molecular Bioscience has a strong interest in the discovery and development of new antimicrobial agents. We have several ongoing projects at various stages of maturity, from early discovery through to hit-to-lead, lead optimisation and pre-clinical development. Each project is unique in terms of targeted organism and medicinal chemistry focus.

Project 1: Probing Structure-Function of Octapeptin C4

Our COListin/OctaPeptin medicinal chemistry program (COLOP) targets drug resistant Gram-negative (G-ve) bacteria such as *P. aeruginosa* and *K. pneumoniae*, two organisms that often cause high mortality infections due to their inability to be killed by most antibiotics. Polymyxin (Pmx), a cyclic lipopeptide natural product discovered in 1947, is a last-resort clinical treatment option. However, its utility is highly compromised by dose-limiting nephrotoxicity and the emergence of Pmx-resistance (Pmx-R). The octapeptins (Oct) are an unexplored class cyclic lipopeptides structurally similar to Pmx. Despite their similarities, Oct possess the intriguing ability to kill multidrug-resistant (MDR) and extensively drug-resistant (XDR) G-ve bacteria that are also highly resistant to Pmx. Importantly, no cross resistance is observed.



Octapeptin C4



We have synthesised ~200 Oct analogues using solid phase synthesis (SPPS), and have identified compounds that are less nephrotoxic than Pmx with retain activity against Pmx-R G-ve bacteria and equivalent efficacy to Pmx in a mouse infection model. SPPS can be tedious when making many structural analogues as each peptide has to be made in stepwise fashion. A more efficient approach would be to make an advanced intermediate and diversify late in the synthetic sequence. This convergent approach would facilitate the generation of structure-activity relationships (SAR) data. Oxime ligation is a reliable and versatile method for conjugating molecules, with stability at physiological pH. Here, we propose to insert an aminoxy functionalised amino acid into several key positions of octapeptin C4 (Oct-C4), a representative member of the Oct class, and then chemoselectively ligate aldehydes onto the side chain to generate a series of oxime derivatives. The initial goal is to determine if the native activity of Oct-C4 is tolerant of such changes at several key positions. If so, we would undertake SAR by oxime formation to further optimise our current lead Oct lead series.

Project 2: Strategies to Target Plasma Membrane Phospholipids of Bacteria

Many of the antimicrobial agents developed in the Cooper group exert their action by targeting the fidelity of the bacterial membrane, either through physical disruption of membrane integrity or by impairment of the biosynthetic machinery required for the synthesis of critical membrane precursors. The unique lipid composition of Gram-positive bacterial membranes, which often contain an abundance of negatively charged phospholipids, provides an opportunity to rationally design antibiotic candidates that preferentially target bacterial membranes over eukaryotic membranes, which are essentially neutral. Indeed, our Vancaptin program is a successful example of this approach, where we have restored the activity of vancomycin toward vancomycin-resistant bacteria using vancomycin-peptide conjugates. Cardiolipin is a unique phospholipid found in both Gram-positive and Gram-negative bacterial membranes, and constitutes an important component of the inner mitochondrial membrane of eukaryotes. Several recently discovered antibiotics have been proposed to target cardiolipin, suggesting it may be a new molecular target for antibiotics. This project will explore new strategies to target bacterial cardiolipin using short peptide sequences designed to interact with this unique phospholipid.

Techniques you will learn in our group may include: The candidate will have the opportunity to understand the unique challenges of antibiotic discovery and development in a globally recognised research group, and contribute to a high impact research area. In particular, the candidate can expect to gain first-hand experience as an independent researcher in a medicinal chemistry setting, learning how to conduct small molecule and solid phase peptide synthesis. Opportunities will exist to purify and characterise compounds using the usual suite of analytical tools (LC/MS, NMR, HPLC etc). An analytical mind and attention to detail is essential for the successful completion of these projects.



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Lewis lab: Discovery of cone snail venom peptides as modulators of pain

Overview

Cone snails are venomous marine molluscs that hunt fish, molluscs and worms depending on their prey preference. The major components of *Conus* venom are small structured peptides (conopeptides or conotoxins) that are injected using a hollow, barbed radula tooth for prey capture or defense. There are ~ 850 species of cone snails identified with each expressing many thousands of unique peptides that selectively target a diverse range of voltage- and ligand gated ion channels, transporters and G-protein couple receptors. Given their high potency and isoform selectivity, cone snail venom peptides provide a natural reservoir of potential drug leads. The ability of cone snails to switch between separately evolved predatory and defensive venom regimes appears to underpin this remarkable structural and functional diversity.

Project Description

Unravelling the complexity of cone snail venoms using advanced proteomic and transcriptomic and pharmacological methods : A guide for rapid bio-discovery of pain modulators

Recent developments in the field of “venomics” (integrated proteomic and transcriptomic analysis of venoms) have opened up a vast potential to tap into this largely untouched resource. Moreover, the ability of cone snails to switch between a predatory and a defensive venoms and their remarkable venom individuality (intraspecific variation) increases the venom variation and hence the peptide pool. This opens up an urgent need for rapid identification of driving peptides with specific physiological functions.

