Discover your future in research

PROJECT OPPORTUNITIES FOR:
• UNDERGRADUATE
• HONOURS
• MASTERS
• PHD

monash.edu/discovery-institute
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Acknowledgement

We acknowledge the traditional lands of Indigenous peoples.

The Faculty of Medicine, Nursing and Health Sciences incorporates the Aboriginal and Torres Strait Islander Curriculum Framework in educating future health professionals. You will learn skills in respect, communication, safety and quality, advocacy and reflection to improve Indigenous health.

Monash is committed to facilitating the entry of Indigenous students into courses. There are a range of pathways, entry points, bursaries, scholarships, accommodation, tutorial support and cadetships. To learn more about entry requirements and our Indigenous Access Interview, contact Gukwonderuk Indigenous Health staff via email at med.indigenoushealth@monash.edu or 03 9905 3828.
Behind every treatment that improves human health is a story of discovery. At the Monash Biomedicine Discovery Institute (BDI), we are making the discoveries that will relieve the future burden of disease. We do this by tackling the big research questions that address the underlying causes of major global health issues.

The Monash BDI brings together more than 120 research teams from multiple disciplines into six global health priority areas. Our six Discovery Programs are Cancer, Cardiovascular Disease, Development and Stem Cells, Infection and Immunity, Metabolism, Diabetes and Obesity, and Neuroscience.

But tackling the big questions in biomedical research demands new perspectives to find new solutions. Spanning six Discovery Programs, we are one of the largest and highest quality biomedical research institutes in Australia. This allows for the cross-pollination of ideas, as it is at the intersection of these global health issues that truly innovative discoveries will be made.

Our exceptional research is possible because our scientists are led by internationally-renowned researchers and they have access to truly world-class technology and infrastructure.

Discoveries will only lead to better health if we partner with the most innovative companies and the best clinical scientists. We have a well-developed record of working with major pharmaceutical companies and a number of our researchers have successfully developed drugs for clinical use. The Monash BDI is at the heart of one of the largest – and fastest growing – medical research hubs in Australia thanks to our relationships with Monash Partners and the Monash Academic Health Science Centre.

Research has no borders and requires an international outlook to be competitive with the best in the world. We encourage strong international networks and partnerships in research and research training, and our scientists have more than 200 productive international collaborations.

Combining our commitment to outstanding research with our capacity to engage both clinicians and industry means we are well placed to fulfil our aim of having an impact on global health.

Training the next generation of scientists is central to what we do and we have students contributing to our research at undergraduate level through our Research in Action electives and through our Summer and Winter Research Scholarship Program, and at graduate level through our Honours, Masters and Doctoral (PhD) programs. All of these programs provide outstanding research training and career development opportunities for our students.

We are always looking to recruit outstanding scientists and students. Please get in touch if you’d like to help us make the next big discovery.
OUR STRATEGIC PRIORITIES

DISCOVER
Pursue excellence in discovery research within and across these six global health priority areas:

• Cancer
• Cardiovascular Disease
• Development and Stem Cells
• Infection and Immunity
• Metabolism, Diabetes and Obesity
• Neuroscience

TRANSLATE
Translate and commercialise our research to impact on health outcomes.

COLLABORATE AND CONNECT
Collaborate globally to conduct outstanding research.

DEVELOP OUR PEOPLE
Attract, support and develop the science leaders of the future in a diverse and supportive environment.

ENGAGE
Engage with the wider community in all that we do, to inform, influence and advocate.

WHO WE ARE

An institute with the scale and scope to tackle major research questions

We are one of the largest and highest-quality biomedical research institutes in Australia. With more than 120 internationally-renowned research teams, we work with national and international collaborators on global health priorities.

WHAT WE DO

Discover and innovate to enhance lives

Our scientists are passionate about discovery research and committed to establishing a culture of excellence and collaboration to enable the most important research questions to be addressed.

With strong international networks and partnerships with researchers, health precincts and industry, together with access to unparalleled, world-leading research infrastructure, our discoveries accelerate the ability to prevent, diagnose and treat disease.

TACKLING THE BIG QUESTIONS IN BIOMEDICAL RESEARCH IS NO LONGER THE DOMAIN OF INDIVIDUAL SCIENTIFIC DISCIPLINES – IT DEMANDS A CROSS-DISCIPLINARY APPROACH
We are part of Monash’s Faculty of Medicine, Nursing and Health Sciences RANKED 46 IN THE WORLD and TOP 3 IN AUSTRALIA according to the 2017/18 Times Higher Education Ranking for Clinical, Pre-clinical and Health.

Our translational partners include the Monash Institute of Pharmaceutical Sciences, the Monash Institute of Medical Engineering, the Monash Health Translation Precinct, the Alfred Medical Research and Education Precinct and Monash Partners Academic Health Science Centre.

The Monash BDI is proud to host the Directorate of the European Molecular Biology Laboratory (EMBL) Australia. We also lead the ARC Centre of Excellence for Advanced Molecular Imaging and play a major role in the ARC Centre of Excellence for Integrative Brain Function.

**DISCOVERY TO IMPACT: THE WIDER CONTEXT**

**A NEW FRAMEWORK FOR RESEARCH EXCELLENCE**

**MONASH BIOMEDICINE DISCOVERY INSTITUTE**

- Industry partners
- Health precincts
- Clinical partners & hospitals
- Research collaborators & consortia

**Impact**

- Research excellence
- Improved health outcomes
- Economic benefit & growth
- Global reach
WE'RE TACKLING THE BIGGEST HEALTH ISSUES IN AUSTRALIA AND AROUND THE WORLD

In Australia, it is estimated that one in two men and one in three women will be diagnosed with cancer in their lifetime. The disease accounts for three in 10 Australian deaths.1

Cardiovascular disease is the leading cause of death worldwide. It is responsible for 30 per cent of deaths in Australia, killing one person every 12 minutes.2

Adult health is determined by both the quality of the sperm and egg, and environmental exposure in early life (during conception, pregnancy, infancy and childhood.) With one in four couples affected by infertility3, the ability to control fertility and the promotion of healthy development is critical to future generations’ health.

