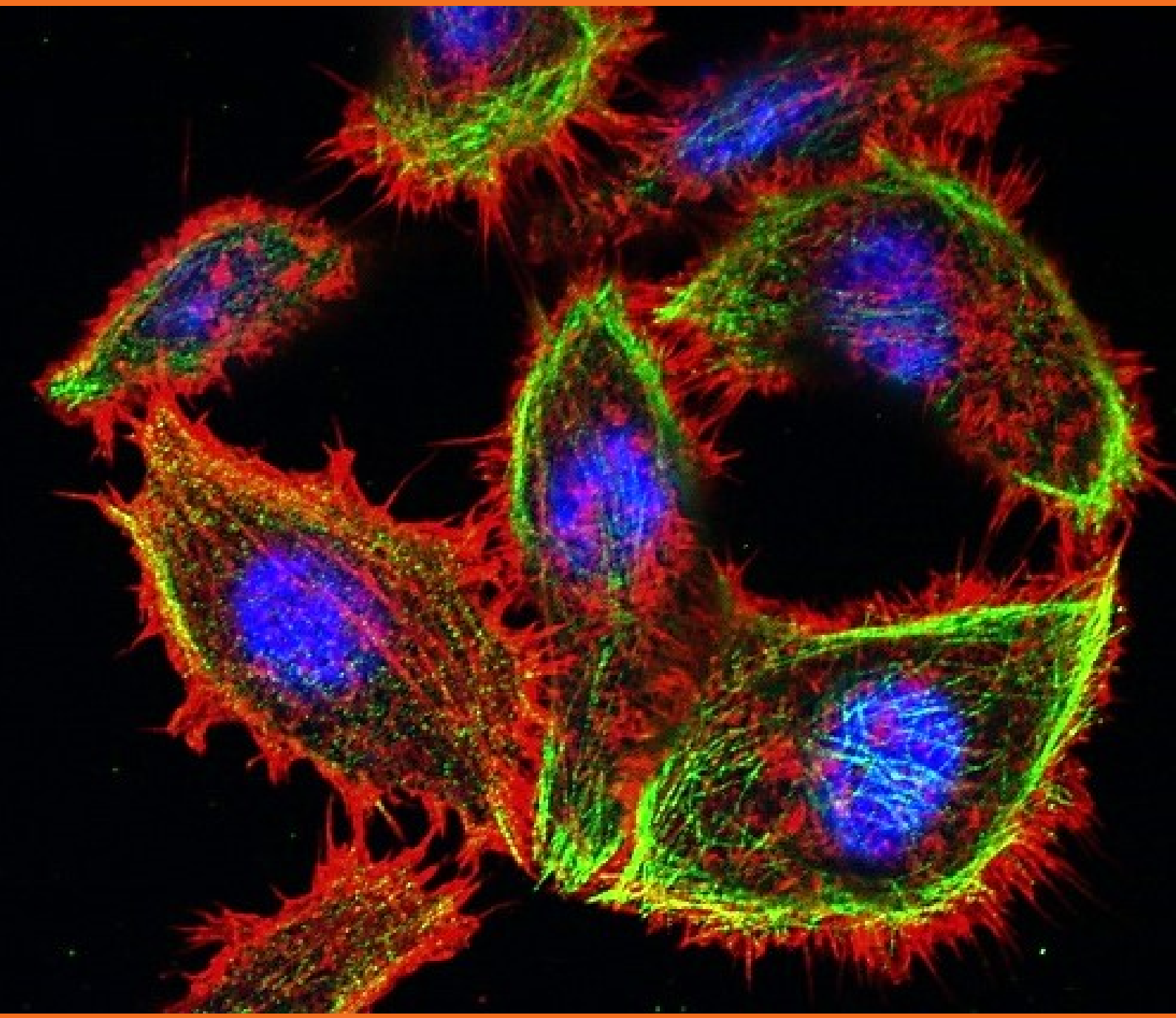
LA TROBE
UNIVERSITY • AUSTRALIA

Department of Biochemistry and Chemistry

School of Agriculture, Biomedicine and Environment

Scientists at the forefront of knowledge in research areas including synthetic, organic, inorganic and analytical chemistry, molecular, cellular and structural biology, fundamental and applied biochemistry in microbes, plants and animals, as well as biomedical applications in human health and disease



latrobe.edu.au/school-agriculture-biomedicine-and-environment

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Cover Photo: Immunofluorescence microscopy of the cytoskeletal network in human PC3 prostate cancer cells. Photo credit: Guneet Bindra, PhD student Hulett lab

About the School of Agriculture, Biomedicine and Environment

The School of Agriculture, Biomedicine and Environment is one of the largest in the University, with more than 170 continuing and fixed term staff across multiple campuses. Over the last three years the School has seen significant growth in both research and teaching revenue. Staff in the School currently generate a significant proportion of the University's teaching revenue and research income, and supervise more than 270 higher degree research students. The School is responsible for 7 undergraduate degree courses at the main Bundoora campus in Melbourne, and our regional campus at Albury-Wodonga. It is a leader in teaching innovation and student satisfaction within the university.

The School undertakes teaching and research across a broad range of disciplines, including: Agriculture, Botany, Soil Science, Animal Science, Plant Science, Ecology, Environmental Geoscience, Evolution and Genetics, Conservation Biology, Zoology, Neurobiology, Microbiology, Physiology, Pathophysiology, Pharmacology and Anatomy, Biochemistry, Chemistry and Cardiovascular Physiology. The School is a major contributor to research strengths in both the Biological and Agricultural Sciences, achieving the highest possible rating '5 - well above world standing' from the Australian Research Council in the fields of Ecology, Zoology, Plant Biology, Physiology, Microbiology, Biochemistry and Cell Biology, Crop and Pasture Production, Genetics, Soil Science, and Veterinary Science, and rated as '4 - above world standing' in Ecological Applications.

The 5 departments in the School are:

- Animal, Plant and Soil Sciences
- Baker Department of Cardiovascular Research, Translation and Implementation
- Biochemistry and Chemistry
- Environment and Genetics
- Microbiology, Anatomy, Pharmacology and Physiology

The School of Agriculture, Biomedicine and Environment research environment is dynamic and growing, and includes these major research centres:

- La Trobe Institute of Agriculture and Food (LIAF)
- ARC ITRH (Industry Transformation Research Hub) for Medicinal Agriculture
- ARC CoE (Centre of Excellence) Plant Energy Biology
- Centre for Livestock Interactions with Pathogens (CLiP)
- Centre for Cardiovascular Biology and Disease (collaboration with the Baker Heart and Diabetes Institute)
- Research Centre for Extracellular Vesicles
- Centre Research Biomedical and Environment Sensor Technology (BEST)
- Research Centre for Molecular Cancer Prevention
- La Trobe Institute for Molecular Science
- Research Centre for Future Landscapes (collaboration with the Arthur Rylah Institute of DELWP)
- Centre for Freshwater Ecosystems (formerly the Murray-Darling Freshwater Research Centre)
- Research Centre for Applied Alpine Ecology
- Mallee Regional Innovation Centre (MRIC)(a joint venture with The University of Melbourne)

Professor Shaun Collin Dean, School of Agriculture, Biomedicine and Environment, Co-Director of AgriBio

Department of Biochemistry and Chemistry

The Department of Biochemistry and Chemistry is the largest academic department in the School of Agriculture, Biomedicine and Environment at La Trobe University. The Department consists of more than 75 continuing and fixed-term academic staff, including two NHMRC Senior Research Fellows, two ARC Future Fellows, two ARC DECRA Fellows, one Victorian Cancer Agency Research Fellow, and one Tracey Banivanua Mar Fellow. Professor Mark Hulett serves the role of Head of Department.

We teach over 2000 students enrolled across undergraduate and master's subjects. We take great pride in providing a friendly and supportive environment, taking particular care to ensure a positive experience for our students. We oversee La Trobe's courses in undergraduate Biomedicine, Masters in Biochemistry and Biotechnology, and Masters in Biotechnology Management, as well as teach in to La Trobe's undergraduate Science course and offer fully online subjects through Open Universities Australia. A number of our teaching staff have been recognized as Fellows of the UK's Higher Education Academy and have received university and national awards for innovation and excellence in curriculum design and delivery.

Our department trains graduates who are ready to take up a diverse range of job opportunities, with potential careers in research institutes, manufacturing and chemical industries, pharmaceutical and biotech companies, government departments and agencies, as well as pathology laboratories and hospitals.

The Department has a dynamic Higher Degree by Research (HDR) program that reflects the multidisciplinary interests of the staff. We are currently training 80 PhD and Masters students and 20 Honours students from Australia and overseas.

Research carried out in the Department is world leading and focusses on some of today's biggest challenges in biomedicine and biotechnology. Staff and postgraduate students research molecular structure and design, the molecular basis of human health and disease, and have a strong focus on translating our fundamental discoveries into new diagnostics and treatments. Indeed, our department has several embedded biotech companies including Hexima Limited, Adalta Limited, and Immunexus. Our breadth of expertise and co-location in the world-class facility of the La Trobe Institute for Molecular Science (LIMS) creates opportunities for new discoveries in molecular science and the important health challenges of cancer, neurodegenerative diseases, infection and immunity, and cardiovascular disease. Through this research, members of the Department are key contributors to La Trobe's new Research Theme Understanding and preventing disease.

The Department's research activities also underpin La Trobe Universities rating of '5-well above world standard' in latest round of Excellence in Research Australian (ERA) in the broad areas of Chemistry and Biology, and in the discipline areas of Analytical Chemistry, Biochemistry and Cell Biology, Medicinal and Biomolecular Chemistry. The department has also contributed to similarly high ratings in are areas of Microbiology and Neuroscience.

The Department's research environment is dynamic and multidisciplinary and includes strong collaborative ties with world-renowned medical research institutes such as The Olivia Newton John Cancer Wellbeing Centre, and The Baker Heart and Diabetes Institute, as well as facilities such as the Australian Synchrotron. We are home to these major research centres:

- Research Centre for Extracellular Vesicles
- Centre Research Biomedical and Environment Sensor Technology (BEST)
- Research Centre for Molecular Cancer Prevention

We are also the founding department for LIMS (the La Trobe Institute for Molecular Science).

Research Centres

- Biomedical and Environment Sensor Technology (BEST) Research Centre
- La Trobe Institute for Molecular Science
- Research Centre for Extracellular Vesicles
- Research Centre for Molecular Cancer Prevention

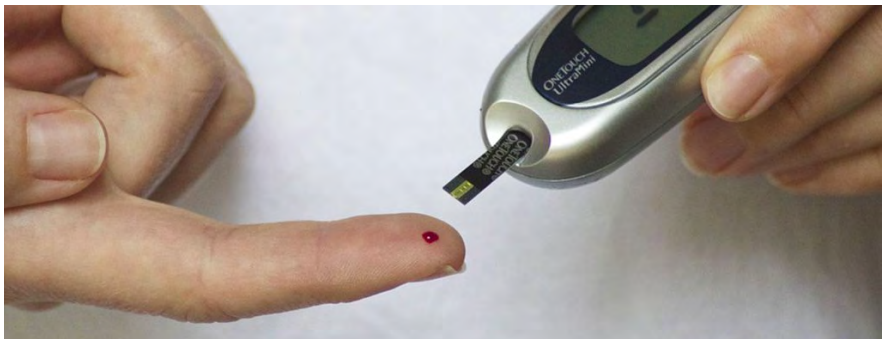
Biomedical and Environment Sensor Technology (BEST) Research Centre

The Biomedical and Environmental Sensor Technology (BEST) Research Centre holds a goal of improving the quality of life for people within our society. We aim to do this by developing new and better sensor technology. Sensor technology is an important research field. Chemical sensors and biosensors provide essential information about our chemical and biological environment. In doing so, they enable better quality of life through accurate and personalized medical diagnoses, efficient energy use, better industrial processes, safer and more ethical food, and a cleaner environment. Because sensor technology is a very broad topic, we have brought together a range of varied expertise from academia and industry. Through collaboration, we can create better sensors, and improve quality of life. The BEST Centre is focused on developing the next generation of sensor technology. Our research covers a broad range of areas from health and disease diagnosis to sensing for transport and energy networks.

Nanofabricated molecular imaging devices for disease diagnostics and environmental monitoring
Development of nanostructured microscope slides to detect the presence of diseased or abnormal cells (e.g. cancer or MS) and also to monitor changes in chemical composition at the nanoscale through combination with microfluidics.

Optical nanoscopy of lipid membranes
Using the newly developed La Trobe near-surface optical microscope we will continue to develop quantitative optical microscopy methods for characterising the composition and topography of cell membranes.

Fluorescent reporters for sensing and imaging proteostasis dysfunction
Developing novel fluorescent probes to quantify proteostasis, which ensures proper protein folding and function, and prevents accumulation of unfolded and misfolded proteins. Methods to quantify proteostasis capacity and the impact on individual proteins on a global scale in cell are currently lacking. Therefore, we are developing novel fluorescent probes which are being tested by collaborators in the Royal Melbourne Hospital, and the Nationwide Children's Hospital, Ohio, USA.



Nanoscale phase contrast imaging combined with metal-conjugated antibody detection
X-ray fluorescence measurements conducted at the Australian synchrotron using metal-conjugated antibodies permit molecular tracking with a much larger parameter space than current optical approaches. When combined with ultrasensitive phase contrast mapping (ptychography) this project will deliver a new X-ray based technique for molecular imaging in-situ which simultaneously characterises the tissue microstructure.

Functional heterobimetallic probes for sensing sugars
Development of new molecular organometallic probes for sensing biologically important carbohydrates and glycalated proteins. This project will result in improved methods for diagnosis and management of diseases associated with these markers such as diabetes and Alzheimer's disease.

Innovative approaches to sensing based on synthetic biology
The rapid detection of contaminants at low concentrations is essential to prevent the spread of nefarious substances through the environment. Sensitivity and specificity of detection is vital to prevent environmental and economic damage. Synthetic biology provides a systematic approach to rationalising molecular pathways within microbes allowing the programming desired outputs from specific inputs such as heavy metals.

New miniaturised instruments for point-of-care immunodiagnostic applications
This project epitomizes in many ways the principles of BEST. A collaboration which seeks to translate some of the high impact fundamental science emerging from the chemistry discipline in recent years, by leveraging expertise in the physics discipline in instrument development; and the largely untapped resource comprising the electronics and product design capabilities of the School of Molecular Sciences workshop. Underpinned by solid market research, this project will provide a new platform to showcase next generation diagnostics.

Mobile phone-based based point-of-care diagnostics
Detection of Sepsis and Malaria biomarkers utilising only a cheap disposable sensor strip and the built-in audio and camera of a mobile phone to carry out sophisticated electrochemical and luminescence-based analyses. More broadly, making inexpensive, quantitative sensors for medical sensing applications to make chemical and biochemical analysis, usually confined to the lab, widely available through similar "instrument free" analysis.

New Electrochemiluminescence based detection strategies
Develop novel supramolecular assemblies that exhibit electrochemically-sensitized luminescence (ESL) by coupling metal complex donors to either luminescent nanoparticles or fluorescent proteins. These assemblies are predicted to have unique sensing properties using simple analytes and bio-markers.

Director:
Professor Conor Hogan

Strategic Partners:
Advanced Molecular Technologies; Metrohm AG; MiniFab Pty Ltd; Universal Biosensors.

La Trobe Institute for Molecular Science

The La Trobe Institute for Molecular Science (LIMS) brings together La Trobe University's leading researchers to work on some of the most critical problems facing our world today. The research agenda of LIMS is supported by a state of-the-art facility where scientists in different disciplines work together in well equipped, shared work-spaces to achieve outcomes that would not be possible in traditional academic settings. The Institute's vision is achieved through excellence in four thematic areas of research strength: Cancer, Infection and Immunity, Molecular Design and Nanoscience.

Cancer

The Cancer theme investigates the mechanisms of cancer initiation and progression, the crosstalk between cancer cells and the surrounding environment, and the potential of novel therapeutic approaches for combating disease.

Infection and Immunity

The Infection and Immunity theme studies the molecules used by viruses, bacteria, parasites and fungi to infect humans, animals and plants, and the immune response associated with this.

Molecular Design

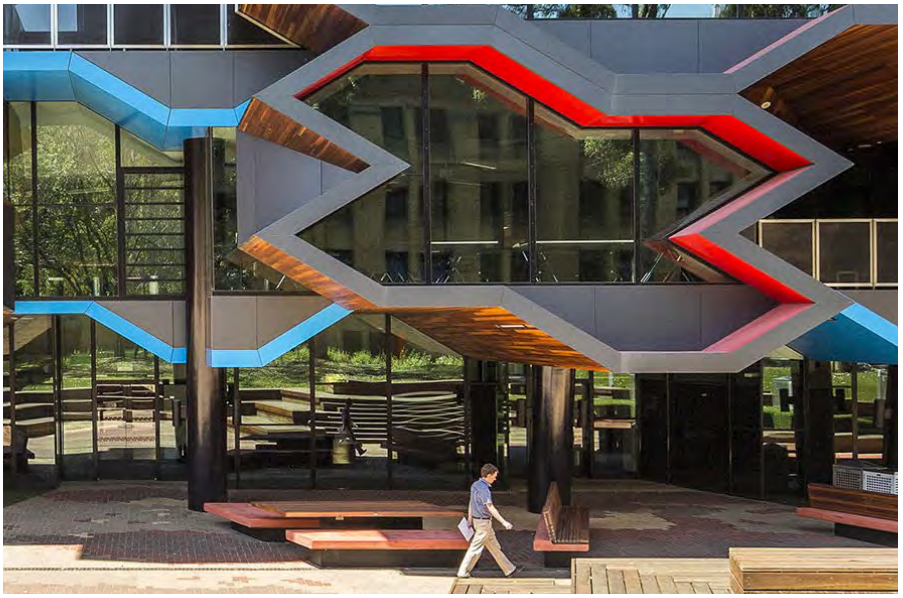
The Molecular Design theme uses molecules to solve real world problems across a broad range of disciplines.

Nanoscience

The Nanoscience theme uses a broad range of methods to characterise molecular structure and function, and to identify and quantitate key chemical and biochemical species in the environment and in the human body.

LIMS Facilities

The Institute's research agenda is supported by a state-of-the-art facility where scientists from different disciplines work together in well equipped, shared work-spaces to achieve research outcomes that would not be possible in traditional academic settings.



LIMS has in-house facilities for bioinformatics, flow cytometry, microscopy, genomics, nuclear magnetic resonance (NMR), and mass spectrometry. It additionally houses inductively coupled plasma (ICP) equipment, atomic absorption spectrometer (AAS), X-Ray diffractometer, crystallography, and laser research. As well as a comprehensive Proteomics Platform, suite of Surface Science and Surface Analysis equipment and a Histology Facility.

Embedded Biotech Companies

LIMS also has several embedded biotech companies including: **Hexima Limited,** which is developing plant-derived proteins and peptides for applications such as human therapeutics and the genetic modification of crops; and **AdAlta Limited,** which is developing the next generation antibody platform, the i-body, to deliver high affinity and specific biologics against a variety of therapeutic and diagnostic targets. **Imunexus** is the latest biologics company to join LIMS. LIMS has outstanding links with the **Australian Synchrotron**. Several of the Institute's physicists design and build synchrotron components.

Game-changing partnerships also enhance the Institute's efforts to raise its research capabilities to new levels of national and international significance. An important collaboration with the **Olivia Newton-John Cancer Research Institute** facilitates the sharing of knowledge, skills, training and facilities.

LIMS Fellowships

The LIMS Endowment Fund was established to create new and sustainable opportunities for scientists with outstanding potential via the inaugural Bruce Stone Fellowship in Chemical Biology and Nicholas Hoogenraad AO Fellowship in Molecular Sciences.

LIMS Fellows Society

The LIMS Fellows Society fosters support, communication and career development for postdocs at LIMS and La Trobe University's partner institutions, such as Olivia Newton-John Cancer Research Institute, AdAlta and Hexima.

Director:

Professor Patrick Humbert

Research Centre for Extracellular Vesicles

The La Trobe Research Centre for Extracellular Vesicles (RCEV) integrates a diverse group of internationally recognised researchers sharing a major interest in the study of extracellular vesicles (EVs). Our team explores EVs and their critical role in cell and tissue communication. We are based in the School of Agriculture, Biomedicine and Environment. Our team has expertise in the isolation and analysis of extracellular vesicles from cells, biofluids and tissues and next generation deep sequencing of EV cargo (especially small RNAseq and available workflow/technology).

We provide our national and international collaborators and industry partners a unique hub, for research, learning and engagement. Our objective as a research centre is to work with national and international groups to study how and why EVs mediate cell-cell communication. We hope to explore ways of harnessing this power.