In this background the overall objective of this study is to utilise proteomic, transcriptomic and high-throughput pharmacological approaches for the accelerated discovery of bioactive peptides that can be developed as selective pain modulators.

Techniques you will learn in our group may include: Cell culture, FLIPR based high throughput bioassays, Mass spectrometry, transcriptomic analysis, HPLC, zebrafish and *c. elegans* based behavioural assays, Cone snail venom collection, extraction

Scholars would get an opportunity to contribute for publications upon the successful completion of the projects. Students will also be acquiring skills on data management and presentation.



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Muttenthaler/Alewood Lab /Neuropeptide Research

Neuropeptides are key mediators in many biological functions and understanding of their interaction with target proteins is fundamental to unravel the underlying mechanism of diseases. Over the years, an increasing number of bioactive peptides from animals, plants, and bacteria have been characterised, with the overwhelming realisation that these molecules often show better therapeutic performance than their human counterparts, particularly in terms of in vivo stability.

Our main research efforts situated in this field of Chemical Biology focus on the exploration and translation of these vast and untapped natural libraries towards the development of useful research tools and therapeutics. Solid-phase peptide synthesis, the main tool to access these compounds, is a powerful technology for the assembly and chemical modification of these highly chiral and structurally complex peptides. This complexity is also responsible for their remarkable selectivity and potency as well as for their low side effect profile observed in the clinic.

Project 1: *Oxytocin and Vasopressin Research*

The oxytocin and vasopressin signalling system regulates many fundamental physiological processes such as reproduction, water balance, cardiovascular responses and complex social behaviour. It is also a high-profile target for autism, schizophrenia, stress, depression, anxiety, cancer and pain. Our group is particularly interested in creating a complete molecular toolbox to study this signalling system as well as in discovering novel therapeutic leads for autism, pain, gastrointestinal disorders and breast cancer.

Project 2: *Gastrointestinal Disorders*

The gastrointestinal epithelium is a major physical barrier that protects us from diverse, and potentially immunogenic or toxic content. A damaged epithelium results in increased permeability to such content, thus leading to inflammation, uncontrolled immune response, and diseases, such as irritable bowel syndrome and inflammatory bowel disease that affect 10-15% of the population. Our group is involved in the identification and validation of novel drug targets and therapeutic strategies that can protect or repair this important barrier in order to prevent or treat such disorders.

Project 3: *Neuropeptides and long-term Memory Formation*

Memory is probably the single most important brain process that defines our personality and gives us the sense of individuality. Emotional events often cause the generation of strong memories that exist for many years, yet the underlying mechanisms are still poorly understood. Neuropeptides are key players in regulating emotions and have been associated with long-term memory formation. Our group is involved in the development of advanced molecular probes to understand how neuropeptides can influence long-term memory formation.

Project Description: *Venoms to Drugs*

Venoms comprise a highly complex cocktail of bioactive peptides evolved to paralyse prey and defend against predators. Homology of prey/predator receptors to human receptors render these venom peptides also

active on human receptors and they have become a rich source for neurological tools and therapeutics. Our group is involved in the discovery, synthesis and structure-activity relationship studies of these venom peptides with the goal to develop novel probes for neuroscientists as well as therapeutic drug leads.

Techniques you will learn in our group may include:

Solid phase peptide synthesis

Organic Chemistry

Medicinal Chemistry

High-performance liquid chromatography

Mass spectrometry

Compound stability assays

Cell culture and pharmacological assays

Gastrointestinal wound healing assays

Proliferation and transmigration assays



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The Role of the cell surface in health and disease

We are interested in features of the cell surface which are able to protect against membrane stress, and/or are involved in the trafficking pathways implicated in human diseases. Currently, we are using both tissue culture and zebrafish models in combination with live imaging and electron microscopy to understand muscle diseases and cancer.

Project 1

Dissecting the role of a novel protein involved in membrane stability, using zebrafish.

We have recently identified a protein which localises to the necks of caveolae, small invaginations on the surface of the plasma membrane. They are thought to confer mechanical stability and release signalling factors upon membrane stretch. Our new protein is present in the zebrafish notochord (the precursor of the spine), and we will focus on this experimental paradigm to dissect the specific functions of this protein at the plasma membrane.

Project 2

Modelling centro-nuclear myopathies using zebrafish.

Several proteins have been associated with centronuclear myopathies in humans, including Bin1, dynamin2 and myotubularin. However, the relationships between these proteins and how they contribute to the human pathologies are not well understood. This project will involve CRISPR-Cas9 knockout of one or more of these genes and assessment of the effects on membrane transport in developing muscle cells.