Diseases caused by infections killed almost 6.5 million people in 20154 and the World Health Organization has identified antimicrobial resistance as one of the greatest threats to human health.5 Autoimmune diseases are one of the top 10 leading causes of death in the US of women under the age of 65.6

About 40 per cent of adults worldwide are overweight.7 Obesity is a major risk factor for many diseases, including type 2 diabetes, cancer, liver disease and heart disease.

Losing vision, hearing or movement because of a brain injury or disease can be debilitating. Furthermore, in an increasingly ageing population, dementia and neurodegenerative diseases are the second most common cause of death in Australia.8

WE ARE DEVELOPING PREVENTION, DETECTION AND TREATMENT STRATEGIES FOR THE FOLLOWING DISEASE AREAS

- Prostate, pancreatic, colorectal and gastric, breast, liver and brain cancers
- Cancer development and progression

- High blood pressure
- Heart attack, aneurysm and stroke
- Chronic kidney disease
- Heart, kidney and lung tissue injuries and scarring, for example cystic fibrosis
- Chronic lung diseases, including asthma

- Organ development and congenital disease
- Male and female infertility and reproductive health
- Genetics and human development
- Stem cells and regenerative therapies

- Infectious diseases, caused by viruses, bacteria, fungi or parasites, including HIV, influenza, golden staph, thrush and malaria
- Hospital-acquired infections
- Antibiotic-resistant superbugs
- Autoimmune diseases

- Obesity and liver disease, cancer and cardiovascular disease
- Type 2 diabetes
- Obesity and the central nervous system
- Mitochondrial disease

- Nervous system and brain injury
- Restoring neural function through brain computer interfaces
- Neurodegenerative diseases including Parkinson’s and Alzheimer’s disease, multiple sclerosis and others
TARGETING THE INTERSECTION OF DISEASE AREAS

Some of the most significant breakthroughs in biomedical research occur at the intersection of disease areas. Our scope and scale enables our scientists in different Discovery Programs to work together to make major advances in our understanding of disease. These are a few examples.

3. World Health Organization [www.who.int/reproductivehealth/topics/infertility/burden/en]

We have shown how a bacterial infection can induce chronic gastritis leading to cancer in our stomach. This insight helps us to develop new cancer therapeutics. 10

We have uncovered cells of our immune system involved in the development of high blood pressure, showing the potential to design new immunotherapies to prevent hypertension. 11

We discovered that when our calorie intake is reduced, a hormone protects our brain from neurodegeneration. Our findings open new possibilities to slow or prevent diseases, such as Parkinson’s. 13

www.monash.edu/discovery-institute
Be supervised, mentored, surrounded and inspired by some of the world’s leading biomedical scientists in an internationally-regarded university with state-of-the art facilities, located in Melbourne, which is not only recognised as one of the globe’s most liveable cities but also Australia’s biomedical capital city.

Our academic program has direct application to your future career. Monash biomedical science students work with industry partners and on genuine research, leading to genuine post-degree employment opportunities, plus we offer opportunities to study abroad as part of your learning.

With more than 150 students enrolled in our Honours programs and more than 300 in our Masters and Doctoral programs, it’s obvious many students choose to start their future in research with us. Here’s a few reasons why.

**THE SCOPE AND SCALE OF OUR RESEARCH**

Research that finds solutions to complex global biomedical challenges requires scale. We bring together more than 700 of Australia’s most creative and innovative minds, with expertise spanning a range of biomedical and related research areas. You’ll have the opportunity to attend – and present at – national and international scientific meetings, and to hear from high-profile researchers at seminars.

**EMPLOYABILITY FOCUS FROM DAY ONE**

Monash BDI offers a huge head start in empowering you to enter the workforce. As a working research institute, partnering with industry every day, we offer an environment where our students are involved in genuine biomedical projects, regularly mixing with senior corporate, scientific and non-academic personnel and building crucial networks of peers and potential future employers. We also have a range of internships and mentoring programs with industry partners.
GROW YOUR FUTURE NETWORK
You won’t only emerge from your research training with a degree, you’ll also boast genuine achievements for your curriculum vitae and an already powerful contact book.

PIONEERING LEARNING SPACES
Our purpose-built Biomedical Learning and Teaching building is set to open in 2019. You’ll have access to wet and dry labs with state-of-the-art equipment to develop your technical skills.

AN INTERNATIONAL OUTLOOK
We are expanding our international footprint. Recently, more than 20 research teams have joined us from countries including Germany, Canada, the US and Denmark, and we have more than 200 established international collaborators. Our students hail from more than 40 countries.

WE BREAK DOWN BARRIERS
Our experts from different fields work together in collaborative multi- and cross-disciplinary teams. This approach ensures each scientific problem can be examined from a range of perspectives and each research program benefits from a diversity of expertise.

STUDY IN AUSTRALIA’S INNOVATION CAPITAL
Victoria is home to a wealth of major medical research institutes and teaching hospitals, and over 180 biotechnology companies.

ESTABLISHED INDUSTRY PARTNERSHIPS
These valuable partnerships boost research excellence and deliver solutions to current industry challenges. We are committed to working with industry, business, government, and the community sector to find innovative solutions to today’s global health problems.

ACCESS TO EXPANDING TRANSLATIONAL PRECINCTS AND HEALTH NETWORKS
These networks accelerate the translation of our discoveries into health outcomes and enable clinical imperatives to inform our innovative research agenda. Our work begins in the laboratory with fundamental discovery research and ends with impactful treatments.

OPEN ACCESS TO UNPARALLELED, WORLD LEADING RESEARCH INFRASTRUCTURE
Monash University has invested significantly in high quality research infrastructure and expertise to establish our platforms. The platform network brings together leading researchers from different fields to engage with local, national, and global, academic and commercial research sectors. Coupled with certification from the International Organization for Standardization (ISO), these platforms are a game-changer for academic and industry collaboration.

AND FINALLY – IT’S NOT ALL WORK – YOU’LL ALSO HAVE ACCESS TO A RANGE OF FUN SOCIAL EVENTS ORGANISED BY WELL-ESTABLISHED STUDENT COMMITTEES.
Biomedical research is no longer the domain of individual disciplines. Today, it’s about pursuing discovery research with experts from different fields who work together in collaborative multi and cross-disciplinary teams.

This approach could help to answer cutting-edge research questions such as the impact of immunity on cancer, how diabetes leads to cardiovascular problems, and the role metabolic inventions can play in killing cancer cells.