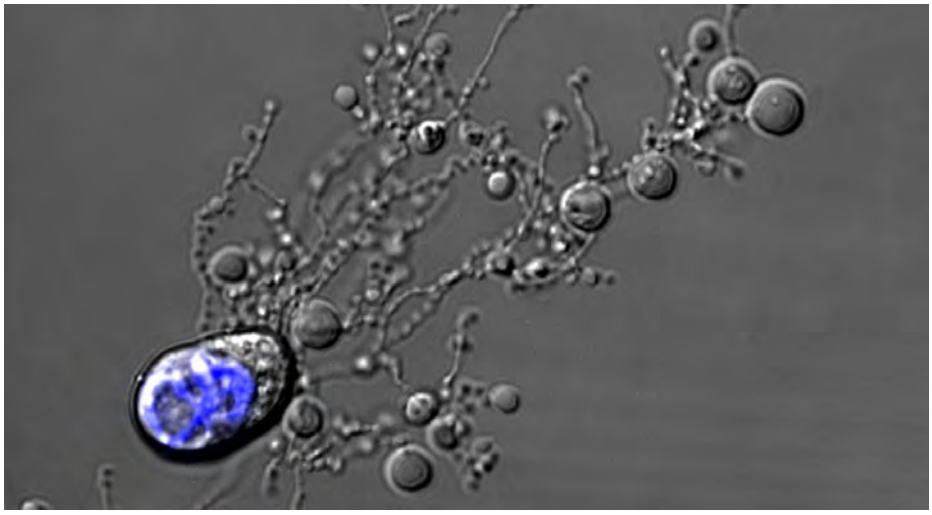
We do this by:

- building an Australian Research Centre encompassing academic researchers, industry partners and educational activities to gain knowledge about EVs in intercellular communication.
- spearheading a multidisciplinary, collaborative program of research to understand, monitor and exploit EVs in the normal and disease processes of all organisms, from plants to humans.

We are studying EVs to advance our understanding of their novel role in the fundamental cellular processes of cell to cell communication and potential biological applications. In the future, we will translate results from these basic biological studies to outcomes with real world impact. Our ultimate aim is to develop methodologies to use EVs for diagnostic purposes in medicine and agriculture and as tools to deliver therapeutics in humans, animals and plants.

New methodologies

We are developing new, rapid and rigorous methodologies for EV isolation and characterisation. This enables extraction and functional analysis of distinct EV subtypes from biofluids and clinical samples, quantification of the biophysical, genetic, protein, and lipid makeup and how this exerts functional changes in target tissues.



White blood cell (monocyte) undergoing programmed cell death (apoptosis). Photo credit: Georgia Atkin-Smith and Ivan Poon

Vesicle biogenesis

Our researchers are also dissecting vesicle biogenesis - the cellular pathways that regulate how different EVs, called exosomes, microvesicles and apoptotic vesicles are formed and released by cells. Once we understand this, it may be possible to manipulate different stages in a targeted way and control cell to cell communication.

Biomarkers

EVs represent a reservoir of new biomarkers for pathogenesis and susceptibility to disease and as drug delivery vehicles for novel therapeutics. We are studying novel and specific disease associated biomarkers in EVs isolated from clinical samples, including cancer, neurodegenerative diseases and the early stage of pregnancy.

Host-pathogen communication

We are also studying the role of EVs in host-pathogen communication during fungal and bacterial pathogenesis and in the transfer of antibiotic resistance.

Director:
Professor Suresh Mathivanan

Strategic Partners:
The University of Adelaide
Baker Heart and Diabetes Institute
Curtin University
The Florey Institute of Neuroscience & Mental Health
Garvan Institute of Medical Research
Hudson Institute of Medical Research
The University of Melbourne
Monash University
Murdoch Children's Research Institute University of Sydney
QIMR Berghofer Medical Research Institute
University of Queensland
University of Technology Sydney
Walter and Eliza Hall Institute of Medical Research University of Western Australia
Aalborg University, Denmark
University of Auckland, NZ
Beijing Genomics Institute, China
University College London, UK
University of Gothenburg, Sweden
Hallym University, South Korea
University of Hohenheim, Germany
Kings College London, UK
University of Oxford, UK
Institute for Systems Biology, Seattle, USA
University of Texas, USA
University of Virginia, USA
University of Utrecht, Netherlands

Research Centre for Molecular Cancer Prevention

The Research Centre for Molecular Cancer Prevention (RCMCP) is a research program for the discovery and implementation of molecular cancer prevention strategies. We are based in the School of Molecular Sciences and collaborate with key local, national and international researchers and conduct multidisciplinary research. Our objective is to lead innovative research and research training in molecular cancer prevention.

We do this by:

- integrating the expertise and capabilities at La Trobe University into new and innovative research programs, enabling molecular targeted cancer prevention therapies that benefit and impact society.
- providing cross-discipline education, training and career development opportunities in cancer prevention research and related skills.

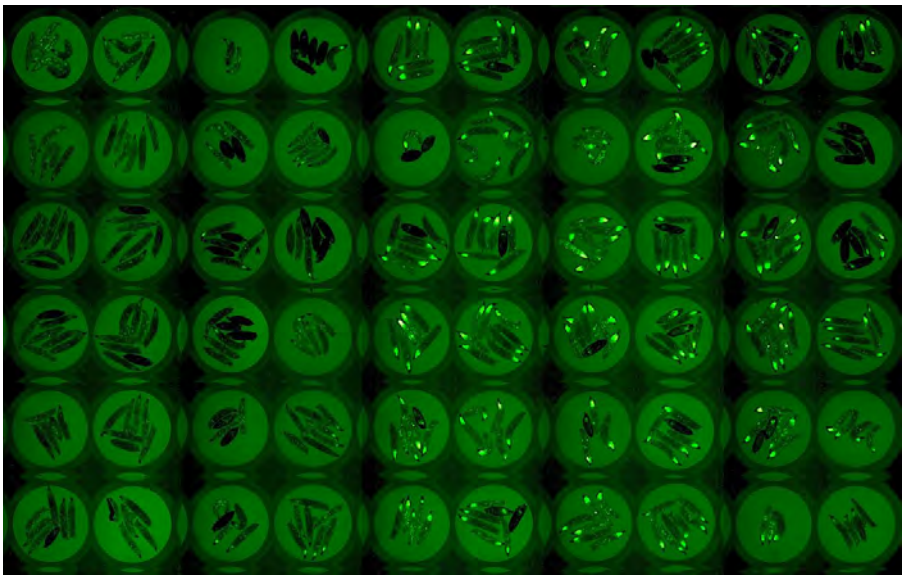
Why study cancer prevention?

There is a 1 in 2 lifetime risk of developing cancer. Breast and prostate cancers are the most common cancers and by age 50, the majority of Australians will already carry silent, premalignant lesions.

Evidence-based economic and health burden studies show preventative approaches to cancer therapy are cost-effective and improve patient wellbeing. However, a major hurdle for new cancer prevention strategies is that we do not understand the biology of cancer initiation.

We need to develop new and improved preventative therapies, specifically designed to target the early biology of breast and prostate cancer. We also need to develop effective strategies for the uptake and implementation of promising molecular prevention therapies.

We are studying the earliest cellular events in cancer to develop new chemo-preventative strategies for breast and prostate cancer. Our research will involve proof of principle basic and pre-clinical studies.



Ultimately, we want to undertake human clinical trials of novel therapeutic agents to implement early intervention and prevention of cancer.

Cancer initiation and the microenvironment

To identify and test biomarkers, we are studying the first molecular changes in cancer cells and the immune surveillance systems that protect us from cancer.

Precision Medicine

To generate specific targets for drug discovery, our researchers will also probe the molecular mechanisms that underlie lifestyle factors such as diet and nutrition that may alter cancer risk.

Barriers to molecular cancer prevention

Uptake of molecular treatments and delivery to the community are barriers to cancer prevention programs. We are developing new implementation models and guidelines to overcome this.

New cancer prevention therapies

We will translate our findings to patients via clinical trials of candidate and newly identified preventative therapies.

Director:

Professor Patrick Humbert

Strategic Partners:

Our centre promotes cross-disciplinary networks and research in the scientific and wider communities. The relationships include:

La Trobe University

School of Cancer Medicine
School of Psychology and Public Health
School of Allied Health, Human Services and Sport

National

Olivia Newton John Cancer Research Institute Olivia Newton John Cancer Wellness and Research Centre
Peter MacCallum Cancer Centre
Victorian Comprehensive Cancer Centre (VCCC)
Royal Melbourne Hospital
The Royal Women's Hospital
Austin Hospital
Community members and cancer survivors.

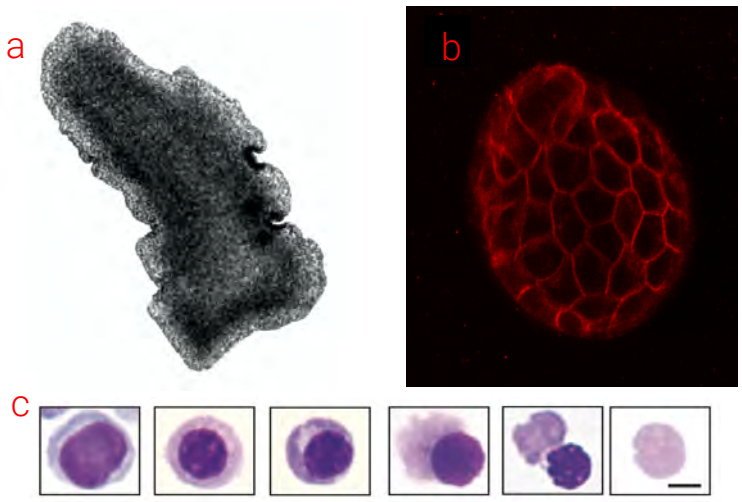
International

International Centre for Genetic Engineering and Biotechnology, Trieste, Italy
University of Veterinary Medicine Hannover, Foundation (TiHo), Germany
University of California San Francisco, USA
University of California Santa Cruz, USA

Research Groups

Cancer Biology, Cell Polarity, and Tissue Architecture Group

Cell polarity, or asymmetry, a basic property of all cells, is encoded by an evolutionarily conserved genetic program that coordinates the differential division of stem cells, the positioning of cells within an organ, and the precise architecture of the organ. Disruption of this genetic program leads to tissue disorganisation and can promote the first steps of cancer. Our laboratory studies how cell asymmetry and tissue organisation can regulate cancer initiation, progression and metastasis. We aim to devise therapeutics to help tumours to "reorganise" themselves, thereby stopping the cancer's growth and spread. We also study how the cell polarity genetic program's involvement in tissue regeneration on earth and in space, as well as in developmental processes (e.g. blood cell production and function). Our multi-disciplinary approach encompasses state of the art imaging, genetically engineered mouse models, and the use of powerful genetic and chemical screens. We work closely with cancer clinicians and pathologists.



a), Trichoplax adherens, one of the simplest and most ancient animals; b), Expression of cell polarity protein Scribble (Red) in 3D MDCK cell cultures; c), enucleation of a mouse red blood cell

"Re-organising" early breast and prostate cancer as a preventative approach

Loss of the proper orientation of cells within a tissue, known as cell polarity, is one of the hallmarks of breast and prostate cancer and is correlated with more aggressive and invasive cancers. How loss of cell polarity occurs and how it contributes at the molecular level to tumour formation remains unknown. Using approaches including RNAi screening, we identified genes that mediate the tumour suppressive functions of cell polarity. We use this new molecular information to re-establish normal tissue architecture through clinically approved drugs and aim to stop early tumour growth.

The evolutionary origin of cancer

How did cancer begin? The advent of the first multicellular animals from single cells required new molecular mechanisms that allowed cooperation between cells and suppressed any conflicts that enhanced the individual fitness of any one cell, stopping them from "cheating" to the detriment of the organism. We study these very first cancer protective mechanisms in one of the oldest and simplest animals on earth, *Trichoplax*. Most human disease genes including cancer suppressing genes are found in this organism. By studying how it escapes cancer, we hope to gain insights into the origins of cancer that will be translated to humans.

The role of gravity in tissue organisation and regeneration

Since life began on Earth four billion years ago, gravity has been the only constant environmental factor accompanying the evolution of life. The role gravity has played with respect to the establishment and maintenance of tissue organisation in multicellular organisms is unknown. Physiological effects resulting from hypergravity or microgravity (weightlessness) have been noted with detrimental effects on bone and muscle turnover, and wound healing in humans. This is a crucial factor for international space programs which aim at a long-term stay of humans and bioregenerative life support systems in space. Through our close connection with the German Aerospace Centre (DLR), and in partnership with TiHo, Hannover, we are testing for the first time how altered gravity may affect the development of tissue architecture and regenerative programs in the simplest and most ancient animal, *Trichoplax*. We use short-term space flights in sounding rockets and ground-based microgravity simulators to provide new insights into how all animal tissues are organised and regenerated.

How did the red blood cell lose its nucleus?

Red blood cell enucleation (extrusion of the nucleus) is a feature of mammalian blood required for proper circulation of red blood cells (RBCs) through the microvasculature and increased haemoglobin concentration in blood. A major challenge for transfusion medicine is the difficulty obtaining sufficient supplies of specific RBC subtypes. Despite advances in *in vitro* production of human RBCs from hematopoietic, embryonic, and induced pluripotent stem cells, the reduced ability of these cultured cells to fully enucleate remains a major hurdle. We study the molecular mechanisms regulating the enucleation process to provide improved strategies for the efficient and rapid production of RBCs for self-generated patient transfusion.

Lab Head: Professor Patrick Humbert
Lab members: Ms Bree Mellberg; Mr Lucas Newton; Ms Yuliya Stepkina

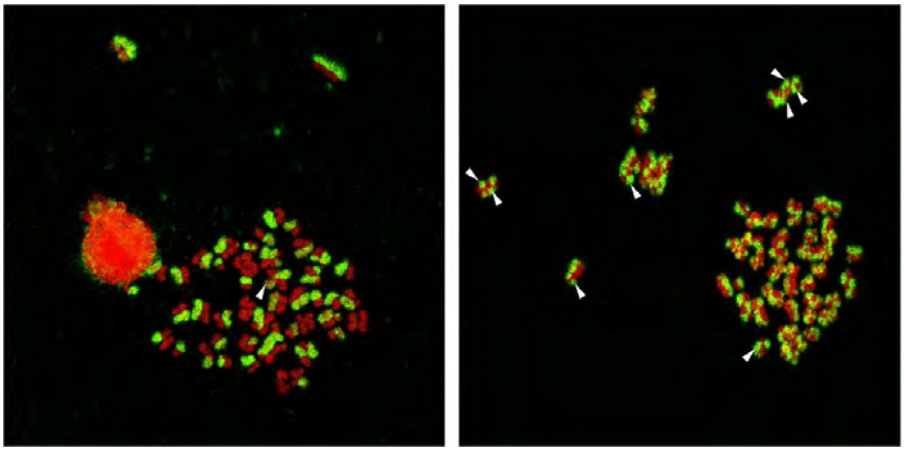
Fields of Study:
Cell development, proliferation and death; Cellular interactions; Cancer cell biology; Space Sciences; Cell Polarity; Erythropoiesis

Capabilities and Techniques:
3D cell cultures; Animal models of disease; Functional screening; CRISPR-Cas9 gene editing; Microscopy – electron, confocal, light; Flow cytometry; Protein biochemistry; Microgravity simulation; Real microgravity experimentation, sounding rockets

TranslationalOpportunities:
Human patient-derived 3D organoid cultures; Pre-clinical animal models of cancer for drug screening.

Cancer Cell Death Group

Cells can die, or be killed, by physical or biochemical damage. Some cell death mechanisms are "programmed" (cell death is caused by the cell's own proteins, encoded in its own genes). This enables the elimination of dangerous cells that could wreak havoc in the individuals that habour them. Apoptosis, necroptosis and pyroptosis are regulated processes that destroy surplus and dangerous cells. Excessive apoptosis has been linked with degenerative diseases, while defects in apoptosis can promote cancer, infection and autoimmune disease. Necroptosis can eliminate infected or cancerous cells that are unable to undergo apoptosis. Pyroptosis is primarily implicated in the destruction of cells following bacterial, viral or protozoal infection. By understanding the proteins that control cellular self-destruction pathways, and their aberrations in cancer and infectious diseases, we are pursuing diagnostic and therapeutic approaches to target these conditions.



untreated cisplatin treated

DNA repair in chemotherapy-treated cells (Photo credit: Mark Miles)

Yeast systems for identifying new drugs and proteins that regulate cell death

Researchers have been mapping the biochemical pathways that control cell survival and susceptibility to apoptotic, necroptotic or pyroptotic cell death. We reconstituted these pathways in yeast, a simple, single-celled organism that shares many features of cellular structure and biochemical pathways with more complex species like humans. Our yeast systems enable rapid, high-throughput screening for novel drugs that can either enhance or suppress apoptotic, necroptotic or pyroptotic cell death pathways. We use these platforms to characterise or identify proteins from host cells or pathogens that regulate or perturb these cell death pathways.

Animal models of sarcomas

We developed multiple mouse models of bone and soft tissue cancers that typically arise during teenage years, including osteosarcoma and Ewing sarcoma. Our model faithfully emulates "metastatic disease", the dangerous phase in which tumours spread from their original sites (e.g. bone or muscle) to other organs in the body, (e.g. lungs). This transition heralds poor outcomes for patients; current anti-cancer treatments are often powerless to cure these metastatic cancers. We developed a technique that allows cancer cells injected into the blood of mice to form tumours in their lungs, mimicking metastatic bone and soft tissue cancers. We use these models to evaluate potential new drug treatments that we hope will improve cancer survival rates.

Smac mimetics/IAP antagonists

Drugs resembling the cellular protein "Smac" can disable other proteins (called "IAPs") within cancer cells that allow some tumour cells to withstand stimuli that would otherwise destroy them. These "Smac mimetics" or "IAP antagonists" are promising anti-cancer agents. We have discovered that a subset of these drugs are able to control and sometimes eliminate bone cancers growing in the lungs of mice, modelling an often-fatal manifestation of this type of cancer.

Curing cancer without causing cancer

About 20% of cancer survivors develop new tumours, many of which are caused by cancer therapies. Chemotherapy and radiotherapy cause DNA damage in cancerous cells. Cells respond by triggering apoptosis, which hopefully eliminates the cancer. Other cells can be damaged during chemotherapy or radiotherapy treatment, if these cells survive, they can form new cancers. Recent research has been focused on the development of drugs that directly kill cancer cells, rather than provoking DNA damage to indirectly induce tumour cell death. Some new drugs have shown robust anti-cancer activity in animal experiments and clinical trials. As direct apoptosis inducers do not need to damage DNA to kill tumour cells, we hypothesised that they may provoke fewer mutations in surviving cells, so may be less likely than current therapies to cause secondary cancers. We found that drugs that trigger necroptosis failed to provoke mutations in surviving cells, in contrast to highly mutagenic chemotherapy drugs. It is hoped that cancer survivors treated with necroptosis-inducing agents will have a lower risk of developing therapy-related cancers.

Lab Head:
Associate Professor Christine Hawkins
Lab members: Mr Yanhao Ji; Mr Michael Harris; Ms Matilda Mikic; Ms Seirian Hart; Mr Dushan Peiris.

Fields of Study:
Biomedicine; Cancer; Molecular Genetics; Biochemistry.

Capabilities and Techniques:
Animal models; Cell Biology; Fluorescence microscopy; Flow cytometry; Microbiology; Molecular Biology; Biochemistry.

Translational Opportunities:
Oncology; Biotechnology; Pharmaceuticals.

Cell Death and Survival Group

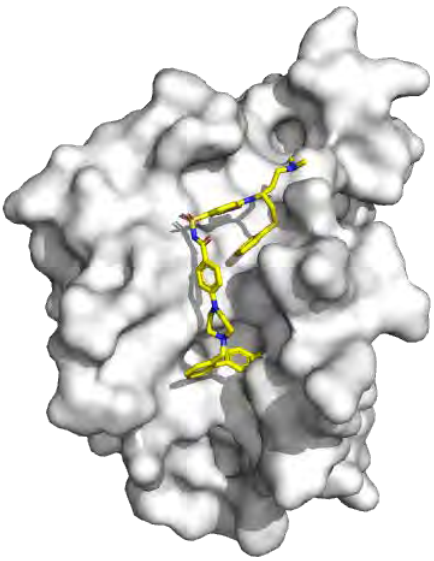
Our group is uniquely positioned at the cross-roads of SABE and the School of Cancer Medicine (Olivia Newton-John Cancer Research Institute). Our research investigates how our cells determine their fate. In particular, we aim to understand what goes wrong in this decision-making process in disease and to then utilize this knowledge for therapeutic intervention. Using a combinatorial approach based on biochemistry, cell biology, and animal-based techniques, we seek to decipher the molecular mechanisms regulating cell fate decisions. Our research focuses on the pathways of cell death known as apoptosis, and of cell survival known as autophagy. Deregulation of these processes have been implicated in diseases such as cancer and inflammatory bowel disease.

Targeting apoptosis for cancer treatment

Our Group has a long and productive track record in the study of the intrinsic apoptotic pathway regulated by the BCL-2 family of proteins. Deregulation of this pathway can result in insufficient cell death and is a hallmark of cancer. Over the years, we have made significant contributions to how this pathway is regulated and to international collaborations that have led to the development of clinically approved drugs targeting it. Our current program investigates the clinical application of drugs that induce apoptosis in incurable and aggressive solid cancers with low overall survival rates. As part of this program, we collaborate with pharmaceutical companies such as AstraZeneca and AbbVie.

Novel regulators of intestinal homeostasis

We also have a research program that focuses on the cell survival pathway of autophagy. This evolutionarily conserved process of cell recycling enables unwanted cellular material to be degraded by the lysosome and is critical for maintaining a healthy cell. Mutations in the pathway have been strongly associated with inflammatory bowel disease. We are currently investigating how well-established regulators of autophagy regulate intestinal homeostasis at a molecular level. Our studies have yielded unexpected but exciting results showing that a key autophagy regulator also has a moonlighting role in another pathway that is critical for maintaining a healthy gut.



BH3-mimetic drug (yellow) bound to its target protein (BCL-XL; white).
Photo credit Doug Fairlie and Erinna Lee.