Project 3

The zebrafish as a model for nano-particle mediated therapies

Our laboratory has developed an experimental nano-particle based system for the targeted delivery of therapeutics. Currently, in vivo laboratory testing is limited to mice, and determination of efficiency is slow and laborious. In this project, we plan to develop the use of transgenic zebrafish, which are optically transparent, to rapidly assess tissue localisation and efficacy of targeting to sites of interest.

Techniques you will learn in our group may include: CRISPR-Cas9 knockout, microinjection, live imaging, in situ hybridisation, confocal and fluorescence microscopy.



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CO-ADD / Predictive Models for Antibiotics against Multi-Drug Resistant Bacteria

CO-ADD is an initiative of the University of Queensland and the Wellcome Trust (UK) to find new antibiotics among the chemical novelty of academic research labs from around the world. As part of this initiative CO-ADD has received and screened a large number of compounds from 40 countries and screened them against bacteria, including Gram-positive and Gram-negative bacteria. This large, unique and consistent data set provides a high quality data set to generate predictive models using state-of-the-art machine learning techniques. CO-ADD will use these models to find new antibiotics able to combat the ever increasing threat of multi-drug-resistant bacteria.

Help us to find the new antibiotic.

Deep Antibacterial Models

The size and the consistency of the data set allows the application of deep learning algorithms for the prediction of antibacterial activity from a chemical structure. Deep belief nets in combination with chemical fingerprints are being used in the lab to develop models able to predict the cell based activity of compounds. The deep neural networks are ideal to model the complexity of both chemical information (input) and cell-based biological activity (labels). The project will use GPU assisted deep-learning packages, such as Tensorflow, in combination with chemoinformatic packages, to optimize the representation of chemical structures with different neural networks. The project requires good coding knowledge (i.e. python or c++) as well as good chemical knowledge.

Penetration Models

One of the key properties of antibiotic is their ability to penetrate the membrane of bacteria. In particular, Gram-negative bacteria, such as *Pseudomonas aeruginosa*, possess an extra membrane and an efficient efflux pump system, to prevent the penetration of many antibiotics or to remove them quickly from the cell. This intrinsic resistance is the main reason only very few new antibiotics are being discovered. CO-ADD has accumulated a large data set from assays evaluating the compounds ability to penetrate these bacteria. The project is to build predictive models specific for the membrane penetration of Gram-negative bacteria. The project will use GPU assisted deep-learning packages, such as Tensorflow, in combination with chemoinformatic packages, to optimize the representation of chemical structures with different neural networks. The project requires good coding knowledge (i.e. python or c++) as well as good chemical knowledge.

Techniques you will learn in our group may include:

Machine Learning, Deep Learning (Tensorflow), Chemoinformatic, Antimicrobial Drug Discovery

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Cancer immunology (Lab head: Prof Ian Frazer)

Our lab investigates the role of the immune system in cancer, with a focus on HPV-driven cervical cancer and Squamous cell carcinoma (SCC) of the skin.

Project Description 1: Immune evasion of SCC of the skin (Dr. Katharina Noske)

Human epidermal keratinocytes undergo several steps of transformation during their progression to skin cancer, from normal over sun-damaged to pre-cancerous Actinic keratosis (AK), to finally become SCC. While AKs are highly immunogenic and can mostly be controlled by the immune system, some of these cells escape from immune surveillance and become cancerous. This project investigates how keratinocytes change during their progressive transformation, under the influence of UV irradiation, and which properties of the cells allow them to modulate their immune environment. In particular, the research focuses on the antigen processing and presenting capabilities of transformed cells compared to normal cells, their immune secretome and subsequent potential to activate immune cells. These studies will be performed in a human SCC progression model.

Techniques you will learn in this project may include:

Immunofluorescence, Microscopy, FACS, 3D *in vivo*-like model of human skin, ELISA, *in vitro* cell-based assays, cell culture, co-culture of immune cells, isolation of cells from tissue

Project Description 2: Development of Potent Nano-adjuvants for Therapeutic HPV Vaccine (Dr. Meihua Yu)

Cervical and other anogenital cancers account for about 5% of the global cancer burden, generally caused by persistent infection with human papillomavirus (HPV). Currently available prophylactic HPV vaccines have the potential to prevent HPV related cancers. However, development of effective HPV specific immunotherapy to treat existing HPV infection and associated invasive cancers has proven challenging. We have developed innovative nanomaterial based adjuvants, eliciting strong cytotoxic T lymphocyte responses against HPV16 E6/E7 solid tumour. The available Honours project aims to investigate this nano-adjuvant mechanism in primary immune cells and in mice. Successful completion of the proposed project will provide insights into the biological pathway of our innovative therapeutic HPV vaccines.

Techniques you will learn in this project may include:

Mice handling, primary cell culture, FACS, vaccine formation, etc.