The Monash BDI offers a number of pathways for you to join one of more than 120 world-renowned research teams and work on exciting ground breaking research projects looking at a range of global health issues.
RESEARCH IN ACTION
At Monash, you can begin working on meaningful research projects as an undergraduate student through our third year Research in Action elective units. These units enable you to undertake exciting research that contributes new knowledge to the field under the guidance of leading researchers and educators.

HONOURS PROGRAM
The Honours program, which is available to graduates of the Bachelor of Biomedical Science and Bachelor of Science degrees, is one year in length and allows you to gain a broader understanding of the biomedical sciences and contribute new knowledge to the field.

The program consists of a significant research project and a coursework component. For your research project, you’ll select and undertake a research topic from any area of biomedical science, working within a research team. The program will enable you to develop research and professional skills, as well as advanced knowledge in your chosen research area. The Honours program increases your employment opportunities and allows you to determine if you want to pursue a career in research.

MASTER OF BIOMEDICAL AND HEALTH SCIENCE
Discover how to conduct and commercialise your research with the Master of Biomedical and Health Science. This program provides you with comprehensive knowledge of multiple disciplines within biomedical sciences. With an employability focus from day one, you’ll be trained in collaboration, professionalism and entrepreneurship. A three-month internship will allow you to develop a highly sought after professional skill set that can be applied in research and industry.

PHD PROGRAM
A PhD in biomedical science at Monash enables you to make significant contributions to the field through original research. At the core of the program is an extensive, independent research project on an agreed topic, supported by at least two expert academic supervisors. This research component is enhanced by professional development activities, which provide you with the skills required to make an impact in academia, government or the wider community. Completing a PhD can also open doors to a research career or high-level roles in the biomedical industry and government.

RESEARCH PATHWAYS

Bachelor of Biomedical Science
Research in Action units
Bachelor of Science (major in a biomedical science area of study)
Honours (1 year)

Career in research or biomedical industry

Master of Biomedical and Health Science (1.5 - 2 years)

Master of Biomedical and Health Science (1.5 years)

PhD (3 - 4 years)

www.monash.edu/discovery-institute
The Monash Biomedicine Discovery Institute offers Research in Action units for students studying the Bachelor of Biomedical Science or Bachelor of Science course. These third year units provide the opportunity for high achieving students to work on a real life research project in a biomedical research laboratory under the supervision of a research scientist. These units are a great way to gain experience and further your interest in biomedical research.

How to apply:

Step 1  Check eligibility requirements:
monash.edu/pubs/2018handbooks/units/index.html

Step 2  Find a supervisor and project:
monash.edu/medicine/research/supervisorconnect

Step 3  Apply:
med.monash.edu.au/sobs/teaching/current/enrolment.htm
SUMMER AND WINTER RESEARCH SCHOLARSHIP PROGRAM

The Monash University Summer and Winter Research Scholarship Program is run over the summer and winter breaks. These scholarships can be undertaken within research laboratories in the Monash Biomedicine Discovery Institute giving undergraduate students an early opportunity to experience research and gain first hand insight into careers in biomedical research.

How to apply:

Step 1 Check eligibility requirements: monash.edu/students/scholarships/current/research-projects

Step 2 Apply: monash.edu/students/scholarships/current/research-projects

Location: On-Campus at Clayton

Duration: Summer and winter breaks - variable duration

Details
- Biomedicine Research 100%

Scholarships value
Amount $200 – $500 per week

Contact
sebs.csu.documents@monash.edu

Further information:
monash.edu/students/scholarships/current/research-projects

www.monash.edu/discovery-institute
A full-time Bachelor of Biomedical Science Honours year gives students the opportunity to undertake a specific avenue of research selected from the range of research interests in any area of biomedical science. The course is made up of a coursework component and an independent research project. Students select and undertake an individual research project working within a team or research group under close supervision. As part of the Honours course students receive training in oral communication, data analysis and advanced discipline-related knowledge. At the end of the year students report their findings to Institute or Departmental staff and write a research thesis.

How to apply:

**Step 1**  
Check eligibility requirements: [monash.edu/study/courses/find-a-course/2018/biomedical-science-m3702](http://monash.edu/study/courses/find-a-course/2018/biomedical-science-m3702)

**Step 2**  
Find a supervisor and project: [med.monash.edu/biomed/honours](http://med.monash.edu/biomed/honours)

**Step 3**  
Apply: [med.monash.edu/biomed/honours](http://med.monash.edu/biomed/honours)
BACHELOR OF SCIENCE HONOURS (BSc (Hons))

This degree aims to provide students with a higher level of experience in independent analysis and research in their chosen field of expertise. This experience has vocational aims, but also provides a preparation for study by coursework and/or research for the higher degrees of Master of Science or Doctor of Philosophy (PhD). The Honours program involves coursework through seminars and a major research project.

How to apply:

Step 1  Check eligibility requirements: monash.edu/study/courses/find-a-course/2018/science-s3701

Step 2  Find a supervisor and project: med.monash.edu/sobs/teaching/honours/science-projects.html

Step 3  Apply: monash.edu/science/current-students/science-honours

Location:
On-Campus at Clayton, On-Campus at Malaysia

Duration:
1 year full-time; 2 years part-time

Course details:
» Biomedicine Research Project (75%)
» Advanced Studies in Biomedicine (25%)

Fees:
Fees subject to change annually.

Course Code: S3701
CRICOS code: 030489K

Contact
Student Academic Services Office
Email: sci-enquiries@monash.edu
connect.monash.edu/s/

Further information:
monash.edu/science/current-students/science-honours
BACHELOR OF MEDICAL SCIENCE (HONOURS) (BMedSc (Hons))

The Bachelor of Medical Science Honours is a one year honours program for medical students and graduates. This honours program provides medical students with the opportunity to be at the forefront of medical research. Students are introduced to research practice and trained in research skills whilst working on a selected research topic. Students can join multidisciplinary biomedical research teams within the Monash Biomedicine Discovery Institute to work on disease focused research projects.

How to apply:

Step 1  Check eligibility requirements: monash.edu/pubs/handbooks/courses/M3701.html

Step 2  Find a supervisor and project: monash.edu/medicine/som/bmedsc-hons/research-placements

Step 3  Apply: monash.edu/medicine/som/bmedsc-hons/how-to-apply

Location:
On-Campus at Clayton,
On-Campus at Malaysia

Duration:
1 year full-time

Course details
» Research project (75%)
» Research skills (25%)

Fees
Fees subject to change annually.