Mechanisms of novel cancer drugs

Drugs that inhibit the growth or survival of cancer cells can be developed without necessarily knowing their precise molecular targets or mechanism of action. However, in many cases these mechanisms involve the apoptosis and/or autophagy pathways. As a consequence of our long-term interest in these areas, we have developed relationships with a number of pharmaceutical companies to evaluate drugs they are developing and establish the mechanisms underlying their anti-cancer effects. This work provides further insights into novel approaches for targeting cancer cells and important data to support clinical approval of these compounds by regulatory bodies.

Drug screening

A recent successful grant application has enabled the ONJCRI to purchase a liquid handling robot. Our lab has now established an efficient experimental pipeline using this robot that allows for the screening of drug libraries on cancer cells. We now plan to initiate a new screening platform that enables researchers to collaborate with us on projects that facilitate the discovery of new strategies for targeting cancer cells.

Lab Heads:

Associate Professor Doug Fairlie and
Associate Professor Erinna Lee

Lab members:

Dr Laura Jenkins;
Ms Sharon Tran;
Ms Julie Juliani;
Ms Tiffany Harris;
Mr Kristian Caracciolo.

Fields of Study:

Apoptosis;
Autophagy;
Cell Biology;
Cancer;
Gastrointestinal Biology and disease.

Capabilities and Techniques:

Cell survival and death assays; high throughput drug screening; genetic editing of apoptosis and autophagy pathways; genetic mouse models of disease.

Translational Opportunities:

Drug screening;
Mechanism of action studies;
Drug validation.

Cell Polarity, Cell Signalling and Cancer Group

Our group uses the vinegar fly, *Drosophila,* to model cancer to understand how regulators of cell shape (polarity) impact on cell signalling and cancer development. We also aim to understand the signalling pathways in the tumour microenvironment that dictate whether polarity-impaired mutant cells live or die. *Drosophila* is a great organism to model cancer due to the high conservation of critical genes and signalling pathways between flies and man, its low genetic redundancy, short life cycle and cheap maintenance costs. We seek to translate our findings from *Drosophila* to mammalian systems by collaboration with Professors Patrick Humbert and Marc Kvansakul at LIMS.

Genetic analysis using the Drosophila adult eye validates Tsp29Fb as a tumour suppressor

Determining how cell polarity proteins control signalling pathways
We discovered that the cell polarity regulator, Lgl, regulates the Notch signalling pathway by effecting vesicle acidification and γ-secretase activity. Using mass spectrometer analysis we identified proteins involved in linking Lgl to the vacuolar-ATPase (v-ATPase), which regulates vesicle acidification. We also found that Lgl and the v-ATPase are involved in regulating the Hippo negative tissue growth control pathway by using genetic, cell biological and biochemical approaches. These studies will potentially provide new avenues for targeting polarity-impaired human cancer.

Modelling Cooperative Tumourigenesis: Determining the link between cell polarity, signalling, tissue growth and tumourigenesis.
We identified novel tumour suppressors that cooperate with oncogenic Ras (Ras^{V12}) in cancer progression in a genetic screen. These novel tumour suppressors include membrane proteins, autophagy, vesicular trafficking, cytoskeletal and metabolic regulators. We aim to determine how knockdown of these tumour suppressors results in cooperative tumourigenesis with Ras^{V12}. We found that knockdown of autophagy genes cooperates with Ras^{V12} to promote hyperplasia of the *Drosophila* eye tissue. Also, autophagic gene knockdown together with Ras^{V12} leads to an upregulation of Reactive oxygen species (ROS) and the JNK signalling pathway, which is crucial for the cooperation. We also studied the tumour suppressor role of a Tetraspanin, Tsp29Fb/TSPAN6, (a four-pass membrane protein) and found it regulates EGFR-Ras signalling in *Drosophila* and mammalian systems. We now wish to study the involvement of the novel tumour suppressors that we discovered in Ras-driven human cancers.

Analysis of a surveillance mechanism involved in preventing cancer initiation.
Cell competition is a surveillance mechanism that acts to remove less-fit cells in an epithelium. We have shown that a phosphatase, PTP61F (ortholog of mammalian PTPN1/PTPN2) is involved in the elimination of polarity-impaired cells in the *Drosophila* developing eye epithelium by inhibiting JAK-STAT signalling in mutant cells. It also has a role in the surrounding normal cells where it functions non-cell autonomously to limit elimination of the mutant cells. We also study the receptor phosphatase, PTP10D (ortholog of mammalian PTPRB/PTPRJ), in cell competition of cells with impaired polarity or with cytoskeletal defects. These studies will reveal new approaches for targeting pre-cancerous lessons by identifying ways in which to augment the cell competition process.

Discovery of novel anti-cancer drugs using Drosophila tumour models.
We established a screening platform using *Drosophila* larvae carrying Ras-activated polarity-impaired tumours marked by green fluorescent protein (GFP). The effect of different drugs on tumour development were revealed by quantifying the amount of GFP. We found that a MEK inhibitor (Ras signalling pathway blocker), Tramtinib, was highly potent in reducing tumourigenesis. Our screen revealed compounds that target diacyl-glycerol kinase, are synergistic with low doses of Trametinib, and specifically kill Ras-driven polarity-impaired tumours in *Drosophila* and human epithelial cells. Using a modified system, we will screen for novel compounds that normalize or kill polarity-impaired cells and senescent cells, which are early defects that occur in cancer initiation. We aim to develop a therapeutic cancer 'de-tox' treatment, similar to the HPV-vaccine for cervical cancer.

Lab Head:
Associate Professor Helena Richardson
Lab members: Dr Eddie La Marca; Mr Peter Burke; Ms Natasha Fahey Lozano.

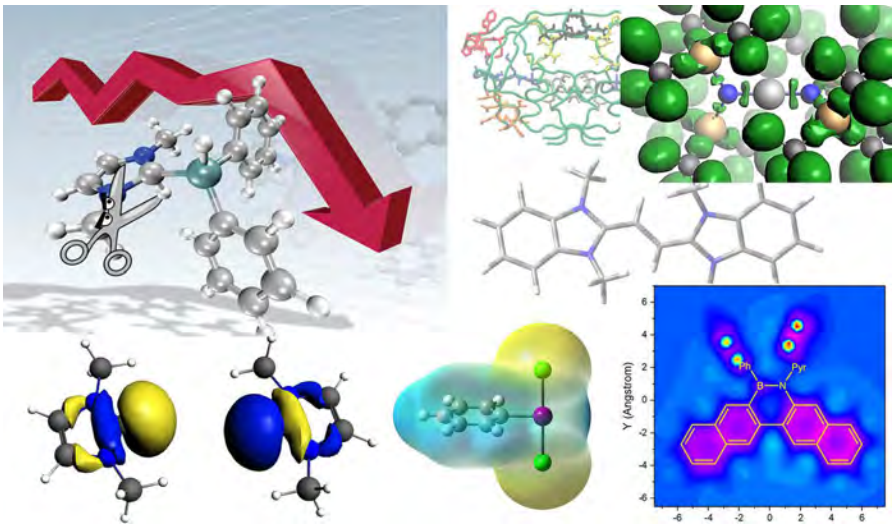
Fields of Study:
Cell Biology; Genetics; Biochemistry.

Capabilities and Techniques:
Drosophila model organism expertise; Immunofluorescence techniques; Confocal microscopy; PCR and Molecular Biology techniques; Genetic analysis; In vivo compound screening.

Translational Opportunities:
In vivo compound screening to identify and develop novel anti-cancer drugs.

Computational Chemistry Group

Our group does chemistry by computer to better understand the structures and properties of molecules and how they react. Our research is highly interdisciplinary and lies at the interface of materials, biology, physics, and chemistry. The goal of our research is to develop quantum chemical tools to calculate accurate chemical properties and then apply these tools to problems of chemical structure, mechanism, and design. We employ a range of computational techniques including empirical force fields, density functional theory, and ab initio quantum chemical methods. Our applied studies range from optical materials design to medicinal drug design, including the computational design of optical materials for use as LEDs, new materials for hydrogen storage, efficient catalysts, and accurate modelling of biological molecules. The research is collaborative and involves local, national, and international partners.



Various molecular chemistry structures

Designing new chemistry

Chemistry is in an age where our ability to rationally design and tailor new molecular systems has led to remarkable developments in materials science, drug design, catalysis, and green chemistry. The capacity to engineer new molecules for specific roles is in large part underpinned by advancements in computational chemistry, which is now able to reliably predict the structures and function of molecular systems. Our group has a strong track record in predicting new chemistry and designing molecules for specific use as chemical reagents, medicines, and materials. In collaboration with Professor Jason Dutton and Professor Robert Gilliard, we are demonstrating the remarkable benefits that arise from the synergy of computational chemistry together with advanced synthetic chemistry that provides the capacity for molecular engineering.

Understanding Chemical Reactivity

Optimization of chemical processes is enhanced by an understanding of the mechanism of reaction; it is difficult to optimize an industrial process if the mechanism is not known, if the reacting species in the flask are ill-defined, or do not even exist. Our group has significant expertise and experience in probing chemically important reactions. Current projects include the mechanism of reaction of halogenation reactions with iodine reagents. Techniques to introduce halogen atoms into organic molecules are of fundamental importance to industry because of the ubiquity of these atoms in useful molecules such as medicines, agricultural chemicals, materials, and specialty chemicals.

Light-emitting materials

Our group is focused on the design and understanding of optical properties of molecular systems, including boron-doped organic molecules and metal-based (ruthenium, iridium) complexes. These are projects are often carried out in collaboration with experimental scientists. One current focus is the Incorporation of boron into polycyclic aromatic hydrocarbons (PAH), which has become a key strategy in the search for new molecular materials such as LEDs. Our research seeks to harness the potential of boron, which is increasingly occupying a prominent position in both molecular optoelectronic materials and medicinal drug discovery due to its 'magic' qualities of its ability to form a variety of bonds and capacity to mimic metal properties.

Molecular Shape

Our research is driven by a curiosity of molecular structure and chemical bonding. Molecular science is underpinned by a fundamental relationship between structure and function; understanding the function of molecules as medicines, industrial chemicals, and useful materials, requires a fundamental understanding of molecular structure and shape. We apply the full array of computational chemistry tools to probe the shape and structure of molecules of importance to biochemistry, astrochemistry, optoelectronics and sensing, and materials chemistry.

Lab Head: Associate Professor David Wilson
Lab members: Mr Andrew Molino; Ms Aishvaryadeep Kaur; Mr Johnny Agugiaro; Ms Ishara Peiris; Mr Matt Gosch.

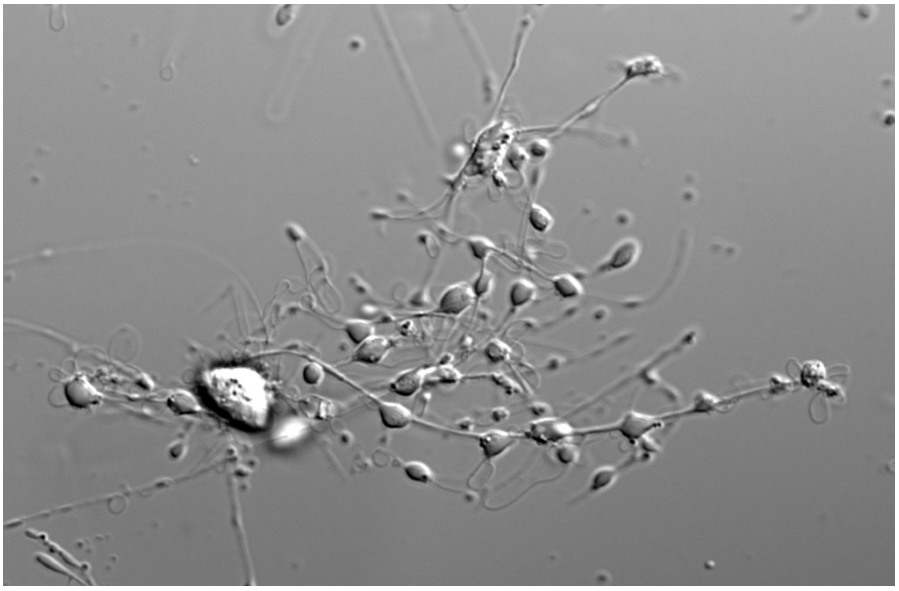
Fields of Study:
Theoretical and Computational Chemistry.

Capabilities and Techniques:
Computational chemistry; molecular structure analysis; reaction mechanism.

Translational Opportunities:
Reaction design and optimisation; optoelectronic materials design.

Dying Cell Clearance and Disassembly Group

Billions of cells die daily as part of normal turnover in various organs. It is vital that dying cells are rapidly removed as their accumulation has been linked to inflammation, autoimmunity, cancer and infection. To aid efficient removal of dead cells, dying cells often disassemble into smaller fragments for neighbouring cells to engulf. Certain cellular components can be packaged selectively into these fragments to regulate tissue repair and immunity. We aim to understand the machinery that controls how dying cells can disassemble into smaller pieces, the importance of cell disassembly in disease settings (e.g. influenza A infection and atherosclerosis), and identify new drugs to control this process.



Dying cancer cell undergoing disassembly. (Photo credit: Stephanie Rutter)

Mechanism of dying (apoptotic) cell disassembly

Apoptosis (programmed cell death) occurs in all tissues as part of development, homeostasis, and pathogenic processes including infection and cardiovascular disorders. Apoptotic cells often disassemble into smaller membrane-bound extracellular vesicles called apoptotic bodies. We have demonstrated that the formation of apoptotic bodies is a highly regulated process in T lymphocytes and monocytes. We discovered a new type of membrane protrusion (coined "apoptopodia") that facilitates the separation of membrane blebs during apoptosis to generate individual apoptotic bodies. The molecular machinery that controls the formation of apoptopodia is undefined. We aim to determine the molecular machineries required for the formation of apoptopodia.

Function of apoptotic cell disassembly in pathophysiological settings

Extracellular vesicles including apoptotic bodies have been implicated to regulate physiological and pathological processes via the molecules they carry inside or exposed on their surface. The importance of generating apoptotic bodies during apoptosis in pathophysiological settings is poorly understood. We study the role of apoptotic cell disassembly in the context of viral infection. During viral infection, infected cells often undergo apoptosis to shutdown cellular machinery as a defence mechanism to limit viral replication. Phagocytic removal of infected apoptotic cells/fragments may also facilitate the spread of infection, and the phagocyte could become infected following the engulfment of apoptotic cells/fragments containing viral particles. Viral proteins have been suggested to accumulate in apoptotic bodies during apoptosis, but the role of apoptotic cell disassembly in the context of viral infection is underexplored. We study apoptotic body formation in influenza A and SARS-CoV-2 infection.

Discovery of novel drugs to modulate the apoptotic cell disassembly process

Apoptotic body formation is a key cellular process for efficient removal of apoptotic debris and intercellular communication in certain disease settings. There is a lack of drugs to target this process so identifying drugs that could modulate apoptotic cell disassembly is important. Using a novel flow cytometry-based drug screen approach, we have identified a number of drugs that can inhibit or enhance the formation of apoptotic bodies without having an impact on the level of apoptosis. Some of these drugs are FDA approved and are currently being used clinically. We aim to characterise these novel inhibitors and enhancers of apoptotic cell disassembly in detail, in particular how these compounds could modulate the morphological steps of apoptotic body formation as well as the activities of known molecular regulators of apoptotic cell disassembly (e.g. ROCK1 kinase and pannexin 1 channel). Furthermore, whether these drugs can be used to control the apoptotic cell disassembly process in disease settings will also be examined.

Lab Head: Associate Professor Ivan Poon

Lab members:
Dr Amy Baxter; Dr Kha Phan; Dr Georgia Atkin-Smith; Ms Gemma Ryan; Ms Amy Hodge; Ms Bo Shi; Ms Jascinta Santavanond; Ms Dilara Ozkocak; Ms Stephanie Rutter; Mr Omar Audi.

Fields of Study:
Cell Biology; Cell Death; Cell Clearance; Extracellular Vesicles.

Capabilities and Techniques:
Time-lapse microscopy; flow cytometry; cell death analysis; drug screening.

Translational Opportunities:
Treatment and diagnostics for infection, cardiovascular and autoimmune diseases.

Electrochemical Sensing Group

Our group conducts a range of both fundamental and applied multidisciplinary research focused on expanding the bounds of Analytical Science. We pursue the development of new chemistries and new technologies which will result in exquisitely low detection limits and enhanced selectivity. Building on breakthrough fundamental science, we seek to develop novel sensing technologies and miniaturised instruments for use outside the laboratory setting. For example, we hold several patents in the use of personal electronic devices such as mobile phones for sensing applications from environmental analysis to medical diagnostics. We also have on-going collaborations with a range of industries and government bodies around sensor development. Working at the interface of electrochemistry and photochemistry, we have pioneered several new approaches to detection science. Our group is a world leader in the application of electrochemiluminescence (ECL) detection to mobile phone readable paper microfluidic sensors and the development of potential resolved multi-coloured ECL or 3D ECL.

Photophysics and electrochemistry of highly luminescent transition metal complexes

We are interested in developing and investigating materials which are electroactive, materials which are luminescent and in particular, materials which exhibit both of these properties simultaneously. One area in which we are are very active, is in the applications of highly luminescent Iridium, platinum and ruthenium complexes. We explore the use of such molecules (with Dr Peter Barnard and others) for applications in ultra-sensitive medical diagnostic and health testing applications.

Ultra-sensitive Electrochemiluminescence (ECL) sensing

Electrochemiluminescence, (ECL) facilitates extremely low (sub-femtomolar) detection limits for bioanalytical measurement, often outstripping fluorescence by several orders of magnitude; but current ECL detection technology consists of large laboratory instruments. We are developing new minimally invasive diagnostic technologies based on electrochemiluminescence (ECL) detection chemistry. This will provide superior detection limits ultimately enabling the detection of biomarkers in saliva.

Android Voltammetry: A simple but powerful smartphone-based biosensing platform

The development of simple, inexpensive (yet quantitative and sensitive) sensors for environmental, medical and other sensing applications is an extremely important emerging area because it has the potential to make chemical and biochemical analysis, usually confined to the lab, more widely available. Such technology can be transformational, particularly in remote areas and in the developing world, where levels of health expenditure are low. Our patented sensing technology called Android voltammetry, developed in the Hogan lab eliminates the requirement for an instrument and harnesses the e xisting audio capabilities of mobile phones to facilitate electrochemical detection. Our first application for this platform (the "ElecTrobe") is set to save millions of dollars for the Australian wine industry each year. By using the audio jack to provide electrochemical stimulation we have replicated what is usually done using expensive laboratory instruments to perform "instrument free" analysis. As the data and associated metadata can be readily shared, this opens up a range of exciting possibilities for e-Health, telemedicine and "crowd sourced sensing". See http://youtu.be/X6zSgFEhFd4 and https://youtu.be/XUXvdd5nMcM. We are currently developing a range of exciting new applications for this platform in the fields of environmental analysis and medical diagnostics.

Design and printing of disposable sensors for electrochemical and ECL detection

Our laboratory hosts a Diamatix materials inkjet printer, a state-of-the-art technology for the production of bespoke printed sensors in significant quantities.

Mobile phone based wine analysis using Fourier Transform AC voltammetry

The materials printer affords unprecedented scope for printing novel sensor designs. We use it to explore the influence of novel sensor geometries on sensitivity in electrochemical and ECL sensing.

Lab Head: Professor Conor Hogan
Lab members: Dr Mohammad Reza Moghaddam; Dr Robert Sikos; Ms Laena D'Alton; Ms Samridhi Bajaj; Ms Helmini D G Dona; Mr David Macedo.

Fields of Study:
Chemistry; Analytical Chemistry; Electrochemistry; Luminescence, Biosensors.

Capabilities and Techniques:
Unique combination of expertise in electrochemistry, photophysics and sensor technology; Proven ability to translate / commercialise basic science for real-world sensor technology applications.

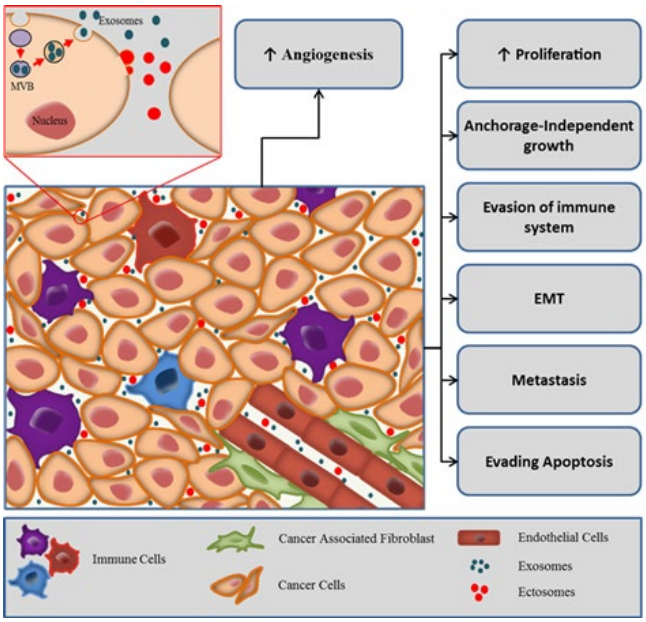
Translational Opportunities:
Proven ability to translate / commercialise basic science for real-world chemical and biosensor technology applications.
Follow us on Twitter @hogansheroeslab and Facebook.