Course Code: M3701
CRICOS code: 068848A

Contact
Course Administrator
Email: med-bmedsc-hons@monash.edu

Further information:
monash.edu/pubs/handbooks/courses/M3701.html
POSTGRADUATE

MASTER OF BIOMEDICAL AND HEALTH SCIENCE (MBiomedHlthSc)

The Master of Biomedical and Health Science is a degree that prepares students for a career in the biomedical field with an opportunity to take an internship within Victoria’s biotech industry.

Candidates undertake an initial year of intensive coursework in how to conduct research followed by a second year of a full-time research project under the direct supervision of a member of the academic staff of Monash University. This culminates in an internship which may be within or outside the University, depending on merit.

Areas of specialisation:
- Cancer biology and therapeutics
- Infectious diseases and population health
- Neuroscience
- Regenerative medicine and stem cells
- Cardiovascular diseases

How to apply:

Step 1  Check eligibility requirements for this degree: monash.edu/pubs/handbooks/courses/M6003.html

Step 2  Check eligibility for scholarships: study.monash/fees-scholarships/scholarships

Step 3  Apply: monash.edu/admissions/apply/online

Location: On-Campus at Clayton
Duration: 1.5 or 2 years full-time depending on prior qualifications
Intake: Second semester (July)

Course details
- Intensive research preparedness training (25%)
- Biomedical theory (25%)
- Specialist biomedical research and application (50%)

Fees
Fees subject to change annually.

Course Code: M6003
CRICOS code: 085118E

Contact
Professor Ramesh Rajan
Program coordinator
Email: ramesh.rajan@monash.edu
Telephone: +61 3 9905 2525

Further information:
monash.edu/study/courses/find-a-course/2018/biomedical-and-health-science-m6003

www.monash.edu/discovery-institute
DOCTORAL PROGRAM IN BIOMEDICAL SCIENCES (PHD)

This program provides doctoral (PhD) students with the opportunity to focus on developing knowledge and expertise in their chosen research area, as well as developing professional skills that will support their career ambitions. The core of the PhD is a cutting edge research project conducted under the guidance of at least two researchers and aimed at making novel scientific discoveries. The results and conclusions of PhD research are reported in a thesis and typically published in leading international journals.

In addition to hands-on training within their research labs, Monash BDI PhD students participate in institute-wide and faculty offered activities and undertake a structured program of professional skills training. Together, these mechanisms hone the students’ competency in five key areas: subject area knowledge; technical abilities; critical thinking; communication; and professionalism. This ensures students have the research experience and transferable skills necessary to be successful in their future careers.

A number of scholarships are available from Monash University and the Monash BDI.

How to apply:

Step 1  Check eligibility requirements for this degree and for scholarships: monash.edu/graduate-research/future-students/eligibility

Step 2  Find a supervisor and project: monash.edu/medicine/research/supervisorconnect

Step 3  Apply for a course and scholarship: monash.edu/graduate-research/future-students/apply/register

Location: On-Campus and off-Campus at various locations

Duration: 3–4 years equivalent full-time

Course details

» Applications can be accepted and students can start anytime throughout the year
» Applications for scholarships are considered four times a year. International students apply March 31st and August 31st. Domestic students apply May 31st and October 31st
» Students are required to complete a significant original research thesis as well as 120 hours of formal skills training

Course Code: 0047
CRICOS code: 041047

Contact
Dr Shae-Lee Cox
Email: shae.cox@monash.edu
Telephone: +61 3 9905 5673

Further information:
monash.edu/discovery-institute/graduate-program

www.monash.edu/discovery-institute
# MONASH BDI GROUP LEADERS AND THEIR DISCOVERY PROGRAM AFFILIATIONS

For more information, please visit monash.edu/discovery-institute/our-people

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Perturbations in cellular signalling play a fundamental role in human cancer and provide the rationale for many targeted therapies. The goal of the Signalling Network Laboratory is to characterize at the molecular level how signalling is altered in cancer, and thereby identify novel therapeutic strategies for particular poor prognosis human cancers, as well as biomarkers that aid classification of patients towards optimal treatments. Ultimately this work will lead to improved treatments for cancer patients with resulting reductions in morbidity and mortality. We utilise a variety of molecular, cellular and biochemical techniques, including mass spectrometry (MS)-based phosphoproteomics and kinomics, siRNA library screens and CRISPR/Cas9, cellular imaging and protein-protein interaction analysis. In addition, bioinformatic approaches are used to analyse our datasets and integrate these with publicly-available data from cancer genome studies and functional genomic screens.

Research Projects

1. Characterization of the SgK269 and SgK223 pseudokinase scaffolds
2. Definition and functional characterization of the Src-regulated kinase
3. Novel oncogenic drivers, therapeutic targets and biomarkers in triple negative breast cancer (TNBC)

Selected significant publications:


Research Background

We wish to understand the detailed molecular events that underlie the recruitment and regulation of chromatin-modifying complexes by their co-factor proteins, RNAs and DNA. We are aiming to uncover the function of long non-coding RNAs (lncRNAs) that have been widely linked to this process, even though their binding specificity and molecular mechanisms are still obscure.

Our current focus is on Polycomb-group (PcG) proteins, which mainly appear as histone modifier complexes. They function in epigenetic silencing during differentiation and in multiple types of cancer. We seek to understand, down to atomic resolution, how the function of these chromatin-modifying complexes is modulated by their environment and various binding partners. We combine next-generation sequencing-based techniques with molecular biology and biochemical approaches, in vitro and in vivo, for coherent functional study. We also study the structural basis for the function of chromatin-modifying complexes, at low and high resolution, using structural biology approaches such as high-resolution cryo-electron microscopy (cryo-EM), X-ray crystallography and small-angle X-ray scattering (SAXS).

Research Projects

1. How Polycomb-mediated epigenetic repression takes place?
2. How are chromatin-modifying factors regulated by lncRNAs and RNA transcripts?
3. How epigenetic de-repression takes place during development and in cancer?

A/Professor Chen Davidovich

EMBL Australia Fellow
Head, Epigenetic Regulation, Structure and Function Laboratory

Monash Biomedicine Discovery Institute
Cancer Program

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Selected significant publications:


Alterations in the finely tuned balance of signalling pathways underlie the pathogenesis of a host of diseases from cancer to inflammation. Capturing an atomic view of ‘signaling in action’ by determining the structures of key signaling components is central to the development of targeted therapeutics. The laboratory’s research vision is to determine structures of critical multi-component protein complexes formed by tumour-suppressor proteins, and oncogenes. This resolution is enabled by combining the latest advances in single-particle cryoEM and crystallography with advanced single-cell fluorescence techniques. Importantly, the incorporation of proteins into signalling complexes often reveals unique sites that can be therapeutically exploited to both increase specificity of medicines and decrease unwanted ‘on target’ side effects. In parallel, the team has a long-term aim to translate key mechanistic findings on the anti-inflammatory signalling of IL-1 family cytokines to the clinic.

Research Projects

1. **Structural characterisation of the co-inhibitory complex formed by the tumour suppressor PTEN and the metastatic factor PREX2**

2. **Structural and functional characterisation of the oncogene PREX1**

3. **Structure and function of interleukin-37 (IL-37) in inflammation and disease**

The laboratory harnesses advanced techniques including single-particle cryoEM, X-ray crystallography, and single-cell fluorescence to understand the role of the GTPase activation cycle in cancer.

Selected significant publications:


Our lab uses cryogenic electron microscopy (cryo-EM) to elucidate the structure and dynamics of large macromolecules involved in processes of fundamental biological and medical importance. In addition, we develop new computational methods for solving the most challenging problems in cryo-EM image processing and integrative structural biology. Biological topics include cancer biology, transcription regulation & mRNA export. Cryo-EM images will be acquired at the newly established Clive & Vera Ramaciotti Centre for Structural Cryo-EM, housing the world-class FEI Titan Krios instrument.

Research Projects

1. Cryo-EM of the housekeeping transcription initiation complex
2. Molecular basis of protein import into the mitochondrion using cryo-EM (Collaboration with Professor Trevor Lithgow)
3. New Computational Methods for Cryo-EM Image Processing & Integrative Structural Biology

Selected significant publications:

Approximately 1 in 8 cancer related-deaths in Australian males is due to prostate cancer. Dr Furic’s laboratory uses biochemical and molecular biology approaches to gain a better understanding of the molecular mechanisms responsible for prostate cancer progression. His research program is centred on survival signalling in prostate cancer cells and its role in the transition from hormone-sensitive to castrate-resistant prostate cancer. Dr Furic is an expert in mouse models of prostate cancer and cellular signalling regulating mRNA translation initiation and RNA stability. His current research projects are focussed on the identification of new combination therapies targeting protein synthesis, estrogen signalling and cell motility and invasion.

Research Projects

1. Role of mRNA translation initiation complex in tumour growth and metastasis
2. Role of estrogen receptor alpha in aggressive prostate cancer
3. Development of combination therapies targeting the ribosome in prostate cancer

Pre-clinical efficacy of targeted therapy against Pol I (CX-5461) in combination with pan-PIM inhibition (CX-6258), in a genetically-engineered mouse models (GEMM) of prostate cancer. This combination strategy shows promising efficacy in inhibiting MYC-driven prostate cancer and has implications for therapy-resistant disease.

Selected significant publications:

The major research direction of our group has been the characterization of the metabolic pathways that regulate phosphoinositide 3-kinase (PI3K) signalling, specifically concentrating on inositol polyphosphate 5-phosphatases, which exhibit altered expression and/or mutations in human disease and cancer. These include breast cancer, ciliopathy syndromes, diabetes/insulin signalling, neuronal disorders, leukaemia and developmental disorders. In addition, our group also investigates the functional role of inositol polyphosphate 3- and 4-phosphatases in various human diseases. Recently, our group identified PIPP, a P(3,4,5)P3 5-phosphatase, as a tumour suppressor in breast cancer which is downregulated in poor prognostic cases and these findings were published in the journal Cancer Cell. Furthermore, we have also identified and characterized a family of signal adaptor proteins called the four and a half LIM domain (FHL) proteins that play significant roles in muscle development and cancer, and we are currently exploring novel therapeutic agents for the treatment of different types of muscular dystrophy.

Research Projects
1. The role of inositol polyphosphate phosphatases in cancer development.
2. PI3-kinase and development.
Dr Lan Nguyen
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The advent of modern -omics technologies has revolutionised biology and has led us
to view biological processes as interconnected networks rather than as assemblies
of isolated molecules. This paradigm shift has instigated efforts to analyse cellular
networks through computational models, which in turn has revealed new insights
into the mechanisms of fundamental biological processes and their malfunctioning
in disease states. However, the translation of the computational modelling of
cellular networks into medical applications remains limited. In my lab, we ask the
following questions: “How can we harness network biology and modelling to better
understand diseases such as cancer? And can we turn network modelling into
new diagnostic and therapeutic applications?”. We propose to address these using
integrated systems approaches, which combine predictive computational network
modelling with cutting-edge experimental technologies. Our main focus is to exploit
developed and tested mathematical models of cancer-related signalling networks to
rationally: (i) understand the mechanism of drug resistance which arise from network
structures; (ii) find effective anti-cancer drug combinations which either avoid or
overcome developed drug resistance; and (iii) design therapies tailored to patients’
mutational profiles. This model-based approach is applicable to multiple signalling
pathways and cancer types.

Research Projects

1. Predictive modelling of the mTOR network to discover novel therapies

2. Systems analysis of the ErbB interaction network in Breast Cancer (Collaboration with Professor Roger Daly)

3. Mathematical modelling to understand network dynamics and cell-fate decisions

Selected significant publications:

  interactions generate hidden feedback and feed-forward loops to trigger bistable
  switches, oscillations and biphasic dose-responses. Molecular Biosystems (in
  press) (* Correspondence)

  integrated analysis and visualisation framework to probe multi-dimensional
  biological networks. Scientific Reports 5, Article number: 12569 doi:10.1038/
  srep12569 (*Correspondence)

  BN, Kolch W. 2014. Protein interaction switches coordinate oncogenic and

4. Nguyen LK, Cavadas MAS, Scholz CC, Fitzpatrick SF, Bruning U, Cummins
  EP, Tambuwala MT, Marresa MC, Kholodenko BN, Taylor CT, & Cheong A.
  2013. A dynamic model of the hypoxia-inducible factor (HIF) network. Journal of
  Cell Science, doi: 10.1242/jcs.119974. Epub 2013 Feb 6. (Most read paper of
  JCS, February 2013).