Exosomes, secretome and systems biology

Our major research interests are in exploring the role of extracellular matrix components (soluble secreted proteins and extracellular vesicles) in cancer and intercellular communication. Our lab integrates proteomic, genomic and bioinformatics methodologies to study cancer progression. In addition to medical research, we are also interested in basic science projects including the biogenesis of exosomes and the role of exosomes in intercellular communication.

Exosomes in the tumor microenvironment
Exosomes are 40-100 nm diameter membrane enclosed extracellular vesicles released by various cell types, including cancer cells. For tumors to progress, bidirectional crosstalk between different cells occurs within the tumor and its surrounding supporting tissue. A tumor can be considered as a complex tissue or organ with abnormal cells harboring genetic mutations, typically referred to as tumor or cancer cells, enmeshed within the surrounding and interwoven stroma, the epithelial parenchyma, which provides the connective tissue of the tumor. Stromal elements include the extracellular matrix as well as other cell types that are activated and/or recruited to the tumor microenvironment such as fibroblasts, immune and inflammatory cells, fat cells and endothelial cells of the blood and lymphatic circulation. Recent literature indicated that all aspects of cellular tumorigenicity are profoundly influenced by reciprocal interactions between responding normal cells, their mediators, structural components of the extracellular matrix, and genetically altered neoplastic cells. Exosomes have recently been recognized as important mediators of the cross-talk in the tumor microenvironment. Exosomes derived from tumor cells have been shown to have both pro- and anti-tumorigenic properties. Our lab is interested in studying the role of exosomes in the tumor microenvironment.

Proteogenomics analysis of exosomes and extracellular vesicles
Recent studies have highlighted the secretion of oncoproteins including mutant proteins via exosomes. However, a prior knowledge of the mutant protein is a prerequisite in all of the published studies.



Exosomes role in tumor microenvironment. (Picture credit: Gangoda et al. 2015, Proteomics)

A global approach to systematically identify mutant proteins secreted through exosomes will aid in elucidating the functional roles of exosomes. In order to identify the mutant proteins that are secreted by a cell via exosomes, we use global proteogenomics approach. In addition to functional implications, as exosomes may contain disease causing proteins including mutant proteins/RNA, assaying for mutant or disease-causing proteins/RNA as disease biomarkers may provide the required specificity for a biomarker test.

Systems biology - exosomes and colorectal cancer
Constant dynamic interactions between a cell and its surrounding tissue microenvironment are important in maintaining the differentiated state of a cell. While such organised intercellular signalling cascades are pivotal in cellular proliferation, sustained disruption of key signalling events render the cells susceptible to malignancy. Our group uses systems biology or bioinformatics approaches to study the molecular mechanisms of colorectal cancer. We use proteomic and genomic technologies to study colorectal cancer cells and integrate bioinformatics methods to make biological sense of the obtained data. With the explosion of datasets from high-throughput techniques, systems biology approaches hold immense promise to investigate such data and present them at the context of the disease. It has to be noted that high-throughput data should be dealt carefully owing to the noise and systemic pitfalls. Our group develops computational tools to analyze such datasets and integrate them with heterogeneous datasets obtained from similar biological experiments using statistics and computation.

Lab Head: Professor Suresh Mathivanan.
Lab members: Dr Pamali Fonseka; Dr Christina Nedeva; Dr Sarah Stewart; Mr Sai Chitti; Mr Sanjay Shahi; Mr Taeyoung Kang; Mr Rahul Sanwlani; Ms Akbar Marzan; Mr Kyle Bramich.

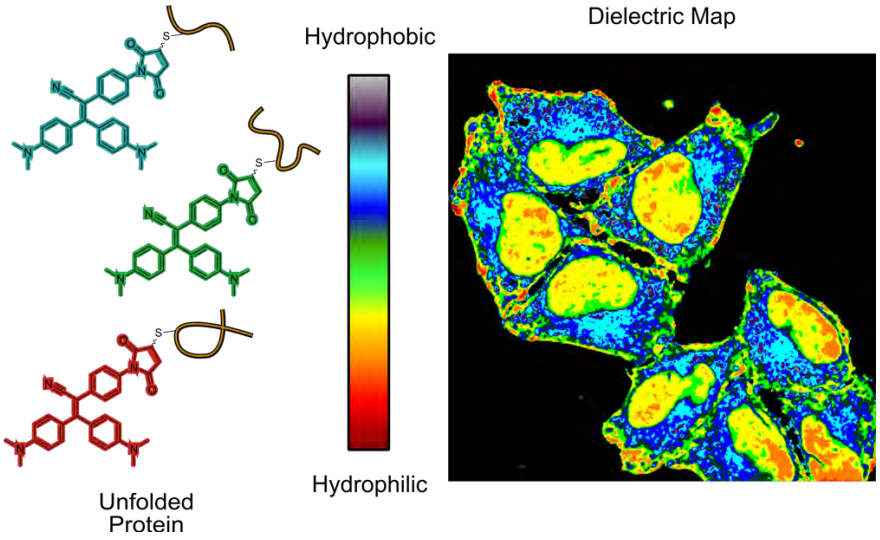
Fields of Study:
Exosomes; Cancer; Extracellular Vesicles; Proteomics; Bioinformatics

Capabilities and Techniques: Extracellular vesicles isolation and characterization; Mass spectrometry; IVIS imaging; Confocal microscopy.

Translational Opportunities:
Treatment for cancer; Therapies to block metastasis; Treatment for cancer cachexia; Cancer prevention.

Fluorescence Chemical Biology Group

Our group develops novel fluorescent probes for understanding and manipulating fundamental biological processes regulating cell fitness and their association with aging and diseases. Our goal is to generate molecular tools that can report on changes such as protein folding, modification and degradation in a native environment such as in live cells and organisms to reveal hidden molecular level mechanisms for the understanding, diagnosis, and potentially treatment of diseases in particular neurodegenerative diseases. The group's work combines multidisciplinary approaches, ranging from synthetic and analytical chemistry, bioconjugation chemistry, molecular and cell biology to bioinformatics, and involves collaborations with local, national, and international partners working on Parkinson's, Huntington's, Motor Neuron Diseases (MND), leukemia and rare diseases.



Mapping Unfolded Proteome (Image credit: Tze Cin Owyong)

Protein Damage in Neurodegeneration

Neurons are postmitotic long-lived cells. Over time, with the accumulated exposure to stress (from ROS production, DNA damage, infection, etc.), the protein quality control system becomes less efficient, leading to accumulation of protein damage and eventually neuron death. Our Group has developed unique chemical tools that can tag on damaged proteins, including those cannot fold properly (e.g. unfolded, misfolded, or aggregated) or undergo aberrant modifications. These tools can selectively tag on damaged proteins, turn on their fluorescence, allowing us to quantify the level of damaged proteins as a measure of proteostasis capacity, imaging unfolded and aggregated protein in cells, mapping subcellular polarity changes in response to protein unfolding, as well as identify those proteins to study protein stability in cells. These tools have been used in the study of Huntington's, Parkinson's, MND, virus infection and antimalaria drugs.

Tracking and Measuring Autophagy

Autophagy ("self-eating") is a cellular housekeeping process in which unwanted components are identified, degraded, and recycled, greatly contributing to cell homeostasis and development, but also the prevention of various diseases. Autophagy is a multi-step, dynamic process. Dysregulation of autophagy has been linked to many diseases, such as neurodegeneration, cancers, cardiovascular and infectious diseases, with different steps of the pathway being impaired. Current tools to study autophagy rely on antibodies or fluorescent protein-based sensors, both of which require modification of the cells prior to the study. Our group develop fluorescent chemical probes that are highly specific to autophagy, which allow us to follow the dynamic process of autophagy and quantify its activity in situ and in a high throughput manner without the prerequisite of genetically modifying the cells. We use these probes in a range of cell models including those derived from Parkinson's patients and model organisms like zebrafish and demonstrate their applications for drug screening, understanding disease mechanisms, as well as studying fundamental biological processes.

Using Luminescence to Fight Antimicrobial Resistance

Antimicrobial resistance (AMR) is a growing health issue recognised by the World Health Organisation (WHO), which has listed AMR as one of the top 10 global public health threats. For example, as a consequence of antibiotic misuse in dental practice, AMR in oral pathogens is becoming more and more prevalent. We develop novel fluorescence for visualizing and inhibiting bacteria growth including those resistant to conventional antibiotics. Some of these molecules also present photodynamic therapy activities, which provide the possibility of using light to kill bacteria in a selective area in a controllable way.

Lab Head: Associate Professor Yuning Hong
Lab members: Dr Bicheng Yao; Dr Siyang Ding; Dr Xavier Zhang; Mr Timothy Gialeris; Ms Soheila Sabouri; Mr Tze Cin Owyong; Ms Karren Jiamin Zhao; Mr Liang Tan; Mr Jack Spencer.

Fields of Study:
Analytical Biochemistry; Bioassays; Biologically Active Molecules

Capabilities and Techniques:
We specialize in fluorescent probe design and synthesis and have developed novel fluorescence probes for protein oligomers, for unfolded protein response, for targeting and imaging organelles, for enzyme activity, for autophagy activity, etc.

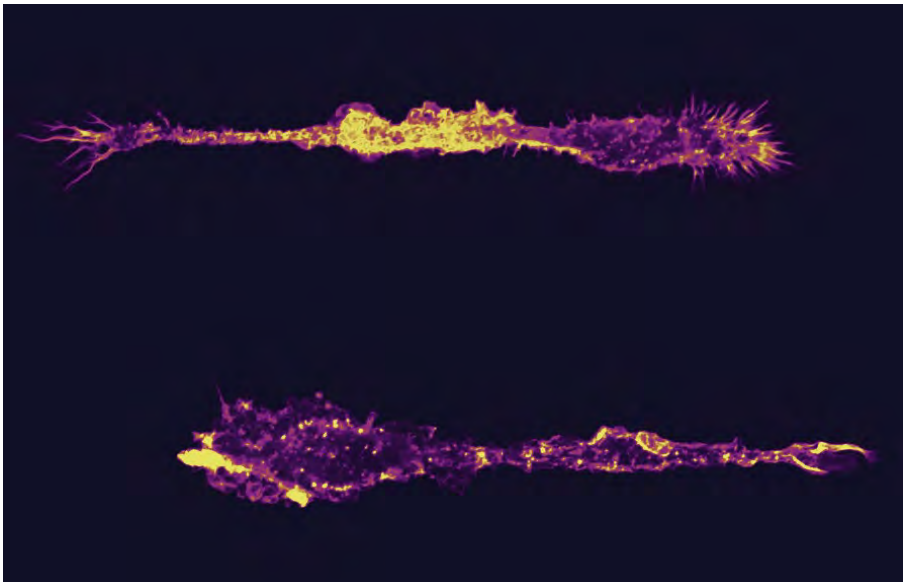
Translational Opportunities:
Material transfer; Early detection of neurodegenerative diseases; Disease treatment evaluation; Assay kits/device development based on our materials.

Immunometabolism and Macrophage Biology Group

Every cell in our body requires energy to perform their specific functions. Generally, this is a well-controlled and ordered process. However, in some settings, the ways in which cells obtain this energy is altered and has important functional consequences.

We are now learning that the metabolism of immune cells is intricately linked to their function, where distinct metabolic configurations are ascribed to different phenotypes.

Our research aims to understand the link between what immune cells 'eat' in our tissues and how this is connected to their normal biology, response to infections, and inflammatory diseases such as high blood pressure and diabetes.



Confocal microscopy image of murine macrophages. (Photo credit: Katrina Binger)

Macrophages go 3D

The cell type we focus on are macrophages, innate immune cells that acquire specialised pro- or anti-inflammatory functions upon responding to stimulatory cues (e.g. toll-like receptor agonists and cytokines) in their local tissue environment. Macrophages therefore have a variety of responsibilities including protecting us from invading pathogens (bacteria, viruses, and parasites), promoting inflammation and tissue repair. Macrophages are also unique in that they are the only immune cells derived from two developmental origins: from progenitors, which seed all tissues during embryonic development, and on command from haematopoietic stem cells, which give rise to circulating precursors that infiltrate tissues throughout adulthood (Wright & Binger. Pflugers Arch 2017).

As the tissue environment is a major controller of macrophage function, understanding their function with classical 2D in vitro culture systems is impossible. The aim of this project is to develop 3D systems that better recapitulate the tissue microenvironment and support TRM function. We are interested in developing in vitro models that better mimic tissue environments. Using 3D printing, macrophages are suspended into different environments and the effect of this on their function is measured. We are particularly interested in modeling tissues like the lung microenvironment to better understand how macrophage function occurs in this specialised environment during infection with respiratory viruses such as Sars-CoV-2, influenza and others.

Mechanosensing metabolism

Our recent data shows that the interaction of macrophages with the extracellular matrix (ECM) is important for their function (McGowan et al iScience 2022). We think that this 'mechanosensing' is a critical, but underappreciated modulator of macrophage biology. In this project students will employ proteomics to identify proteins that regulate macrophage interaction with the ECM, and investigate their role in metabolism.

Dietary salt

It has recently emerged that small molecules, such as metabolites and electrolytes, have significant effects on macrophage phenotypes via 'reprogramming' their cellular metabolism; involving the activation of signalling pathways, expression of metabolic enzymes and proteins, increased uptake and storage of nutrients, and physical remodelling of mitochondria. We previously reported that high dietary salt increased sodium (Na+) in tissues that subsequently modulated macrophage phenotypes: increasing pro-inflammatory responses and glycolytic metabolism, while inhibiting protective anti-inflammatory functions and mitochondrial respiration (Binger et al., J Clin Invest 2015; Jantsch et al., Cell Metab 2015). The aim of this project is to understand how sodium reprograms macrophage metabolism.

Lab Head: Dr Katrina Binger

Lab members:
Mr Sean Cutter; Ms Kaitlyn Ritchie;
Mr Christopher Chong;
Mr Michael Osbourne; Ms Emily Field;
Mr Shohan Johnson.

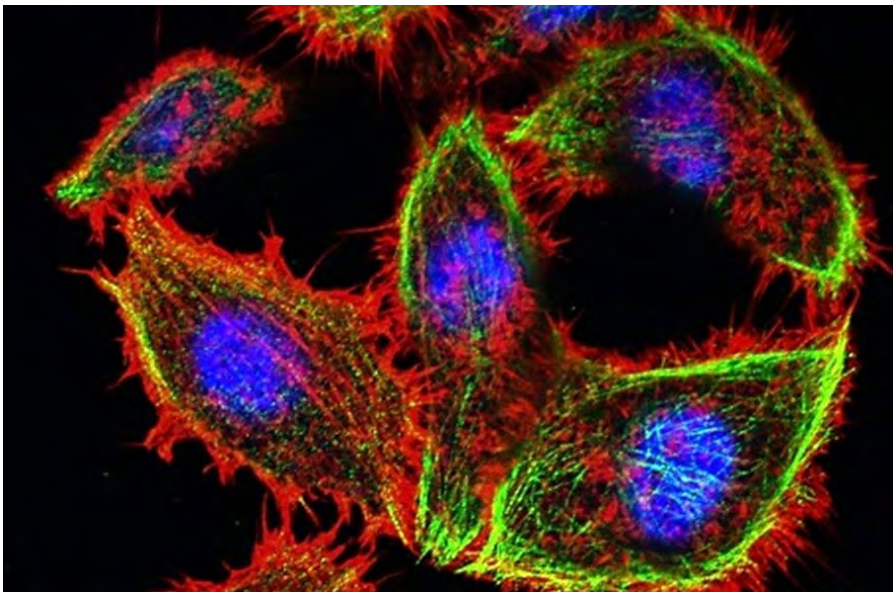
Fields of Study:
Immunology; Cell Biology; Metabolism; Biochemistry; Molecular Biology.

Capabilities and Techniques:
Primary cell culture; infection assays; metabolism analyses.

Translational Opportunities:
Biomedical therapies for infection control and inflammatory diseases.

Inflammation and tumour progression group

Our research aims to understand the structure and function of key molecules in innate immunity and tumour progression and to harness this information for the development of novel therapeutics to treat infectious disease, inflammatory disease and cancer. In particular, we aim to precisely define and translate the unique molecular mechanisms of innate defense peptides and the heparan sulphate (HS)-degrading enzyme heparanase in immunity and tumour progression. Towards this aim, our interests are focused on two main research themes, to define (i) the role of heparanase and investigate its drug targeting in the disease settings of cancer and inflammatory disease, including the important cardiovascular disease atherosclerosis, and (ii) the molecular basis of membrane-targeting by defensins, its importance in innate defense, and to use this information to develop novel antimicrobial and anticancer molecules.



Cytoskeletal proteins in human cancer cells (Photo credit: Guneet Bindra)

Heparanase function and drug targeting in inflammatory disease

Cell migration is critical in the initiation of inflammation and to combat infection. The HS-degrading enzyme heparanase plays a key role in these processes by facilitating the migration of immune cells. As such, heparanase can also promote chronic inflammation that underpins various inflammatory diseases and therefore is an attractive anti-inflammatory drug target. Atherosclerosis is a chronic inflammatory process that is a major contributor to myocardial infarction and stroke – key sources of morbidity and mortality. We have defined heparanase as an important driver of atherosclerosis and are now assessing heparanase inhibitors as novel anti-atherogenic drugs to prevent and treat these cardiovascular diseases.

Heparanase function and drug targeting in tumour progression

The ability of malignant tumour cells to escape from primary tumour sites and spread through the circulation to other sites in the body is what makes cancer such a deadly disease. Essential in these processes of tumour growth and spread, are metastasis - where tumour cells move into and out of tissues and the vasculature, and angiogenesis – where new blood or lymphatic vessels are formed in and around a solid tumour. Heparanase has been linked to promoting tumour metastasis and angiogenesis and therefore represents an attractive anti-cancer target. Our lab has generated unique heparanase knockout mice that we are using to define the precise role and contribution of heparanase to tumour progression in the settings of breast, colon and prostate cancer, towards determining the appropriate application of heparanase inhibitors for treatment.

Antimicrobial and Anticancer Defensins

Antimicrobial peptides such as defensins are natural innate immunity molecules found throughout the plant and animal kingdoms and are attracting clinical interest for their unique antimicrobial properties against bacterial, fungal and viral pathogens, as well as their ability to target and kill cancer cells. We defined a key mechanism of action of defensins involving the specific recognition of membrane phospholipids that results in permeabilisation and death of target and anticancer therapeutics. cells. We focus on defining the precise molecular basis of the specific membrane-targeting activity of defensins to develop new potent antimicrobial and anticancer therapeutics.

Lab Head: Professor Mark Hulett
Lab members: Dr Fung Lay; Ms Gemma Ryan; Ms Guneet Bindra; Ms Tien Nguyen; Mr Scott Williams; Mr Matt Hein; Ms Zoe Day; Ms Serenay Dimir.

Fields of Study:

Biochemistry; Cell biology; Innate immunity; Inflammation; Cancer biology; Cardiovascular disease.

Capabilities and Techniques:

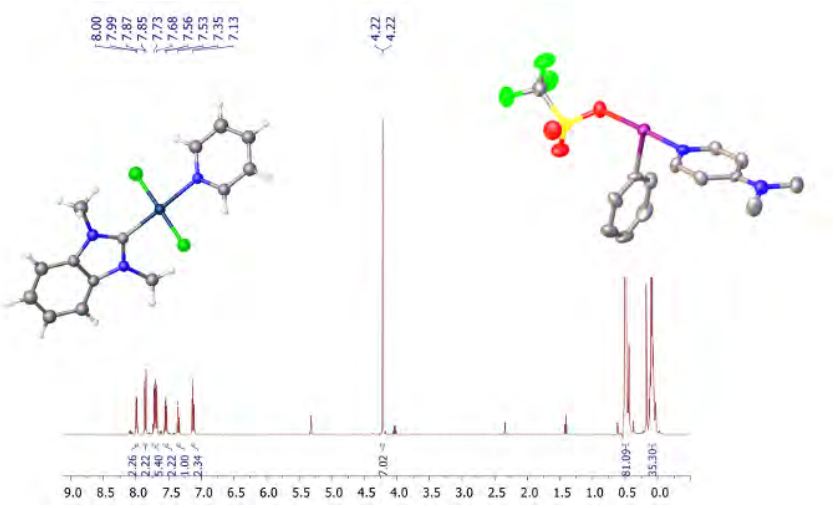
Molecular biology; gene expression analysis; protein expression, purification & quality control; protein-protein & protein-lipid interaction; mammalian cell culture; live cell electron microscopy; cell viability & drug testing; flow cytometry; mechanistic cell death assays; immunohistochemistry; heparanase activity; inflammation/cytokine profiling; in vivo mouse models of tumour progression, inflammatory disease; heparanase conditional gene knockout mouse models.

Translational Opportunities:

In vitro mechanistic & in vivo functional studies for infection, inflammatory disease & tumour progression; peptide & small drug therapeutics development & preclinical testing. Track record of translating research discoveries in partnership with biotech companies e.g. Progen Industries, Hexima Ltd, Wintermute Biomedical.

Inventing Chemistry Group

Our Group seeks to invent new chemistry with a broad philosophy of achieving this by making molecules as uncomfortable as possible. Electrons dominate the properties of molecules and in projects spanning the periodic table we consider molecules that either have too many or too few electrons. These new molecules are typically highly reactive and often result in the discovery of completely new reactions. We use a combined effort to interrogate molecules and reactions involving synthesis, spectroscopy, structural characterization and finally theoretical studies. In the latter area we undertake both predictive theoretical studies, especially in the area of chemical compounds that are too toxic or reactive to handle, and also to rationalize observations that are made by our group and others. Overall the goal of the group is to increase understanding in what is possible in chemical synthesis.