  Kholodenko BK. 2011. Switches, excitable responses and oscillations in the
  e1002317. (Highlighted in the Conway Research Focus)
Cancer is a complex disease that evolves over time and becomes more malignant by acquiring multiple mutations at the DNA level, as well as in the way proteins act within a cell. While a single initial defect can promote tumor appearance, additional mutations may favour development of the disease to more aggressive stages of malignancy.

The PI3K-Akt-mTOR cascade is a key intracellular signalling pathway that mediates several biological processes including cell growth, proliferation, metabolism and migration. As such it is not surprising that mutations in key regulators of this pathway are frequently associated with cancer. PTEN (phosphatase and tensin homology on chromosome 10) is a major negative regulator of the PI3K-Akt-mTOR pathway and is frequently inactivated or silenced in a range of human cancer and cancer syndromes.

Our research focuses on the identification and characterization of signalling pathways and molecular networks responsible for the correct functioning of cells in mammals with a special focus on the tumour suppressor PTEN.

Through a combination of in vitro studies and in vivo analyses, we utilise recently generated mouse models to investigate how loss of PTEN functions alters normal cell behaviour to promote uncontrolled cell growth and survival, at a systemic level and in a tissue specific manner. The final goal of these studies is to identify new therapeutic targets for the development of novel treatments or treatment modalities of human diseases, including cancer.

Research Projects

1. To define the functional role of PTEN in suppression of breast tumourigenesis
2. To characterise the contribution of the mTOR signalling pathway to brain cancer formation and progression

Selected significant publications:

Selected significant publications:


Our lab is focused on the regulation of autophagy, a major intracellular degradation process. In cancer, autophagy plays complex roles and can suppress tumours, but also helps tumour cells survive in other cases. Autophagy delivers cellular and cytoplasmic structures to the lysosome, where they are degraded. This process is tightly linked to cellular metabolism and is an evolutionary conserved survival mechanism that helps cells cope with nutrient starvation. We have recently discovered a link between metabolic control and the Serine/Threonine kinase ULK1, a key regulator of autophagy. We aim to develop a detailed understanding of how these regulatory networks are causing changes in intracellular membrane trafficking during autophagy.

Research Projects

1. High-resolution imaging of the mitophagy pathway
2. Autophagy and Cancer
Prostate cancer is one of the most common forms of cancer in men, affecting 1:6 men throughout their lifetime. Despite all our efforts to find a cure, prostate cancer remains a lethal disease and in Australia, about 60 men die from prostate cancer each week.

Working as a multidisciplinary team, we aim to improve patient treatment and outcome through a better understanding of the mechanisms that drive prostate cancer. Our research utilises state of the art techniques (eg. xenografting, bioengineered in vitro modelling, and transgenic animal models) that allow us to examine the mechanisms that contribute to disease development and progression.

**Research Projects**

1. Patient derived xenograft models of prostate cancer for preclinical studies
2. Defining the features of familial and high risk prostate cancer
3. Novel combination therapies for prostate cancer that target the ribosome
4. Targeting the eukaryotic translation initiation factor 4E in prostate cancer
5. In vitro modelling of the human prostate cancer microenvironment
6. Estrogen signalling and metabolism in prostate cancer
7. Epigenetic regulation of the tumour microenvironment

**Selected significant publications:**


Selected significant publications:


Genetic screens provide global information about how genes are regulated in normal homeostasis and how they are deregulated in disease. Recent technological advances are revolutionizing our ability to use these approaches. Research in the Rosenbluh lab uses state-of-the-art functional genomic tools that include pooled CRISPR and ORF loss/gain of function screens and apply these technologies towards understanding and targeting of β-catenin driven colon cancer.

Research Projects

1. Genetic screens for identifying drug targets in β-catenin driven colon cancers.

2. Identification and characterization of drugs for colon cancer therapy.

Prostate cancer is an androgen dependent disease. Advanced (castrate-sensitive) prostate cancers are managed with hormonal therapy. Inevitably, these tumours adapt to low serum levels of androgens and become castrate-resistant prostate cancers. In both castrate-sensitive and castrate-resistant disease, the Androgen Receptor (AR) plays a major role in driving tumour progression. Additionally, castrate-resistant tumours metastasise to different parts of the body. The most common location is the bone, but more recently soft tissue metastases such as liver, lung and brain have emerged. The origins of each metastatic tumour and the genetic drivers responsible for their growth are currently unknown.

Research Projects

1. Characterising the androgen receptor in castrate-sensitive prostate cancer cells

2. Investigating the origins of metastatic prostate cancer

Selected significant publications:


Breast cancer remains one of the leading causes of death in Australia, with current treatments often causing debilitating unwanted toxic side effects. By determining the underlying cellular differences between cancer and normal cells, we are able to understand the causes of these changes and to develop new drugs and delivery agents to target them specifically.

Similarly, infectious diseases such as those caused by viruses and cellular stress conditions often rely upon or generate changes in the subcellular targeting of various proteins, particularly those involved in transport between the cytoplasm and the nucleus. We identify these protein interactions and harness them to develop novel anti-viral drugs and to uncover the cellular pathways, which underpin these important conditions.

Research Projects
1. Advanced tumour targeting agents for triple-negative breast cancer.
2. The role of nuclear transport in cellular stress, DNA damage and repair.

Selected significant publications:


Our research focuses on the biophysical analysis of macromolecular interactions that underlie important cellular processes in health and disease. These include protein-nucleotide interactions underlying translational control as well as interactions of signalling molecules in cancer. The characterisation of these interactions facilitates the design, synthesis and testing of inhibitor molecules that have therapeutic potential.

Growth factor receptor bound protein-7 (Grb7) is an adapter protein, aberrantly overexpressed in several cancer cell types, that mediates the coupling of tyrosine kinases with their downstream signalling pathways via its SH2 domain. We have developed Grb7-SH2-specific bicyclic peptides that will allow us to better understand the downstream effects of Grb7 and serve as a starting point in the design of therapeutics targeting Grb7.

One of the cell’s primary rapid responses to stress is to sequester specific proteins and RNA into dense clusters known as “stress granules” (SGs). This process is essential for regulating the expression of pro-inflammatory proteins as well as stress-response proteins. Accordingly, improper SG formation is implicated in many pathologies including inflammation, cancer and neurodegenerative diseases. We are currently investigating the way in which TIA proteins recognise RNA and self-associate to form stress granules.

Research Projects

1. Grb7 in cancer
2. TIA proteins in RNA recognition and stress granule formation

Selected significant publications:


Our research interest is to identify new chromatin factors that control chromosome stability and genetic transmission. We aim to uncover fundamental epigenetic mechanisms that regulate transcriptional silencing at repetitive DNA sequences in the genome including telomeres and centromeres. Recent studies have identified the frequent mutations of histone variant H3.3 and its chaperone ATRX in human cancers, including the brain and bone cancers. We use CRISPR CAS9 gene editing system, highly advanced cellular imaging and high throughput DNA and RNA sequencing to investigate the genome-wide epigenetic defects associated with H3.3 and ATRX mutations in cancers.

Research Projects:

1. Investigate how chromatin defects cause brain tumours
2. Investigate epigenetic mechanisms that control transcriptional silencing DNA repeats
3. Investigate chromatin defects associated with Alternative Lengthening of Telomeres, a mechanism used for telomere elongation in cancers

Selected significant publications:

Our group focuses on peptide-based drug design and biomembrane nanotechnology. We are developing novel compounds that allow us to exploit the potential of peptides as drugs. We are currently applying our technology to the development of new compounds for treatments of cardiovascular disease and new biomaterials for regenerative medicine. Our membrane nanotechnology projects probes the role of membranes in the mechanism of Alzheimer’s disease, G protein-coupled receptor function, apoptosis and antimicrobial peptide function. The long-term aim of these studies is to increase our understanding of the molecular basis of peptide and protein function and allow the rational design of peptide and protein based therapeutics.

Research Projects

1. Peptide-Based Biomaterials
2. Role of the Mitochondrial Membrane in Apoptosis
3. New Ligands for Cardiovascular Disease

Selected significant publications:


Our group explores the regulation of smooth muscle function in diseases of the lung and cardiovascular system. These chronic diseases have serious impacts on quality of life, and can be evident following premature birth (bronchopulmonary dysplasia) or may emerge during childhood (asthma), or develop in adulthood (COPD, pulmonary hypertension. Current therapies are not always effective in managing symptoms or preventing disease progression, and they do not provide a cure.

The goal of our research program is to identify new drug targets for these diseases – to protect against the development of the changes in lung structure and function or to treat symptoms under conditions where current drugs are ineffective. We are currently examining multiple novel dilators targeting small airways and arteries using a novel lung slice technique in which contraction, relaxation and calcium signalling can be visualized. These drugs are being assessed in animal models of chronic lung disease and in human lung tissue to support their future clinical development.

**Research Projects**

1. **Characterising changes in airway and vascular reactivity in chronic lung diseases**
2. **Identifying novel bronchodilators targeting intrapulmonary airways in asthma and COPD**
3. **Identifying novel vasodilators targeting intrapulmonary arteries in pulmonary hypertension and bronchopulmonary dysplasia**

**Selected significant publications:**


Images showing airway and artery contraction within a lung slice – uncontracted (left) contracted (right).
Hypertension is the world’s leading risk factor for disease. It strongly correlates with adverse outcomes such as heart disease, stroke and kidney failure. The challenges of managing and preventing the development of hypertension are increasing as it is predicted that 60% of the population by 2025 will be hypertensive. Greater understanding of the mechanisms causing increased blood pressure, and identification of new therapies to prevent hypertensive tissue injury are pivotal in meeting this challenge.

Research Projects

1. The path to hypertension and cardiovascular disease has its origins in early life. Current work is directed at identifying prognostic indicators of disease and developing intervention strategies in the very young.

2. Women prior to menopause are protected against hypertension and cardiovascular disease. Ongoing research focuses on understanding sex-difference in the regulation of blood pressure. Novel treatments to prevent post-menopausal hypertension are being examined.

3. Our work also examines the efficacy and safety of renal artery denervation, an emerging treatment for hypertension.

Selected significant publications:


There is now very strong evidence that tissue hypoxia (low levels of oxygen) is a final common pathway in kidney disease. But the causes and consequences of kidney hypoxia mostly remain a mystery. We also do not know enough about how hypoxia drives kidney disease. We have a range of projects investigating how oxygen levels are normally regulated in a healthy kidney, how the kidney becomes hypoxic in disease, how tissue hypoxia contributes to the development and progression of kidney diseases, and how we monitor kidney oxygenation in patients to prevent acute kidney injury and delay the progression of chronic kidney disease.

Research Projects
1. The roles of kidney hypoxia in chronic kidney disease and acute kidney injury
2. The role of vascular structure in kidney oxygenation
3. Continuous measurement of urinary oxygenation as a biomarker of risk of acute kidney injury

Selected significant publications:
Our current research interests involve identifying novel pharmacological and/or cell-based therapies that can limit the pathophysiology of hypertension and stroke. Associated with the development of hypertension is the accumulation of macrophages in the arterial wall leading to fibrosis and vascular stiffening. Whilst current antihypertensives are effective at lowering blood pressure, they don’t necessarily target vascular stiffening and new therapeutics are sought. Hence, we are studying the impact of chemokines released from macrophages on fibrosis and collagen generation, which may lead to the development of more effective therapies of hypertension.

Currently there are few treatment options available for stroke patients, thus identifying new stroke therapies is vital. Excitingly, stem cells have been shown to improve recovery post-stroke. However, most stem cells have either ethical issues or concerns regarding tumorigenicity. Conversely, human amnion stem cells don’t have these limitations, hence we are investigating whether these placenta-derived stem cells can improve stroke outcome.