Structural characterization and spectroscopy of a small molecule

Discovering Organic Chemistry with an Inorganic Touch

Carbon has a privileged place in. chemistry, and the entire field of organic chemistry is built around it. We however don't view carbon as distinct from any other chemical element and treat it as just another metal. Using this philosophy we have discovered a number of molecule classes and reactions that are very simple, but were completely unexplored simply because a classically trained organic chemist wouldn't think that way. For example in metal chemistry one can generate a molecule by taking away electrons from the metal and replacing them with ligands, or conversely adding electrons and removing ligands. It turns out carbon can behave exactly the same way, which in turn gives carbon based species that are extremely reactive in classic organic chemical transformations.

Super Charged Halogenation Reagents

Halogenation, the addition of fluorine, chlorine, bromine or iodine to simple organic feedstocks are some of the most important transformations in chemistry, occurring on a multi-million ton scale. Elemental halogens (e.g. Cl2) are efficient at this, but are ferociously difficult to handle on a small scale. We are developing improved halogenation reagents based on I-X (X = F, Cl, Br) bonds in extremely electron poor environments that are more reactive than elemental halogens, but offer a vastly improved safety and handling profile. We have also found that organic chemists are frequently wrong in invoking how iodine reagents work and are carrying out a campaign to correct the literature.

Gold Chemistry for Organofluorine Synthesis

Fluorine holds a special place in medicinal chemistry, with half of top selling drugs containing a C-F bond. However, it is difficult to controllably change C-H into C-F. We have discovered that Au-F compounds are effective for performing this transformation. In this project we are using simple and cheap fluoride sources, combined with electrochemistry to generate extremely electron poor and thus reactive Au-F molecules that can catalytically effect the transformation of C-H info C-F bonds without degrading other parts of the druggable molecule of interest. In perusing this goal we have also uncovered a raft of other interesting reactivity surrounding the Au-F bond, which is generally unexplored due to its unstable nature.

Predictive Theoretical Chemistry

Sometimes one has good ideas that for a reason or another can't be actioned. In concert with the Wilson group we have an ongoing program in predictive theoretical chemistry. One of the main focusses is Beryllium chemistry. Beryllium has a very rich reactivity but is hardly explored due to its extreme toxicity. We predict what might be possible in the computer, and international groups with the appropriate skills test our predictions in their labs.

Lab Head: ProfessorJason Dutton
Lab members: Mr Lachlan Sharp-Bucknall; Ms Tania; Mr Lachlan Barwise; Ms Biljana Vujci; Ms Aseel Bakro; Mr Jason Benetts; Mr Benjamin Davis; Mr Luke Vincent-Blood.

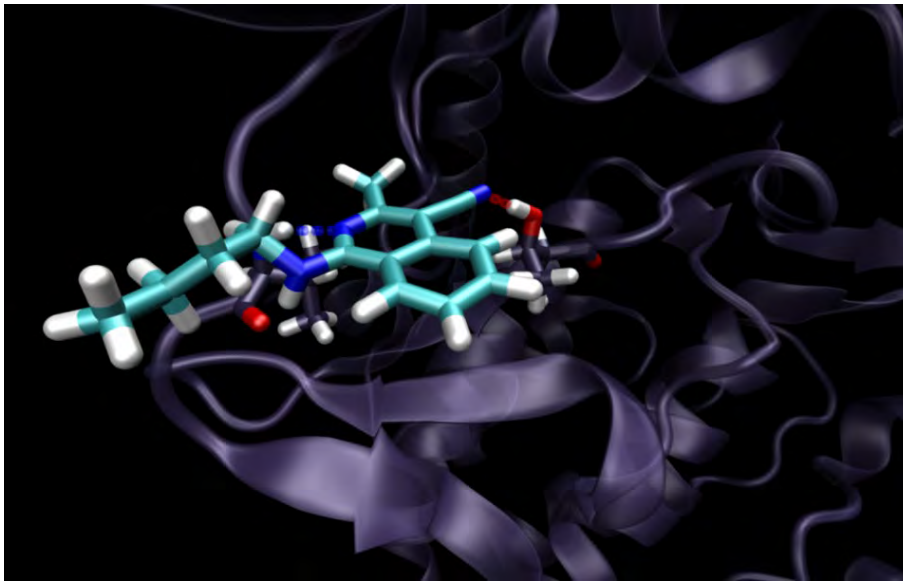
Fields of Study:
Inorganic chemistry; Organic Chemistry; Theoretical Chemistry.

Capabilities and Techniques:
Complex chemical synthesis; Characterization of small molecules by spectroscopy; X-ray crystallography; theoretical calculations.

Translational Opportunities:
Chemical analysis; Prediction of chemical properties; Reaction planning and synthesis.

Medicinal and Biological Chemistry Group

Medicinal chemistry involves the design, synthesis and development of the molecules we need in order to understand, prevent and treat disease. Our research uses chemical synthesis, purification and characterisation techniques to make novel heterocyclic compounds. We partner with collaborators in order to study how these small molecules interact with complex biological systems, allowing us to develop our understanding the structure-activity relationships of our novel compounds with the target of interest. We are then able to use chemical modifications to optimise the pharmacodynamic and pharmacokinetic properties of promising lead compounds for further evaluation as potential therapeutics.



Small heterocyclic compound binding to protein target. (Image credit: M.Buskes)

Exploring FBDD to interrupt bacterial signaling between SRP and FtsY
The bacterial signal recognition particle (SRP) is an essential ribonucleoprotein complex responsible for the delivery of membrane and secretory proteins to the plasma membrane in bacteria. Interrupting the interactions of SRP with the SRP receptor (known as FtsY) represents a promising strategy for the development of novel antibiotics. This project aims to expand fragments obtained from a screening library into high affinity compounds using the approach of fragment-based drug design(FBDD).

Design, synthesis and evaluation of Drp1 inhibitors
The mitochondrial protein dynamin-related protein (A) has been implicated in the development of a number of neurodegenerative diseases, including Alzheimer's disease. To date, no direct small molecule inhibitors of human Drp1 have been identified. Our work aims to develop small molecules which can potently and selectively inhibit human Drp1 to provide important research tools to reveal the specific role of Drp1 in dementia and as potential leads for drug development.

Discovery and synthesis and of inhibitors of Bim expression
Beta-blockers such as propranolol are commonly used to treat cardiac arrhythmia and hypertension but have serious side effects; patients have a 5-year survival rate of 50%. New therapeutics for the treatment of these heart conditions are urgently needed. We are currently interested in two classes of compounds which prevent induction of the pro-apoptotic Bim protein but at the same time not affect CREB phosphorylation, a discovery which may be the key to the development of successful cardiac drug treatments.

Targeting protein transport for the effective treatment of motor neurone disease (MND)
Protein transport is critical to supply a motor neuron with components necessary for its maintenance and survival, and to remove waste products. We have identified a compound that enhances decreases ER stress, preventing the formation of inclusions and prevents apoptosis (cell death). We seek to further develop new compounds with this neuroprotective activity, as there is currently no effective therapeutic treatment for MND.

Inhibiting *P. falciparum* in the search for a new antimalarial agent
Malaria is a severe disease burden on the health and economy of the developing world. Enzymes which are important in the life cycle of the malaria parasite could possibly be attractive targets for novel antimalarial agents. We are synthesising analogues of an isoquinoline compound to evaluate against the malaria causing parasite *Plasmodium falciparum* with the aim of identifying a selective and potent inhibitor against a novel enzymatic target.

Lab Head:
Associate Professor Belinda Abbott

Lab members:
Ms Monica Nguyen; Ms Emily Graham; Mr Jarrod Pontisso; Ms Jordan Matoe; Mr Nicholas Baricevic.

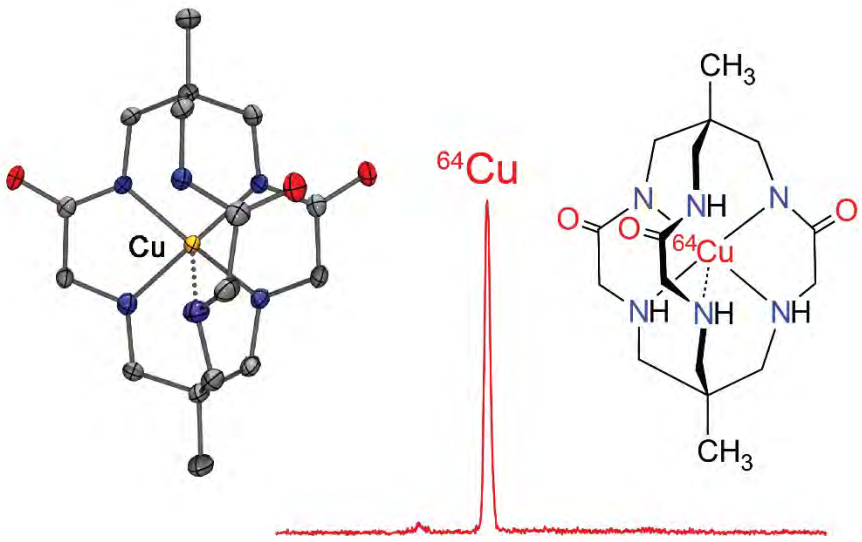
Fields of Study:
Medicinal Chemistry; Biological Chemistry; Organic Chemistry.

Capabilities and Techniques:
Chemical synthesis; Recrystallisation; Flash Chromatography; RP-HPLC; NMR spectroscopy; mass spectrometry.

Translational Opportunities:
Small molecule development; Enzyme inhibitors; Drug discovery.

Medicinal Inorganic Chemistry and Luminescent Sensors

We use chemical synthesis to prepare new organic and inorganic molecules for medicinal and biological imaging applications. Organic synthetic chemistry is used to prepare ligands for the formation of metal-based coordination compounds with properties optimized for use as medicines, imaging agents, and chemical sensors. Our lab has two main areas of research focus, the first is the development of antibacterial silver and gold-based compounds, which are active against multi-drug resistant bacterial strains. The second research area is the preparation of luminescent and radiolabeled molecules for potential chemical sensor and biological imaging applications. To allow for the selective sensing of carbohydrates, boronic acid-based luminophores have been developed as part of a collaborative project with the Australian fine chemical company Boron Molecular.



Triamine cryptate ligand labelled with the positron emitting radionuclide copper-64.

Silver and gold-based antibacterial agents
Medicinal inorganic chemistry is the development of metal-based compounds as potential medicines. We are working on gold- and silver-based complexes of N-heterocyclic carbene ligands as new antibacterial agents. A series of compounds have been prepared that show excellent activity against both Gram-positive and Gram-negative bacteria and significantly also multi-drug resistant bacterial strains. A noteworthy feature of these compounds is that antibacterial resistance does not develop, whilst resistance is developed against the widely used broad-spectrum antibiotic ciprofloxacin in the same bacterial strains. Current work is focused on evaluating the mechanisms by which these compounds are active and the preparation of targeted gold and silver metallodrugs.

Synthesis and Studies of Luminescent and Electrochemiluminescent Metal Complexes
We are developing luminescent and electrochemiluminescent coordination compounds of, iridium, gold, ruthenium and the lanthanide metals. These compounds are of interest as biological imaging agents and as luminescent chemical sensors. A particular focus is electrochemiluminescence where the luminescent emission is stimulated using electrochemical processes. Current efforts are directed toward tuning the luminescent properties of d-f heterobimetallic arrays (containing d-block and f-block metals) to provide molecules that are emissive in the infrared region. We are also interested in developing new compounds that can detect and monitor simple sugars and more complex carbohydrates. To achieve this luminescent boronic acid-based molecules that sense carbohydrates have been prepared as part of a collaborative project with the Australian fine chemical company Boron Molecular.

Radiopharmaceutical Imaging Agents for Disease Diagnosis
In this collaborative project with the Australian Nuclear Science and Technology Organization (ANSTO) we are developing new ligands for radiopharmaceutical imaging applications. A range of ligand systems are being used in combination with metallic radionuclides such as technetium-99m and copper-64. Technetium-99m is the most widely used radionuclide in medical imaging and many technetium-99m labelled compounds are currently used to image a range of disease states. As all isotopes of technetium are radioactive, we develop new chemistry using the metal rhenium and an array of rhenium complexes of N-heterocyclic car bene ligands have been prepared. Significantly, our laboratory was the first to successfully label a N-heterocyclic carbene ligand with technetium-99m.

Synthesis of amide-based cryptate and cage molecules
The amide or peptide functional group is critical to life as it provides the linkage between adjacent amino acid residues in proteins. Amides also display interesting coordination chemistry and we have utilized the amide linkage to synthesize new cryptate ligand systems. In this work, a range of cryptate and cage ligand systems incorporating amide groups have been prepared (for example the triamidetriamine cryptate ligand shown in the picture).

Lab Head: Associate Professor Peter Barnard
Lab members: Mr Michael Dewar-Oldis, Mr Quoc Dat Duong, Mr Rahad Rahman, Ms Neha Jangra and Mr Liam Barron.

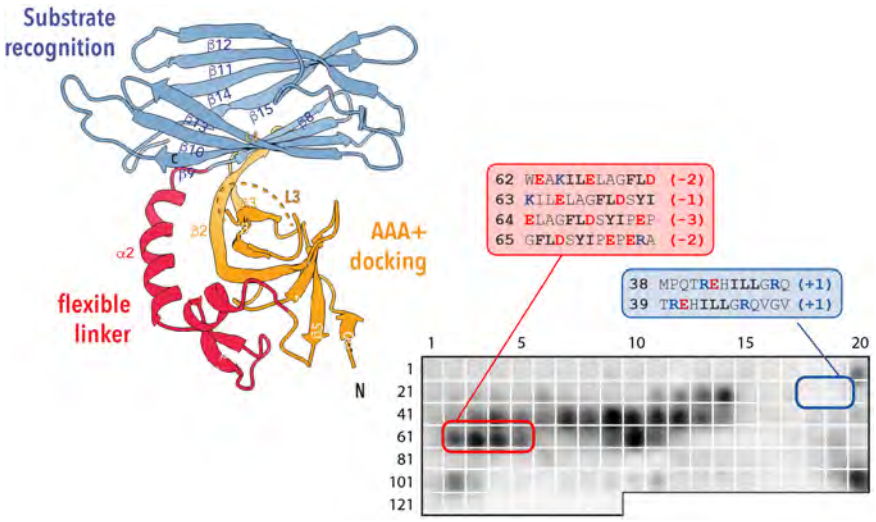
Fields of Study:
Medicinal Inorganic chemistry; Organic Chemistry; chemical luminescence.

Capabilities and Techniques:
Organic and inorganic chemical synthesis; Medicinal inorganic chemistry; Molecular structural characterization by NMR spectroscopy, mass spectrometry X-ray crystallography.

Translational Opportunities:
Chemical synthesis; peptide synthesis; radiochemistry.

Mitochondrial Proteostasis Lab

Mitochondria are critically important organelles that contribute to a wide range of cellular functions. Unsurprisingly, impaired mitochondrial function is linked to many different diseases including cardiovascular disorders, neurodegeneration and cancer. As mitochondrial proteins and protein complexes are separated from other cellular compartments by a double membrane, specific mechanisms are required for the biogenesis, surveillance, and maintenance of the mitochondrial proteome termed protein homeostasis (proteostasis). A key part of this maintenance is performed by ATP-dependent machines and assembly factors which help protect the organism from disease. Our research focuses on the molecular details of substrate recognition by these machines, from how they recognize protein substrates directly, to how these machines are regulated by specialized components, known as adaptor proteins. Our goal is to conduct fundamental research that improves our understanding of mitochondrial proteostasis in human health and disease.



Structure of human POLDIP2, a novel adaptor protein for the mitochondrial AAA+ protease CLPXP. Peptide array illustrating the features of substrate recognition by human CLPX (Photo credit: David Dougan)

Complex II assembly

The mitochondrial oxidative phosphorylation (OXPHOS) system fuels the energy demands of most eukaryotes through the generation of the majority of cellular ATP. The OXPHOS system comprises five multi-subunit protein complexes in the mitochondrial inner membrane, termed Complexes I to V. These multi-subunit complexes are composed of redox active cofactors including flavins, iron-sulfur clusters, copper and heme. Assembly of each complex requires assembly factor proteins, which act at several steps, including membrane insertion, subunit association and cofactor incorporation. Mutations in, or the absence of, these assembly factors lead to assembly defects of the various Complexes resulting in mitochondrial dysfunction.
Complex II is composed of four subunits (SDHA, B, C and D). Assembly of these subunits into the final complex requires four dedicated assembly factors (SDHAF1, 2, 3 and 4). Mutations in SDHAF2 affects Complex II assembly, triggering mitochondrial dysfunction and causing cancer. The molecular details and dynamics of Complex II assembly pathway, however, remain unclear. Notably, our unpublished data has identified several uncharacterized assembly intermediates. This project will determine the composition of these intermediates and the precise role of the assembly factors within these intermediates.

Molecular dissection of protein degradation pathways in mammalian mitochondria

Our group has a strong track record in the study of regulated protein degradation in various model systems from bacteria to mammalian mitochondria. We have made several ground-breaking findings in the field, including the structural and functional dissection of several essential protein degradation components. We previously identified that the AAA+ (ATPases associated with a variety of cellular activity) protease, LONM, is responsible for the turnover of the Complex II assembly factor, SDHAF2, which forms an intermediate complex with SDHA, *en route* to the final functional complex. Importantly, our unpublished data suggest that the turnover of SDHAF2 is facilitated by a short N-terminal degradation (N-degron) tag composed of two elements one of which is occluded in the SDHA-SDHAF2 assembly intermediate. This project will dissect the significance of the N-degron, and the mechanism that triggers release of this degron for progression of SDHA into the final complex.

Lab Head: Dr Kaye Truscott
Lab members: Dr David Dougan
International collaborators:
Prof. Kornelius Zeth (Roskilde University, Denmark); Prof. Kürşad Turgay (MPI, Berlin, Germany)

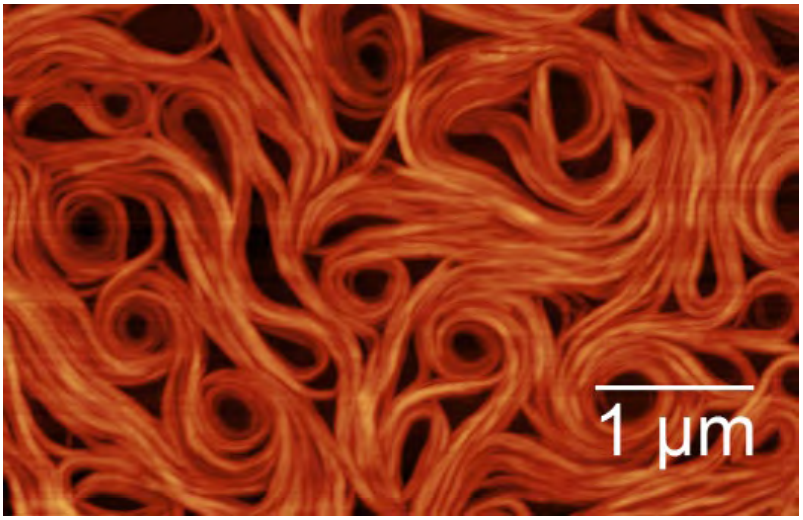
Fields of Study:
Biochemistry; Mitochondrial Biology; Microbiology, Cell Biology.

Capabilities and Techniques:
Biochemistry (protein chemistry, protein structure-function analysis Protein array interactions); Mitochondrial assays, Blue Native PAGE; Bacterial/eukaryotic cell culture.

Translational Opportunities:
Our research is fundamental however it will lead to a better understanding of how chaperones, proteases and assembly factors regulate mitochondrial proteostasis and thus may reveal opportunities for small molecule interventions to prevent late onset mitochondrial diseases.

Molecular Self-Assembly and Nanoarchitecture Group

Our Group studies natural self-assembling systems and uses self-assembly principles to design complex nanostructures. Self-assembly is nature's way of building complex structures from molecular building blocks. Cell membranes, silk fibres and proteins are examples of this process where final structure is the product of a multitude of second order interactions – individually weak, non-covalent bonds between adjacent molecules, the collective effect of which is a strong, stable superstructure. Adapting the self-assembly process to the design of complex nanomaterials from unnatural building blocks requires the study of the natural processes and establishing design rules. This will eventually lead to the development of a "molecular lego" toolbox where the chemical building blocks can be selected to create complex nanostructures.



Self-assembling oligoamides form nano-micro scale hierarchical structures

Phospholipid Self-Assembly

Self-assembled phospholipid bilayers provide the core structure of cell membranes – the physical boundaries of cells and sub-cellular structures that preserve cell integrity while also serving as a platform for life functions related to metabolism, sensing and intercellular communication. Phospholipids, organised into a two-dimensional bilayer, provide the primary membrane structure. We study the formation and physicochemical properties of phospholipid bilayers of various composition, with microscopic and microspectroscopic methods. Our aim is to describe the structural and chemical characteristics of such biomimetic membranes that are deterministic of their collective properties: phase transitions, tension, bending rigidity, as a function of composition and environmental factors. We create artificial biomimetic membranes on arbitrary surfaces to mimic the physiological environment of living cells, for applications in biophysics, while also furthering the fundamental understanding of lipid self-assembly.

Peptide-membraneinteractions

Disrupting integrity of cellular membranes underpins many biophysical processes in biology, from immunity to apoptosis and plays many roles in nature, however the mechanism of membrane disruption is not fully understood. We study membrane disruption by antimicrobial peptides which provide innate immunity against pathogens in most living organisms. They disrupt the cytoplasmic membrane of pathogens, facilitate the efflux of essential ions, and thus disrupt ionic homeostasis. We study the molecular mechanism of these interactions, focusing on identifying the factors contributing to the specificity and selectivity of these peptides towards pathogenic membranes. By studying the role of lipid composition, peptide sequence, the physiological environment and temperature at various stages of the interaction, and the role these factors play in switching between disruptive and non-disruptive interaction pathways, we aim to develop novel peptide-based broad spectrum antibiotics for last resort applications in the clinical setting.

Oligoamide based hierarchical nanosystems and metallosupramolecular frameworks

We developed a unique β3 oligoamide based self-assembling platform that forms fibrous nanomaterials from helical units, like a molecular LEGO set. These molecules fold into highly stable helices with a pitch of 3.0-3.1 amino acids, hence the side chains align in the larger oligomers. The helical form is stable for short sequences and for a wide variation of amino acid side chain geometries and chemistries. Metal coordination crosslinking of these molecular fibres creates a unique metallosupramolecular framework, a platform for development into functional nanomaterials. We study the factors affecting the self-assembly of these molecules, working towards implementing multiple self-assembly motifs and chemical "switches" to create either self-spun fibres, two dimensional arrays, or three dimensional metamaterials. The accessible sidechains offer easy pathways of chemical modification of these oligoamides, which we utilize to implement controlled complexity and physicochemical properties.

Lab Head: Professor Adam Mechler, FRSC

Lab members:
Mr Jose Vilareal-Diaz; Mr Yifan Wang; Ms Zahra Saadatmand; Mr Norton West; Mr Abdalwahab Alshammari.

Fields of Study:
Physical Chemistry; Lipid Self-Assembly; Antimicrobial Peptides; Hierarchical Nanostructured Materials; Surface Chemistry.

Capabilities and Techniques:
Biomimetic solutions for biomedicine; Delivery and effectiveness of antimicrobial peptides and nanoscales.

Muscle Biochemistry Group

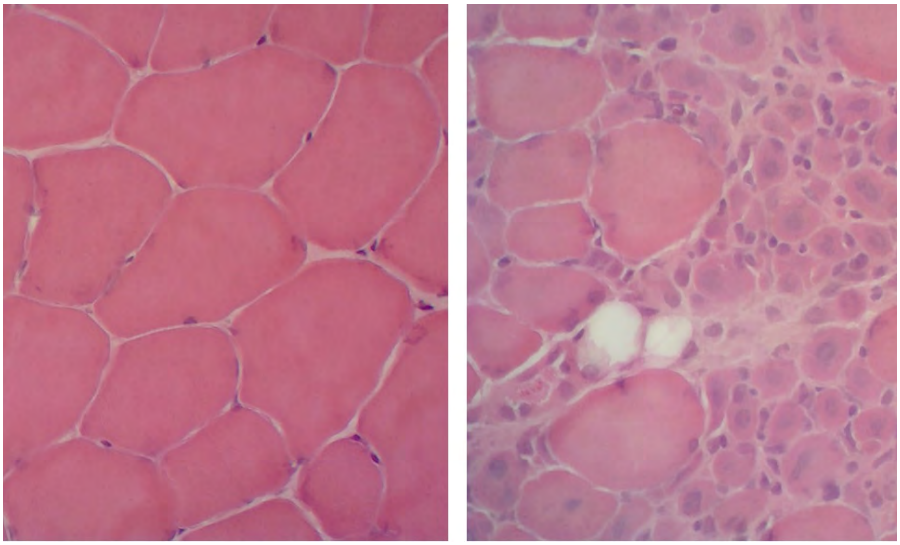
The Muscle Biochemistry Laboratory focuses on understanding aspects of muscle function and biochemistry in both health and disease. The laboratory is situated in the LIMS1 building, with full access to all biochemistry facilities. The overall research interest of the laboratory is in the area of skeletal muscle in health and disease. The laboratory focuses on various aspects of skeletal muscle biochemistry, using exercise and disease models in humans, as well as animal models. In particular, the laboratory pioneered and optimised the measurement of proteins in very small samples sizes. This allows proteins to be measured in small segments of individual muscle fibres allowing issues with the heterogeneity of skeletal muscle to be overcome. We also examine movement of proteins following micro-dissection of fibres, allowing quantitative assessment of the redistribution of proteins following various interventions, in particular exercise.

Calpains and MMPs

Calcium dependent proteases calpains, and metallomatrix proteinases (MMPs) have been touted as playing similar roles in muscle. To understand their potential, improving our understanding of their regulation and functional properties in the physiological milieu is crucial. If an individual has an absent or non-functional muscle specific calpain-3, they develop a type of muscular dystrophy (LGMD2A). We have identified that calpain-3 likely plays a role in muscle repair. MMPs play a diverse role in the body, with MMP2 and MMP9 linked to muscle degenerative processes. We use exercise as a manipulation to alter intracellular calcium levels and to investigate how lengthening, or eccentric contractions can affect the activation of calpains and/or MMPS, and to identify their in vivo cellular targets.

Glycogen related proteins

By removing the surface membrane of a skeletal muscle fibre by microdissection, we can quantitatively assess crude localisation of proteins in muscle.



H&E staining: healthy (left) & damaged (right) skeletal muscle (Photo credit: Robert Barker)

Our research has revealed that glycogen related proteins are differentially associated with the glycogen granule in vivo and also that the important energy sensing molecule, AMPK, along with the glucose transporting protein, GLTU4, are not associated with the glycogen granule. These findings debunk the theory that glycogen utilisation directly affects their function. We continue to explore how these proteins, are involved in skeletal muscle function, in particular in response to exercise and diseases such as type 2 diabetes. Importantly, we are trying to understand what the mechanisms are that result in an improvement in this metabolic disease following exercise interventions.

Mitochondrial dynamics

Mitochondrial content has been described as being reduced with aging, however using our quantitative approaches to protein assessment, we have shown in healthy older adults there is no loss of mitochondrial content or in the ability of mitochondria to adapt to exercise. We identified that an increase in mitochondrial dynamics may be in some way protective to the muscle and overall function.

Lab Head: Professor Robyn M. Murphy

Lab members:
Dr Noni Frankenberg; Dr Barney Frankish; Dr Stefan Wette; Dr Robert Barker; Ms Heidy Flores; Ms Amy Pascoe; Ms Oliva Timson Smith.

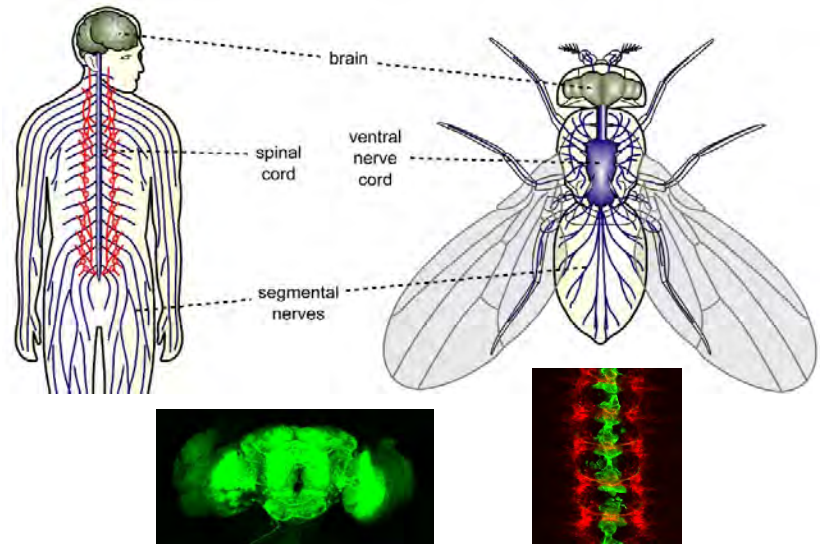
Fields of Study:
Biology with Physiology (cellular, animal and biochemistry); Medical Physiology; Human Movement and Sports Science.

Capabilities and Techniques:
Chemidoc imaging (fluorescent, chemiluminescence & UV lights); Leica semi-automated crysostat, LabConco freeze-dryer; Polytron homogenisor for small volumes; Eppendorf refrigerated benchtop microfuge centrifuge; Ultra-sensitive, low volume western blotting.

Translational Opportunities:
Muscle disease diagnostics; exercise physiology; exercise interventions for aged individuals.

Neural Cell Signalling Group

Our group studies how cells in the nervous system receive and respond to extracellular signals from their environment. An animal's nose can detect thousands of different chemicals in their environment. How does this occur, and how does the animal know what these represent and what the response should be? Other cells in the brain detect environmental signals that determine how fast an animal grows and to what size. How is this controlled? As well as these questions, we are also investigating how neuronal signalling goes awry in the devastating disorder motor neuron disease. We use the model genetic insect *Drosophila melanogaster* for most of our work, as cell signalling in the nervous system is highly conserved between flies and humans, and for flies we have many highly sophisticated genetic and molecular approaches available to study gene function and to interrogate the nervous system.



Drosophila melanogaster is a great model for studying the nervous system. GFP labelling of adult *Drosophila* brain and larval CNS (Photo credit: Dr Katherine Shaw)

Molecular basis of odour detection in insects
In insects the sense of smell is vital for detecting plant or animal hosts for feeding or laying eggs, and for detecting potential mates. We are studying the signalling mechanisms used by the very large family of odorant proteins in insects, and how they evolve across species. As well as fundamental studies, we are investigating the odorant receptor family of the Australian sheep blowfly, a damaging pest of sheep in Australia. We aim to identify receptors for ecologically relevant chemicals, which may in future lead to more environmentally friendly methods of pest control. This project is a collaboration with Dr Trent Perry at the University of Melbourne.

Neuropeptide regulation of developmental timing and growth
In animals developmental timing and growth are controlled by steroid hormones that are under complex regulation by both developmental and environmental cues. We are studying novel neuropeptide receptors involved in controlling steroid hormone production and growth in response to these cues in *Drosophila*. Many of these receptors have human counterparts, thus the knowledge we obtain may inform our understanding of growth in humans, and of disorders such as obesity.

Role of neuronal excitability in Motor Neuron Disease
Motor Neuron Disease (MND) is a devastating and universally fatal late onset disorder for which there are no effective treatments or cure. In MND progressive muscle weakness results in sufferers becoming unable to use their limbs, and eventually being unable to breathe. Development of therapies has been very challenging due to MND being a complex disease, with many genetic and environmental components.

Prior to symptom onset all patients initially exhibit hyperexcitability (over responsiveness) of the motor neurons. We are focused on understanding the mechanisms by which this develops, as its commonality to all patients makes it an attractive therapeutic target. *Drosophila* is an outstanding model for this question - fly models of MND recapitulate the pathology seen in humans and we have the ability to easily experimentally manipulate neuronal function and see how this impacts disease. This project is a collaboration with Prof Tracey Dickson and Dr Rosie Clark at the University of Tasmania.

Lab Head: Professor Coral Warr

Lab members:
Dr Mackenzie Lovegrove;
Ms Emily Kerton;
Ms Natasha Fahey-Lozano;
Ms Sachini Arachillage Mallika;
Mr Stephen Penrose.

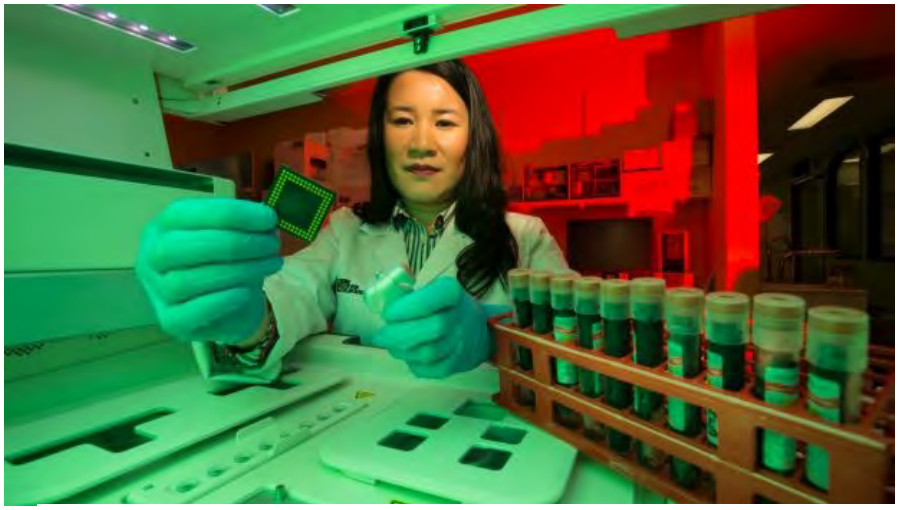
Fields of Study:
Molecular genetics; Cell Biology; Neurobiology; Developmental Biology.

Capabilities and Techniques:
Drosophila molecular genetics; All routine cell and molecular biology approaches; Many biochemical techniques; Many insect phenotypic assays (chemosensory behaviour and physiology, growth and developmental timing, embryo development and patterning, locomotory behaviour, immunity assays, microbiome assessment, ageing).

Translational Opportunities:
Our work is fundamental but may lead to targets for insect pest control methods; to future opportunities to develop better therapies for MND; and to novel targets for growth disorders in humans.

Neurodegeneration Biology and Biomarker Group

Neurodegenerative diseases, such as Alzheimer's disease (AD) is one of the leading causes of death world-wide. At the early stages of AD, neurons that control memory and thinking are attacked by toxic proteins that causes pre-mature neuronal death. Brain tissue becomes damaged, and patients begin to experience symptoms such as dementia related memory and cognitive impairment – a stage of disease when it is difficult to repair with disease-modifying drugs. Currently, the diagnosis process involves invasive procedures such as brain imaging and cerebrospinal fluid testing but is often performed at the symptomatic stage when damage to the brain has begun. Hence, there is currently an unmet need for an early, convenient, low-invasive blood-based test to diagnose AD. Our group focuses on developing diagnostic tests for neurodegenerative diseases such as Alzheimer's and Parkinson's disease but, also other similar dementia disorders to allow for differential diagnosis.



Testing blood samples for neurodegenerative diseases (Photo credit: James South)

It's in the blood – Extracellular Vesicles

Exosomes are extracellular vesicles (EVs) that are secreted from cells and tissues where they can then be found circulating throughout the body. They can carry protein and genetic material which have been shown to reflect the host cell. EVs can be isolated from blood making them a potential source of disease biomarkers. Our hypothesis is that EVs secreted from neurons within brain tissue can migrate through the blood brain barrier (BBB) into the blood whereby brain biomarkers are readily detected and reflective of disease occurring the brain, equivalent to a 'liquid biopsy' of the brain. We utilise 'Next-Generation' deep sequencing to identify all the RNA species, in particular microRNA, in EVs isolated from human post-mortem brain tissue and blood of patients with neurodegenerative diseases.

Brain-derived EVs

Historically, it has been challenging to develop biomarkers for brain diseases as neurological biomarkers do not cross the BBB so sampling peripheral whole blood is not reflective of the brain. However, brain-derived EVs (BDEVs) can cross the BBB through specialised transport channels that allow BDEVs to pass the BBB. Our research group has the capability to isolate BDEVs from human brain tissues, a complete game-changer from using cell culture models. We can now investigate the contents and role of EVs isolated from the brain of patients diagnosed with a neurodegenerative disease from an entirely new perspective.

The role of EVs in neurodegeneration

We use genomics and proteomics to profile the contents of BDEVs in search for proteins and RNA associated with neurodegenerative diseases. Those we identify are used as potential disease biomarkers but are also further studied in cellular and mice models to understand their role in the pathology of neurodegenerative diseases. We use an array of molecular, cell and protein biology methods to discover biological pathways that are implicated in neurodegenerative diseases and determine whether EVs assist and/or accelerate the disease process.

EV biogenesis of the BBB

Our group seeks to understand the endosomal and non-endosomal pathways of EV biogenesis and release from human brain endothelial cells of the BBB. We will use cellular models of the BBB together with super-resolution microscopy to visualise EVs within endosomal structures and track their movement across the BBB to the periphery. Unravelling the biogenesis pathways of EVs at the BBB will allow us to manipulate these pathways to deliver therapeutic EVs to the brain to treat neurodegenerative diseases.

Lab Head: Dr Lesley Cheng
Lab members: Ms Robyn Sharples; Mr Mitch Shambrook; Ms Natasha Vassileff; Mr William Phillips; Mr Christopher Reimann.

Fields of Study:

Neurodegeneration, biomarkers, genomics, diagnostics and extracellular vesicles

Capabilities and Techniques:

Cellular, tissue and biological fluid extracellular vesicle purification and characterisation, Molecular diagnostics, Genomic sequencing, proteomics, qRT-PCR/ Digital PCR, automated laboratory instruments, cell culture, cellular imaging

Translational Opportunities:

This research will develop a diagnostic blood test capable of specifically detecting brain-specific disease indicators associated with neuropathological changes in the brain. This would also allow for monitoring decline or improvements during therapeutic treatment. We are currently working with several industry partners within the R&D sector to investigate the use of EVs in therapeutics and diagnostics.

Neurodegeneration and Neurorepair Group

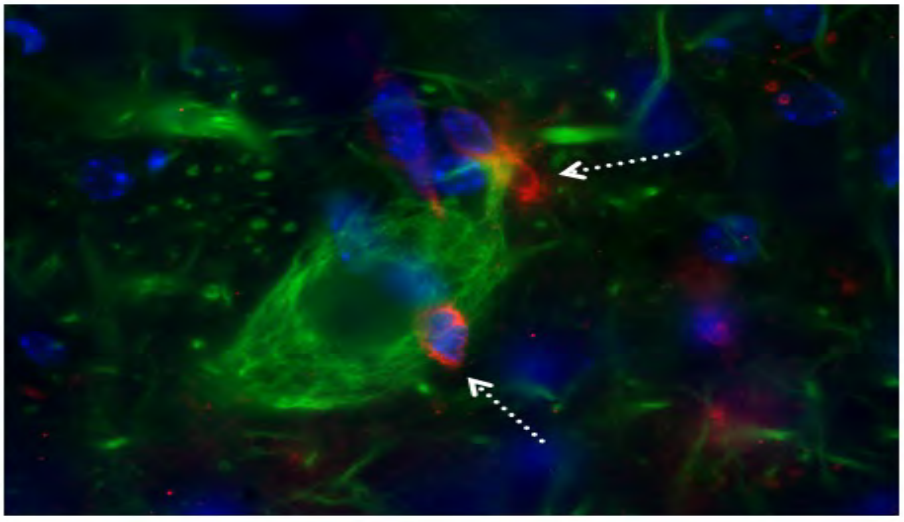
Our laboratory focuses on multiple sclerosis (MS), an autoimmune and neurodegenerative disorder of the central nervous system (CNS). The cause of MS is unknown, but incidence and prevalence of this disease is rising worldwide. Treatment options are unsatisfactory, because of poor understanding of mechanisms underlying tissue destruction, or of the relationship between evolution of these mechanisms and clinical progression. Our goal is to clarify the pathological processes of tissue destruction and the accumulation of neurodegeneration, from the pre-clinical stage. We have developed multiple animal models that mimic facets of MS, as well as approaches including standard histopathological, advanced imaging and molecular techniques. Our long-term aim is to identify primary and targetable mechanisms for early intervention and prevent irreversible neurodegeneration.

Modelling MS

There is no accurate MS model. Instead, experimental paradigms have been developed to study various facets of MS, including virally-induced CNS inflammation (Theiler's murine encephalomyelitis virus model), chemically-induced demyelination (cuprizone, lysophosphatidylcholine) and autoimmune-mediated demyelination (experimental autoimmune encephalomyelitis EAE). The EAE model is preferred because it exhibits both inflammation and demyelination. We have developed EAE variants using defined combinations of neuroantigen: mouse strain. This results in clinical progression exhibiting chronic-progressive, chronic-relapsing, or monophasic disease, which can be T cell or B cell-driven. Clinical progression and pathological hallmarks over the disease trajectory have been mapped. We have investigated the earliest timing and mechanisms of neuronal loss and evaluate drug efficacy. Future developments include chemically-induced demyelination models to investigate remyelination strategies.

Mechanisms of neuronal loss

MS inflammation is relatively well understood and treatable with immunomodulatory drugs. However, neurodegeneration is poorly addressed.



Neuron stained with antibody to neurofilament protein (green) targeted by $CD3^+$ T cells (red) during the acute phase of EAE. Nuclei are stained with DAPI (blue). (Photo credit: Anton Ramp)

Existing MS therapeutics improve quality of life, but do not arrest the neurodegenerative process or actively promote remyelination. Our lab identified an early and critical role for platelets in neurodegeneration in EAE. We identified platelets in the CNS from the pre-onset stage, throughout the whole CNS and specific platelet targeting of neurons. We also demonstrated platelet targeting of myelin. Behavoiural studies have revealed neuropsychological symptoms prior to disease onset. We propose that platelets are the substrate of neurodegeneration and that platelet targeting is a novel strategy for early intervention in MS.

Targeting neuroinflammation

Historically, the inflammatory component of MS has been the focus of drug development, via T and B cell targeting. With respect to T cell targeting, we have demonstrated the efficacy of the S1P analog FTY720 in reducing disease severity. Our studies have revealed high-level complexity responses by the S1P receptor family, whereby each of the receptors expressed in the CNS exhibits differential dose-related and region-specific changes in response to treatment. Using a B cell driven EAE variant, we mapped B cell compartmentalization and showed efficacy of anti-CD20 drugs in disease attenuation. Immunomodulation does not ameliorate neuropsychological symptoms, suggesting that immunomodulation is not neuroprotective.

Platelet targeting in neuroinflammation

In view of the evidence of the early and driving role of platelets in neuroinflammation and the inefficacy of immunomodulatory drugs in promoting neuroprotection, we further investigated the potential of platelet-targeting. Current evidence shows that blocking platelet reactivity is associated with both inhibition of inflammation and restoration of myelination and function. Future studies will elucidate mechanisms underlying the multi-faceted consequences of platelet targeting.

Lab Head: Dr Jacqueline M Orian
Lab members: Ms Jing Ting Vernise Lim (PhD student); Mr Hussam Al-Saraji (Honours Student); Ms Xiaoya Li (Master's student); Ms Sivar Sanjana Iyengar (Master's student).

Fields of Study:

EAE models, multiple sclerosis, myelin biology, neuroimmunology, platelets.

Capabilities and Techniques:

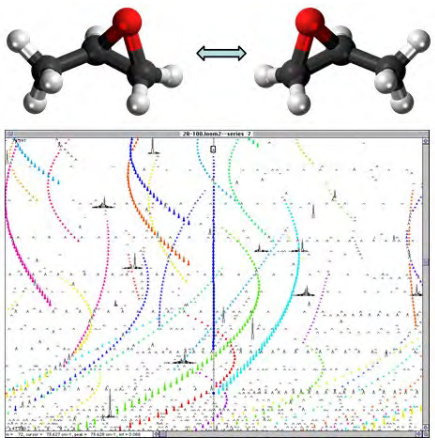
Generation of B and T cell driven EAE variants; Neuroanatomy; Histology; Brightfield and confocal microscopy; Unbiased counting techniques.

Translational Opportunities:

Pre-clinical evaluation of candidate multiple sclerosis and remyelination therapeutics.

Optical Spectroscopy of Atmospheric, Astrochemical and Biological molecules

There is more to light than meets the eye. Light with wavelengths invisible to human sight but detected by sophisticated instruments called spectrometers provide us with a detailed view of the "nanoscopic" molecular world that underpins daily life. We exploit powerful light sources such as infrared, visible and ultraviolet lasers, or the Australian Synchrotron's infrared beamline to study molecules relevant to pharmaceutics, atmospheres and astrochemistry. For example, this type of molecular sensing can reveal the shape of neurotransmitter molecules that act as the 'key' in receptor 'locks' involved with signaling in the brain, the details of how much radiant heat is absorbed by greenhouse gases, the size and temperature of ice nanoparticles like those in high altitude clouds, or the spectral fingerprint patterns that allow molecules in space to be identified through radioastronomy.



Left and right-handed forms of propylene oxide form patterns of spectral lines like those observed by radio astronomy

Molecules in Space

Life on earth is intrinsically chiral. In the building block molecules such as proteins and sugars, "left-handed" or "right-handed" forms are possible, but only one one type is found and the reason for this choice remains unclear. Astrochemistry may well play a role and yet amongst the 200 molecules detected in the interstellar medium outside our solar system to date, propylene oxide is the only one that is chiral. We are undertaking work to increase understanding of its' spectral properties in the crucial microwave region used for detection. Other work is aimed at finding other chiral molecules in space and identifying the molecules responsible for thousands of unidentified absorption lines measured by radioastronomy.

Atmospheric molecules and their greenhouse absorptions

The absorption of infrared radiation by greenhouse gases in the atmosphere is at the heart of human induced climate change. Some of our research into fluorocarbons has revealed the fine details that may be used to efficiently model the complex pattern of IR absorption within the atmospheric greenhouse window. One of our targets has been dichlorodifluoromethane, commonly known as CFC-12 or refrigerant R12, which despite being present in concentrations of less than one part in a billion has a warming contribution exceeded only by carbon dioxide, methane, and nitrous oxide. Aerosols also play a key role in our atmosphere, affecting the climate both directly through absorption and reflection of light, and indirectly by hosting chemical reactions and influencing cloud formation. Research to investigate the formation, composition and behaviour of aerosols is critical to improve the climate models. A specialised cooling cell with unique capabilities at the Australian synchrotron's IR beamline enabled us to measure the first far IR spectra of water ice nanoparticles. Such particles as are found in cirrus and mesospheric clouds on earth, and in non-terrestrial environments such as Mars, Titan and the interstellar medium.

Conformational shape of biomolecules

The conformational shape of biological molecules, and their interactions with the surrounding environment including water molecules are critical to their functioning. Laser-based gas phase spectroscopy combined with appropriate computer modelling generates precise structural information on molecules such as neurotransmitters that provide a rigorous platform for understanding their behaviour and ultimately, rationalizing drug design. The resonant two photon ionisation technique allows electronic and IR spectra to be measured for molecules cooled to a few Kelvin. This results in beautiful, simplified spectra that can be interpreted to reveal the preferred shapes of molecules and how strongly they interact via hydrogen bonding with water.

Lab Head:
Associate Professor Evan Robertson

Lab members:
Mr Luigi Villani,
Mrs Ishara Peiris,
Mr Kaidan Rolfe.

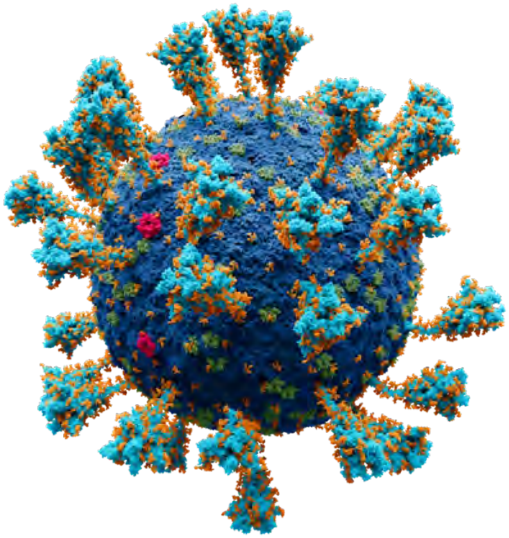
Fields of Study:
Atmospheres, Astrochemistry, Molecular spectroscopy, Vibrational spectroscopy

Capabilities and Techniques:
Infrared and Raman Spectroscopy, pulsed ns laser systems, ab initio quantum chemistry, rovibrational analysis.

Translational Opportunities:
Gas sensing, applications of Raman spectroscopy extending into many fields.

Probing materials-biology interactions using AI and machine learning

Computation is the third arm of research, after theory and experiment. Computational modelling and simulation of molecular systems are becoming indispensable for 21st-century science. However, the size, scale and complexity of realistic materials-biology interactions preclude the application of rigorous, physics-based computational methods like molecular dynamics and quantum chemistry. AI and machine learning are making spectacular inroads into solving these very complex problems. We use a wide range of computational chemistry and AI-based methods to model complex systems and predict their properties. These provide insight into how molecules interact with biology at the molecular level. As these are broadly applicable platform methods, we collaborate with experimental scientists across a wide range of projects, some involving non-biological structure-property relationships problems in materials.



SARS-CoV-2 coronavirus. (Photo credit: CC BY-SA 4.0 Alexey Solodovnikov)

Machine learning for materials and surface science

We apply advanced informatics and machine learning methods to extract new knowledge from surface analysis methods. We are applying these methods to tissue profiling or tumour samples and to libraries of polymers that are candidate coatings for implantable and indwelling medical devices. In collaboration with colleagues from RMIT, CSIRO, HZG Hamburg, we design catalysts and photo-catalysts for CO2 reduction, hydrogen, water splitting and safe organic corrosion inhibitors for addressing the >$1Tn market for these materials. We also use machine learning and evolutionary methods to design porous materials for environment and energy applications and to model the electrical, optical, and mechanical properties of hybrid 2D materials, recently shown to be superconductive.

Next-generation biomaterials

We work on a large University of Nottingham EPSRC project discovering and designing new materials for medical applications. We use data from high throughput experiments to build models of the biological effects of biomaterials.

Drug treatments for cancer and COVID-19

Working with CSIRO, Mt Sinai School of Medicine we developed novel drugs binding to the thrombopoietin receptor that may be the first disease-modifying treatments for the blood cancer myelofibrosis. We also work with Monash University to find biomarkers for colorectal cancer using sparse feature selection and machine learning. We are using very large-scale computational resources to conduct molecular docking and molecular dynamics studies to discover drugs that can be repurposed for treating coronavirus infections such as COVID-19.

Therapeutic gases

Noble gases like xenon are chemically inert but display a wide range of useful biological effects. We work with Air Liquide Sant International to use large scale computational simulations to understand how these gases produce medically relevant properties.

Safe use of nanomaterials

We are part of two EU Horizon 2020 projects on safety by design of nanomaterials: SABYDOMA, (€6M.1) and (NanoSolveIT (€6M) and a Marie Skłodowska-Curie project on the use of AI in drug discovery (AIDD, €3.93 M).

Lab Head: Professor Dave Winkler

Postdoctoral Fellow: Dr Marco Fronzi (UTS).

Collaborators:
Prof Morgan Alexander; Dr Grazziela Figeiredo; Prof Ricky Wildman (Nottingham); Prof Alex Tropsha (UNC Chapel Hill); Dr Ira Katz, Dr Geraldine Farjot (Air Liquide Sant International); Prof Nikolai Petrovsky, Dr Sakshi Piplani (Vaxine Pty Ltd, Flinders); Dr Tim Würger; Dr Sviatlana Lamaka; Dr Christian Feiler (Herzberg Institute Hamburg); Dr Ceyda Oksel, (Izmir Institute of Technology); Prof Joe Shapter (UQ); Prof Mike Ford (UTS); Prof Amanda Ellis (Melbourne); Dr Tu Le; Dr Nas Meftahi; Prof Andrew Christofferson; Prof Rachel Caruso (RMIT); Dr Aaron Thornton (CSIRO); Prof Nico Voelcker; Dr David Rudd (Monash); Prof Michael Morris (Sydney).

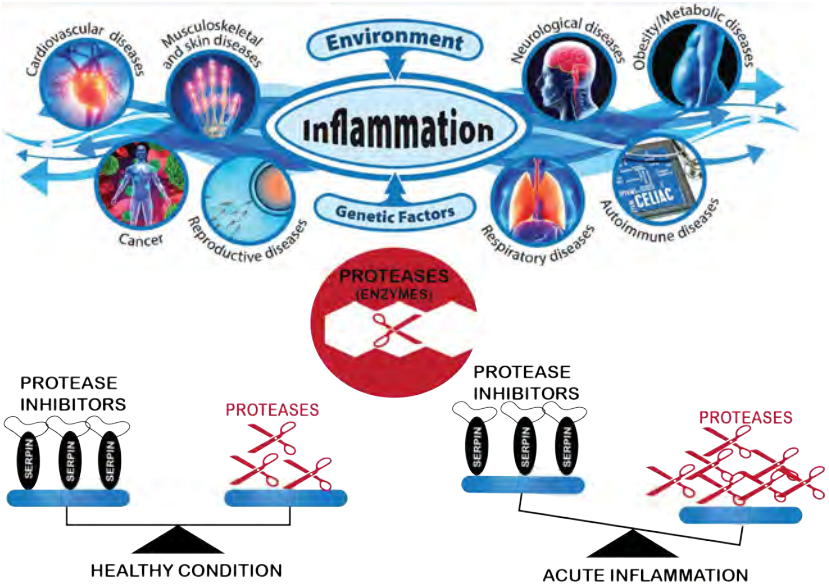
Fields of Study:
Computational chemistry; drug design; AI and machine learning; materials design; complex systems.

Capabilities and Techniques:
Mathematical analysis; visualization; and interpretation of complex data.

Translational Opportunities:
Cancer drugs; biomarkers; materials.

Protease Biology Group

Proteases are involved in multiple biological processes, including the regulation of inflammation. They have been shown to initiate and terminate proinflammatory or anti-inflammatory responses. The dichotomy in the biological roles that proteases exert is essential to drive acute inflammation toward the resolution phase to later return to homeostasis. However, when left unchecked, proteases can also promote inflammatory diseases. Importantly, proteases play both protective and detrimental roles in inflammatory diseases. Therefore, a greater understanding of proteases coupled with development of strategies to monitor and inhibit their activity is likely to have significant positive impact on human health conditions such as thrombosis, cancer, haemophilia, inflammation, and viral diseases.We are a protein biochemistry laboratory using techniques in molecular biology, protein biochemistry and enzymology to understand how the human body responds to infection and disease by dissecting the activity of enzymes called proteases. We use this mechanistic information to study a crucial part of our immune defenses, the Complement system as well as strategies developed by bacterial pathogens and viruses use in order to avoid killing by complement, which results in infections and disease. In the words of Professor Piet Gros, "The challenge lies in understanding the greater picture. It's about understanding the way in which different molecules work together in a process where everything must happen at exactly the right place and at exactly the right time." The moment when you start to understand how the complex system works is the most gratifying element of this job."



Regulation and control of the complement system in immunity

The complement system is vital in preventing disease caused by infections. The system is also implicated in many diseases associated with excess inflammation. We are studying the classical and mannose-binding lectin (MBL) pathways of complement activation, both of which are associated with inflammatory diseases. These pathways involve the sequential activation of proteins by a cascade of proteases. Our lab focuses on the initiating proteases of the two pathways: C1r, C1s and the MBL-associated serine proteases (MASPs). Our lab examines how these proteases interact with their target substrates and their regulatory inhibitor, C1-inhibitor. We plan to develop specific protein and peptide inhibitors of the different proteases to determine their roles in diseases.

The enemy within: targeting the virsl entry facilitator of SARSCoV2

The COVID-19 pandemic caused by SARS-CoV-2 has posed an enormous challenge to public health, and the threat still has a significant impact on humanity. The molecular properties of SARS-CoV-2 infection have been quickly elucidated, paving the way to therapeutics, vaccine development, and other medical interventions. Despite this progress, the detailed molecular mechanism of SARS-CoV-2 infection remains elusive. Given virus invasion of cells is a determining factor for virulence, understanding the viral entry process can be a mainstay in controlling newly emerged viruses. TMPRSS2 is a type II transmembrane serine proteases (TTSP) that has been shown to be crucial for host cell viral entry and spread of SARS-CoV-2, as well as SARS-CoV, MERS-CoV, and influenza A viruses. Our team has extensive expertise in the study of serine proteases involved in infection-driven inflammation and intracellular host responses. We will use our cross-disciplinary expertise to examine the proteolytic signature of viral infectivity by examining the enzymatic function and structure of TMPRSS2. We will then use this knowledge to dismantle the host cell machinery that enables the virus to infect the host cell and spread from one cell to another. We anticipate that this work will provide mechanistic insights into precisely how TMPRSS2 acts as a host factor that is essential for the infectivity of SARS-CoV-2. Many medically significant viruses require host cell proteolytic activation to result in functional infectious particles, making the unravelling of the infection process by targeting host-derived machinery in this study highly relevant to both basic science and potential therapeutic applications.

Lab Head: Dr Lakshmi Wijeyewickrema

Lab members:
Professor Rob Pike; Ms Jing Pang

Fields of Study:
Innate Immunity; Enzymes; Enzyme inhibitors; Coagulation; Viral Entry.

Capabilities and Techniques:
Protein production; Enzyme kinetics; Protein Biochemistry.

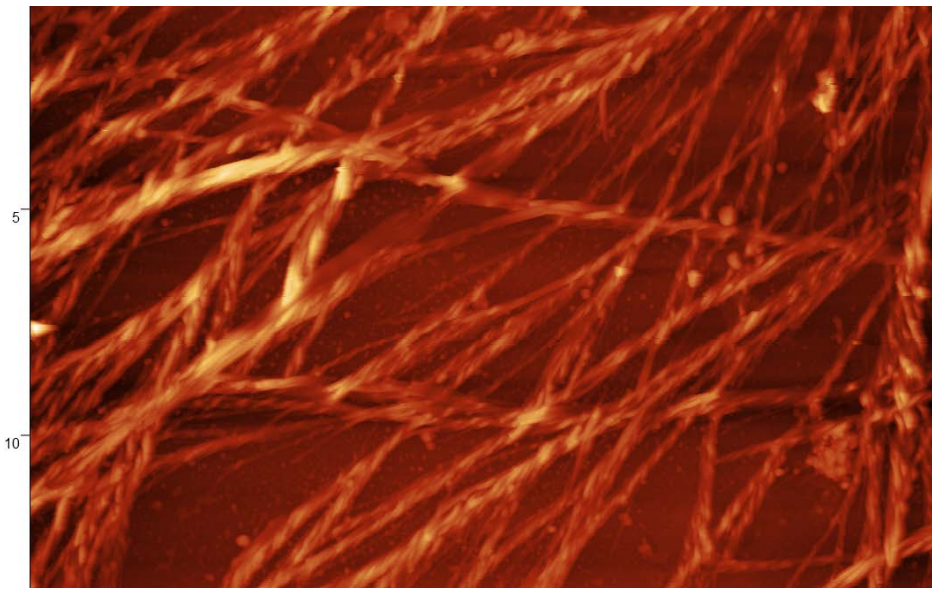
Translational Opportunities:
Development of specific inhibitors.

Self-Assembled Nanomaterials Group

Our group focusses on the design, discovery and characterization of self-assembled nanomaterials. Molecular self-assembly is an evolutionary optimized process where biological molecules with two or more distinct regions (e.g. one part of the molecule may be hydrophilic water loving and the other maybe hydrophobic water hating) organize themselves to form complex structures with distinct nanoscale morphologies (fibrils, micelles, vesicles etc). Such self-assembling materials have applications in diverse technical fields including tissue engineering, drug delivery, antibacterial materials, biological and environmental sensing and understanding disease.

The goal of my groups research is to develop materials, devices or medicines that have real and tangible benefits to communities in Australia and worldwide. For this to be possible, routes to translate our fundamental research to clinics, facilities and factories must be identified. Thus, I work closely with the MedTech industry, clinicians and government agencies to enable the translation of research outcomes into commercial devices, products and therapies.

Self-Assembled Peptide Nanofibrils as materials for 3D cell culture, bioprinting and tissue engineering
We are exploring the applications of a variety of self-assembling nanofibrillar peptides, and their ability to act as 3D culture materials for a variety of cell types. These materials will help us better understand fundamental biological processes, develop new materials for tissue engineering, new cell-laden inks for bioprinting and regenerative medicine.



Atomic Force Microscopy of Self-Assembled Phenylalanine nanofibrils, the toxic culprit in Phenylketanuria (Photo Credit: Jeremy Engwirda & Claire Buchanan)

Understanding the role of protein self-assembly in diseases
Misfolded protein aggregates known as amyloid fibrils are the molecular hallmark of a number of neurodegenerative diseases including Alzheimer's and Parkinson's. However, protein misfolding and amyloid aggregation also play important roles in a number of other maladies that are not traditionally thought of as amyloid diseases. We are interested in studying the amyloid aggregation processes in some of these less well studied amyloid diseases. Currently, we have active projects investigating the role of amyloid assembly in inborn errors of metabolism such as Phenylketonuria (PKU), and investigating if amyloid assemblies are playing a role in some of the neurological symptoms that occur in COVID-19. These fundamental investigations will help us understand the molecular mechanisms that underpin the progression of these diseases, hopefully revealing new potential therapeutic targets that will aid the development of new drugs.

LabHead: Dr Nicholas Reynolds

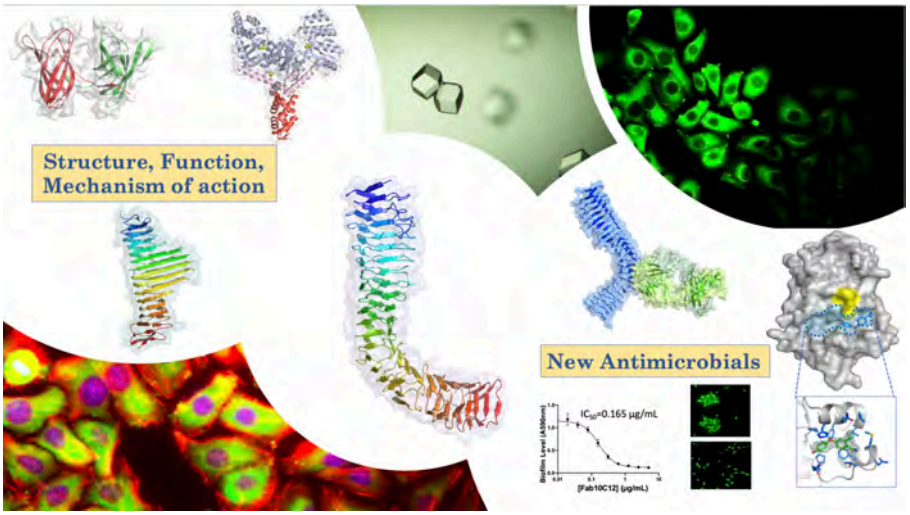
Lab members:
Mr Christopher Chong; Mr Jeremy Engwirda; Ms Bonnie Mclean; Mr Leshy Patchett; Ms Emily Field; Mr Michael Osborne.

Fields of Study::
Nanotechnology; Biomaterials; Colloid Science; Materials Science; Cell Biology.

Capabilities and Techniques::
Bioprinting; Atomic Force Microscopy; 3D Cell Culture; Biomaterials Characterization; Rheology.

Translational Opportunities:
Long standing relationships and collaborations with Clinicians and Surgeons at St Vincents Hospital Melbourne. We also work closely with the bioprinting company CellInk Ltd.

Structural Biology and Bacterial Pathogenesis Group



Antimicrobial resistance (AMR) is recognised by the World Health Organisation (WHO) as a critical threat to human health. The overuse of antibiotics has led to AMR bacteria (superbugs), which are now widespread in hospitals around the world. In 2019, AMR infections were associated with 4.98 million deaths worldwide, placing resistant bacteria among the leading causes of death for people of all ages. Meanwhile, the antibiotics development pipeline is near-empty which demands for the urgent development of new molecules to fight bacterial infections. Our research examines the molecular mechanisms underlying bacterial infections. Our multidisciplinary approach combines X-ray crystallography, molecular biology, biochemistry and biophysics to investigate the structure-function relationships in proteins involved in bacterial pathogenesis. Our work provides new knowledge on therapeutically important microbial proteins and the tools to guide the development of new antimicrobial classes.

Structure, Function and Mechanism of action of bacterial virulence proteins

Bacterial pathogens deploy an arsenal of virulence factors to establish infection and cause disease. Autotransporter proteins, the largest group of outer membrane and secreted proteins in bacteria are involved in host cell adhesion and toxicity, and promote the formation of aggregated communities and biofilms, which are critical strategies bacteria use to resist the host immune response and antibiotics. Autotransporters are also highly immunogenic and are integral components of human vaccines. We study how autotransporter proteins promote disease and allow bacterial survival by forming protective biofilms. We focus on important therapeutic autotransporters and investigate their mode of action at atomic resolution, as well as whether inhibition of autotransporter function prevents infection.

How bacterial pathogens make toxins and antibiotic resistance enzymes

Bacteria produce folding enzymes (foldases) necessary to produce functional virulence factors. These include the Dsb family of proteins, which catalyse a key step in the protein-folding pathway, the introduction of disulfide bonds. Mutants defective in the Dsb pathways have reduced fitness and pathogenic potential. Our team, in collaboration with national researchers, is leading the structural-functional characterisation of these key bacterial enzymes. We dissect the molecular mechanisms through which some bacteria catalyse the folding of proteins involved in host infection and bacterial resistance. Our studies provide structural information to guide inhibitor development.

Harnessing structural information to drive the discovery of antimicrobials

The increase of antimicrobial resistant infections highlights the critical need for new therapeutics. We are developing novel antibiotics that target virulence rather than viability. Disarming rather than directly killing bacteria is a new paradigm for antibacterial therapy that will lead to lower resistance rates than current antibiotics. We are developing small drug-like molecules or antibody inhibitors against key enzymes, secreted toxins and biofilm forming proteins from multidrug-resistant *Enterobacteriaceae.* For example, we have developed monoclonal antibody-based inhibitors that bind to specific autotransporter proteins and prevent the formation of bacterial biofilms. We have patent-protected this novel technology, which represents an entirely new strategy for targeting bacterial biofilms and meets all four innovation criteria defined by the World Health Organisation (WHO) - new mode of action, no cross-resistance to antibiotics, new target and new chemical class.

Lab Head: Associate Professor Begoña Heras
Lab members: Dr Jason Paxman (Snr Postdoc); Dr Tony Wang (Adjunct); Dr Pramod Subedi (Adjunct); Dr Lilian Hor (Adjunct); Mr Carlos Santos; Ms Akila Pilapitya; Ms Kaitlin Clarke; Ms Taylor Cunliffe; Ms Stephanie Penning.

Fields of Study:

Structural biology; Biochemistry; Microbiology; Host-pathogen interactions.

Capabilities and Techniques:

Structural biology (X-ray crystallography, SAXS); Biochemistry (protein chemistry, enzyme kinetics, redox biochemistry, stopped-flow assays, enzyme kinetics); Biophysics (Analytical Ultracentrifugation, CD spectroscopy, SPR); Microbial assays (biofilm and aggregation assays, motility, in vitro susceptibility testing,); Structure-based drug design and computational biology (molecular docking); Bacterial/eukaryotic cell culture; Microscopy.

Translational Opportunities:

Develop new antibiotic classes to counteract antimicrobial resistant infections; develop antimicrobials against critical priority pathogens recognised by WHO; develop small molecules and biologics targetting virulence.

Structural Biology of Host-Pathogen Interactions Group

Our Group investigates the complex interplay of hosts and their pathogens. All life is shaped by the constant struggle between hosts and microbial threats. The interface between host and pathogens represents a major frontier for biomedical and biotechnological applications. We aim to understand at the atomic level three such molecular battlefields. We hope to understand how viruses hijack cellular defence systems to ensure their own proliferation and survival. Our second major area of interest centers on the role of small proteins that act as a first line of defence against microbial targets such as fungi, and the mechanism that these molecules use to destroy target cell membranes. And lastly, we try to understand how viruses assume control of cell polarity signalling and the impact of this on viral disease.

Crystal structure of an African Swine Fever Virus virulence factor. (Photo credit: Marc Kvansakul, Pippa Hawes)

Antimicrobial peptides in innate immunity
Defensins are small cationic proteins that are involved in innate immune processes in plants as well as humans. In plants, defensins have been shown to deliver significant resistance against plant pathogens such as fungi, however their precise molecular mechanism of action is currently not fully understood. Furthermore, defensins are also able to target cancer cells. We are currently investigating how defensins are able to attack and perforate cell membranes of pathogens as well as cancer cells. Recognition of phospholipids has been shown to be critical for the ability of defensins to attack target cells, and we are interested in understanding the structural basis for phospholipid recognition as well as membrane attack. Using X-ray crystallography we recently showed that defensins form large oligomeric complexes with phospholipids, thus for the first time shedding light onto the detailed molecular mechanism employed by defensins during innate defence.

Viral infections and cell death pathways
The programmed death of cells (apoptosis) is a critically important mechanism that enables multicellular organisms to eliminate damaged, infected or unwanted cells during development, growth and tissue homeostasis. Failure to regulate apoptosis leads to a number of diseases including arthritis, autoimmune diseases and cancer. Viruses have evolved a powerful ability to inhibit host cell apoptosis in response to viral invasion to ensure their own survival and proliferation.

Cell polarity
The establishment of cell polarity, and correct definition of where top and bottom, front and back as well as left and right are in a cell, is critically important for the formation of tissues in multicellular organisms. Dysregulation of this process is associated with the development of birth defects, more mobile and aggressive cancers as well as viral infections. Correct establishment of the different polarity axis is controlled by a network of scaffolding proteins that integrate signals from a host of cellular signalling pathways. We are interested in understanding the molecular mechanism underlying cell polarity regulation using a range of structural biology techniques including X-ray crystallography, cryo-electron microscopy and small-angle X-ray scattering.

Evolution of cell death and cell polarity signaling
Our Group's research is driven by a deep curiosity to discover how the natural world works, and a particular interest of ours centers on the evolutionary origins of some of our favorite cell signaling pathways, including those that control cell death and cell polarity. We are studying proteins that control these pathways from a range of ancient animals including Trichoplax, hydra and sponges, to understand the ancient origins of these critical signaling pathways and how they evolved over time.

Lab Head: Professor Marc Kvansakul
Lab members: Ms Airah Javorsky; Mr Ben Espinoza; Mr Bryce Stewart; Ms Janesha Maddumage; Ms Shi Xuan Sum.

Fields of Study:
Structural Biology; Biochemistry; Cell Death; Innate Immunity; Cell Polarity.

Capabilities and Techniques:
X-ray crystallography; Cryo-electron microscopy; Protein interaction affinity measurements.

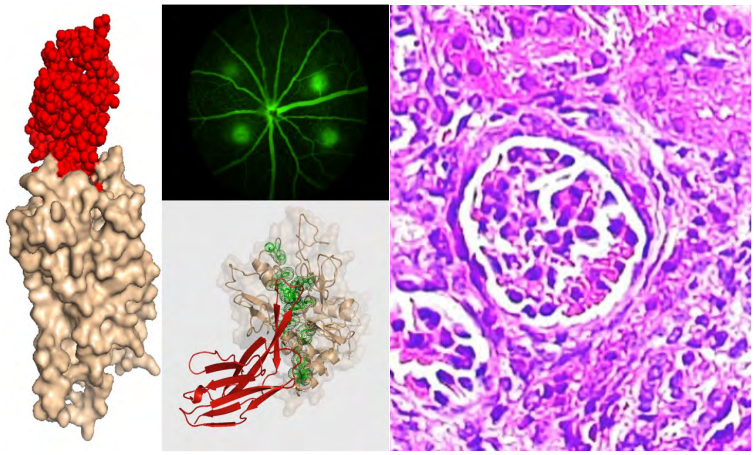
Translational Opportunities:
Drug discovery; vaccine design.

Translational Biology Group

Our group studies the molecular basis of various inflammatory diseases and we aim to develop therapies to combat these. Inflammation is essential in alerting the immune system to infection or tissue injury so that the host's white blood cells can quickly locate and combat the pathogen or engage in tissue repair. This response is tightly controlled, with inflammation waning after infection/injury is resolved – returning to basal levels with the host's white blood cells following suit. An uncontrolled inflammatory response leads to various diseases such as multiple organ failure in sepsis, various fibrotic diseases and auto-immune diseases (e.g. psoriasis, systemic lupus erythematosus and inflammatory bowel disease etc). Our lab has identified upstream cell surface receptors regulating these diseases and we aim to develop therapies by blocking receptor activation.

Treml4 receptor and innate immune memory
We have identified Treml4 receptor as the master regulator of inflammation during polymicrobial sepsis. Genetic ablation of this receptor in mice offers almost absolute protection from sepsis-mediated inflammatory pathology and immune cell apoptosis. Our findings suggest that ablating this receptor can induce neutrophil memory after exposure to sepsis, which enables the mice to combat blood-born Candida infection. This protection can last up to a month despite neutrophils lasting only 24 hours in the blood, and suggests neutrophil memory, which is a new concept. We have evidence this memory is imparted through epigenetic modification in the bone marrow compartment and we are studying the underlying mechanism using ChIP-Seq and single cell RNASeq analyses.

Developing biologicals against Treml4 receptor
We identified the Treml4 receptor in a genome wide CRISPR screening of mice undergoing polymicrobial sepsis and developed an *in vitro* assay to test the functionality of this receptor family. We are also developing humanized mouse models expressing the human receptor to enable us to study the function of this protein in an *in vivo* system and allow testing *in vivo* of any biologicals that we develop (i.e., monoclonal antibodies (mAbs), i-Bodies, shark antibodies and human Fabsas) to treat sepsis, psoriasis, SLE and IBD.



Inflammation in various structures

Single domain antibodies against fibrosis and inflammatory diseases
Shark antibodies (VNARs) are a subset of antibody-like molecules found in sharks and rays. Some VNARs have been shown to possess a long CDR3 loop, which is much larger than those of human and murine antibodies. This extended CDR3 loop is ideal for penetrating cleft-type epitopes such as enzyme active sites and ligand binding sites of surface receptors that are otherwise inaccessible to conventional antibodies. We created a humanized version of these antibodies, called i-bodies, and identified binders from this library that bind to the chemokine receptor CXCR4. This molecule is up regulated in many cancer cells and is expressed in organs that have developed fibrosis and other inflammatory diseases. The i-body that binds to CXCR4 (AD-214) can bind to and block the migration of inflammatory cells towards the site of inflammation thereby preventing the development of fibrosis in animal models of pulmonary fibrosis, kidney fibrosis and eye fibrosis in macular degeneration. The biotechnology company, AdAlta has completed manufacturing, toxicity, and a Phase 1 human clinical trial with AD-214. AD-214 was shown to be safe and is currently progressing towards the clinic for Idiopathic Pulmonary Fibrosis. We are examining how AD-214 can block the molecular signaling pathways of CXCR4 and prevents inflammation and fibrosis.

Single domain antibodies in malaria
The *Plasmodium falciparum* parasite causes severe malaria in humans. We identified VNARs and i-bodies that block invasion of malaria into host erythrocytes. The structural complex of one of these VNARs and its target AMA1, revealed that the long loop of the VNAR can penetrate a hydrophobic trough on this protein and block the function so the parasite is unable to invade the red blood cell. We identified i-bodies that bind to AMA1 from all *P. falciparum* strains and have shown that some can block parasitic invasion into blood cells. We are collaborating with colleagues to develop these i-bodies as potential therapies to understand the molecular tricks that the malaria parasite uses to invade blood cells.

Lab Heads: Associate Professor Hamsa Puthalakath and Professor Michael Foley
Emeritus: Professor Robin Anders
Lab members: Mr Joseph Menassa; Mr Corey Pollock; Ms Valeria Impicheche; Mrs Irvin Jose; Dr Dimuthu Angage; Mr Callum Cairns.

Fields of Study:
Inflammation; Innate immunity; Fibrosis; Antibody development.

Capabilities and Techniques:
CRISPR gene editing; mouse models; i-Body/ Fab library panning; disease models

Translational Opportunities:
Developing biologicals against human inflammatory pathologies.

Viral & Structural Immunology Group

We focus on how to combat viral infections. Viruses are part of day-to-day encounters that our immune system needs to deal with. How the immune system "sees", recognises and eliminates viral infection is not fully understood. Indeed, viruses can mutate and escape the immune system surveillance (viral escape). If we were to develop better vaccine and drugs, it is essential to understand the mechanism of viral recognition and viral escape prior to this. Our laboratory combines both the cellular and structural approaches to understand the immune system action when face with a viral infection. Our goal is to deeper our current understanding of T cell activation and recognition mechanism, especially in the context of viral infection such as SARS-CoV-2, influenza and HIV.

The Gras Lab

Viral Immunology

Our lab is focused on understanding infections by viruses that are a health burden. Trying to understand why some of us are at higher risk of developing severe infection due to those viruses, while other seems to be able to handle the virus and have an immune system allowing them to control the infection.

COVID-19disease

We study COVID-19 disease to understand the immune response to SARS-CoV-2 and its variants. We work in collaboration with other teams in Australia and overseas to fully dissect the T cell, B cell and Antibody responses toward the virus. We aim to map and characterise in depth SARS-CoV-2 peptides able to stimulate T cells in better understand the progression of the disease, the role of T cell in COVID-19. This information can help anticipate or predict which mutation will be an issue for T cell recognition, as well as quickly assessing the impact on the immune system, and immune protection, that new SARS-CoV-2 variants might have. This also will help us understand the risk factor worsening the COVID-19 disease, if some marker can be used to predict the evolution of the disease. In addition, we also aim to study the level of protection from the vaccines against variants, and over time to help inform the need for future booster shot.

Influenza disease

Influenza viruses cause significant morbidity and mortality worldwide. Although a vaccine is available, it primarily induces a humoral response (antibody) and requires updating annually. Also, the vaccine provides protection if the predicted strains match the circulating strains, but sometimes the virus mutate away from the prediction and the vaccine will have minimal benefit. Our aim is to develop a universal influenza vaccine that could provide protection against distinct influenza strains. This will allow a one-short vaccine to be developed, instead of having the "jab" every year. Our immune system has killer T cells that are known to be protective against influenza disease, decreasing the quantity of virus (viral load) and disease severity. Understanding how T cells can be protective, what are their characteristics, would help replicate a protective immunity.

AIDs disease

While antiretroviral therapy (ART) has dramatically improved the health of HIV-infected individuals, comorbidities associated with persisting inflammation have emerged as complications. It is imperative to develop new treatments (and ideally, a vaccine) for this virus. Our work focuses on individuals known to control HIV infection and/or delay disease progression. They have superior T cell responses and understanding the mechanism behind it is central for informing therapeutic or vaccine development against HIV. We aim to understand how HIV controllers T cells are protective, their functional but also molecular features, which could lead to new therapeutic avenues.

Lab Head: Professor Stephanie Gras
Lab members: Dr Emma Grant, ARC DECRA fellow; Dr Dimitra Chatzileontiadou; Dr Christopher Szeto; Mr Dhilshan Jayasinghe; Ms Andrea Nguyen; Mr Christian Lobos; Mr Lawton Murdolo; Mr Samuel Liwei Leong; Ms You Min Han; Ms Ha Pham.

Fields of Study:
Cellular Immunology; viral disease (e.g. influenza, SARS-CoV-2, HIV); T cell activation; epitope presentation; Structural biology.

Capabilities and Techniques:
X-ray crystallography; biochemistry; protein affinity and stability measurement; sample biobank (COVID); cellular assay; immunology; T cell activation and repertoire; single cell sequence; flow cytometry.

Translational Opportunities:
T cell engineering; biomarker identification; risk factor of disease; drug design and anti-viral development.

About La Trobe University

Our Mission

Advancing knowledge and learning to shape the future of our students and communities.

Our Vision

To promote positive change and address the major issues of our time through being connected, inclusive and excellent.

Our Values

Our early reputation as a radical and challenging institution continues to influence the way we enrich the experience of our students and engage with our partners and communities.

We were founded half a century ago to broaden participation in higher education in Melbourne's north and, later, in regional Victoria. We have succeeded for many thousands of students who would otherwise have been excluded from the opportunities provided by a university education.

We continue to support access, diversity and inclusivity while undertaking world-class research that aims to address the global forces shaping our world and make a difference to some of the world's most pressing problems, including climate change, securing food, water and the environment, building healthy communities, and creating a more just and sustainable future.This approach is based on our values of:

- inclusiveness, diversity, equity and social justice
- pursuing excellence and sustainability in everything we do
- championing our local communities in Melbourne's north and regional Victoria
- being willing to innovate and disrupt the traditional way of doing things.

Of all Australian universities, we are the most successful at combining accessibility and excellence, and have become a place where social inclusion and globally-recognised excellence come together for the bene t of our students, our staff and our communities.

Our academics and researchers achieve national and international recognition, our public intellectuals demonstrate an enduring social conscience and influence, and our alumni achieve extraordinary success and impact in government, industry and not for profit organisations.

We strive to be exemplars for the sector in our commitment to gender equity and to inclusivity for marginalised groups; and we work with indigenous peoples and organisations to support their social, cultural and economic aspirations.

We embrace sustainable practices across all our campuses because we are committed to improving environmental, social and economic outcomes for our communities.

We contribute to economic development for our local communities, and our future activity will increasingly be international as we become a globally connected university in everything we do.

Our Culture

La Trobe Cultural Qualities

Our cultural qualities underpin everything we do. As we work towards realising the strategic goals of the University we strive to work in a way which is aligned to our four cultural qualities:

Connected

- We are Connected: Connecting the students and communities we serve to the world outside

Innovative

- We are Innovative: Tackling the big issues of our time to transform the lives of our students and society

Accountable

- We are Accountable: Striving for excellence in everything we do. Holding each other to account, and working the highest standards

Care

- We Care: We care about what we do and why we do it, because we believe in the power of education and research to transform lives and global society.

About Victoria and Melbourne

Experience Melbourne

Melbourne is the capital of the state of Victoria, and Australia's second largest city. It's a multicultural hub with 4.5 million people from over 153 countries. It's one of the world's best sporting cities, and is Australia's art and culture capital. Melbourne is a safe, well-serviced city in which to live. The main campus of the University at Bundoora is close to many world class hospitals, schools, research centres, shopping centres, bike paths and parklands. Melbournians enjoy, affordable healthcare, world-class education, reliable infrastructure, business opportunities and a healthy environment. In Melbourne you'll find just about every cuisine: French, Italian, Spanish, Greek, Chinese, Malaysian, Indian, Thai, Japanese, Moroccan and lots more. Melbourne has over 100 art galleries as well as theatres, international and local opera, ballet, comedy and live music.

Each year Melbourne hosts major international sporting events like the Australian Open Grand Slam tennis tournament, the Formula One Grand Prix, the Rip Curl Pro surfing championship, the Australian Masters golf tournament, the Melbourne Cup and the Grand Final of Australian Rules Football. As well as over 2500 festivals and events including the Melbourne International Arts Festival, Melbourne International Film Festival, Melbourne International Comedy Festival and the Melbourne Spring Racing Carnival.

Find out more: https://liveinmelbourne.vic.gov.au/discover

La Trobe University Campuses in Australia

Each of our seven campuses (Melbourne, Albury-Wodonga, City, Bendigo, Shepparton, Midura and Sydney) is a unique expression of place, people and history that play an important role in social, cultural and economic life. We are located in Victoria's major regional cities, creating a unique network of research, industry and innovation expertise that can be accessed across the state.

Victoria: The Garden State

Victoria has many notable gardens and 36 national parks covering two and a half million hectares. Victoria's many attractions include the Great Ocean Road, (stunning coastal views and the world-famous Twelve Apostles), the Grampians and the High Country.

Find outmore: visitvictoria.com

Melbourne Campus

La Trobe's Melbourne Campus has 27,000+ students and is surrounded by bushland. Students from across the world take advantage of state-of-the-art facilities, including our AgriBio Research Centre, the La Trobe Institute for Molecular Science and our very own Wildlife Sanctuary.

Albury-Wodonga Campus

La Trobe's Albury-Wodonga Campus has 800+ students and is home to our leading regional research centre, the Centre for Freshwater Ecosystems which focuses on water science and policy of the Murray-Darling basin. Here, undergraduate students work alongside Honours and research students on local issues.

School of Agriculture,
Biomedicine and Environment
La Trobe University