Research Projects

1. Exploring the profibrotic actions of CCL18 in the cardiovascular system
2. Role of the inflammasome in the pathogenesis of pulmonary hypertension
3. Using human amnion stem cells to improve stroke outcome
Fibrosis is defined as the hardening and/or scarring of various organs including the heart, kidney and lung; which usually arises from abnormal wound healing to tissue injury, resulting in an excessive deposition of extracellular matrix components, primarily collagen. The eventual replacement of normal tissue with scar tissue leads to organ stiffness and ultimately, organ failure. Despite a number of available treatments for patients with various heart/kidney/lung diseases, patients receiving these therapies still progress to end-stage organ failure due to the inability of these treatments to directly target the build-up of fibrosis. Hence, novel and more direct anti-fibrotic therapies are still required to be established.

Research Projects

1. Signal transduction studies (in models of heart / kidney / lung disease)
2. Head-to-head and combination therapy efficacy studies
3. The influence of ageing and gender on fibrosis
4. Development of new approaches to target airway remodelling in asthma

Selected significant publications:


* Corresponding author.
Our group is investigating mechanisms that reverse hypertensive heart disease and adverse organ remodelling due to extracellular matrix build up (e.g. fibrosis) associated with cardiovascular disease. The renin angiotensin system is one of the major hormonal systems regulating blood pressure and general cardiovascular status. Increased activity of the renin angiotensin system is likely to contribute to a range of cardiovascular diseases including hypertension, heart failure, atherosclerosis and stroke. There are a number of angiotensin receptor subtypes that are activated by endogenous angiotensin peptides as well as by synthetic compounds. The AT₁ receptor subtype mediates most of the classical effects of angiotensin II. While blockade of AT₁ receptors by sartan-type compounds has proven very successful in the treatment of diseases such as hypertension, other non-AT₁ receptors are now thought to counter-balance overactivity of AT₁ receptors and exert protective actions in their own right.

Therefore, a major focus of the Integrative Cardiovascular Pharmacology Laboratory has been to elucidate the (patho)physiological role(s) of various less-recognised components of the renin angiotensin system including AT₂ receptors, Mas receptors and insulin-regulated aminopeptidase (IRAP), and their interactions with endogenous angiotensin peptide fragments and synthetic ligands that we and/or our collaborators have developed. Drug discovery programs in these areas are providing mechanistic data, from initial drug screening through to in vitro and in vivo preclinical testing, of potential drugs for a range of cardiovascular diseases including hypertension, heart failure, stroke, atherosclerosis, aortic aneurysms and ageing. These studies combine ex vivo morphological/histological analysis of organ structure, together with in vivo functional readouts following novel treatments, aimed at preventing and reversing organ fibrosis, inflammation and cardiovascular remodelling. Another therapeutic target of interest is the role of acid sensing ion channels in the pathophysiology of stroke.

Research Projects
1. Novel therapeutic strategies to reverse hypertension, organ fibrosis and remodelling
2. Drug discovery programs to develop new ligands to target AT2 receptors and IRAP
3. Acid sensing ion channels (ASIC) as a novel target for stroke

Selected significant publications:
The intestinal epithelium or bowel lining is a regenerative tissue that is constantly renewed throughout life via a small population of stem cells. We study how growth and differentiation of intestinal epithelial cells is regulated using genetic models and organoid or “mini gut” cultures from mouse and human tissue. Our research is centred on understanding the molecular mechanisms and environmental influences that regulate stem cells during development and regeneration of tissue following damage. The bowel is very vulnerable to a variety of pathologies including cancer which involves the development of polyps before progressing to more invasive, malignant carcinomas. We are aiming to analyse the role of candidate molecules in regulating stem cells in normal tissues, degenerative diseases and colon cancer.

Research Projects

1. Role of stem cell activity in the initiation and progression of colorectal cancer
2. Molecular regulation of intestinal stem cells during development and regeneration of tissue following damage
3. Analysis of environmental influences on the intestinal epithelium
4. Using organoid culture to model tumour responses
Our lab brings together comparative methods and advanced 3D imaging resources to the study of living and fossil mammal anatomy. This ranges from our leading research at multiple fossil human sites in South Africa, to reconstructing the basic and functional anatomy of living and recently extinct Australian marsupials using CT and MRI. We also lead applications of 3D visualisation and printing in human and comparative anatomy research and education, including the development of new teaching tools for medical and clinical training.

Research Projects

1. Evolving landscapes of our early South African ancestors: Palaeobiology and palaeoecology of Drimolen and Haasgat
2. Rediscovering the Thylacine: Cyberanatomy of an Australian Icon
3. The use of 3D printing to create advanced surgical simulators for clinical training
4. The origins and evolution of southern hemisphere seals
5. Advanced imaging applications to reconstructing marsupial structural and functional anatomy

Selected significant publications:


With the advent of personal genomic medicine a detailed understanding of gene function has never been more important. In the future, our health may be monitored by regular "omics" measurements overlaid on our individual genomes. Each of us carries numerous "disease" mutations and countless further genetic variation, with mostly unknown consequences. My lab studies RNA metabolism: the birth, life and death of RNA molecules. A growing list of RNA-metabolic enzymes and binding proteins are implicated in intellectual disability, neuronal disorders and other diseases. I am motivated by a conviction that through the combined use of next generation technologies and evolutionary conservation in model organisms we can significantly accelerate discovery of basic gene function and the network-effect of loss-of-function mutations. And, that the impact that these mutations have on gene expression networks will have direct relevance to human health.

Research Projects

1. Investigating coding and non-coding RNA expression
2. Investigating the switch from silence to activation of translation
3. An Investigation into the host-pathogen synapse
A suboptimal feto-maternal environment can lead to a permanent deficit in the numbers of nephrons in kidney. We have shown that low nephron number in humans and animal models is associated with increased blood pressure and risk of chronic kidney disease in later life. However, how low nephron number increases the risk of these adult diseases remains unknown. We have also recently shown that nephrons formed in a suboptimal feto-maternal environment do not have the normal number of podocytes, cells vital to the filtration function of the kidney. Like the nephron deficit, this podocyte deficit is permanent, and has been directly linked to chronic kidney disease. Understanding the causes and consequences of low nephron and podocyte endowment is our major research focus, together with the mechanisms that link these early life events with disease in later life. High resolution imaging of the kidney in vivo and ex vivo is a major tool in these studies, and we are at the forefront of developing new imaging advances.

Research Projects

1. Podocyte depletion: causes and consequences

2. Understanding how low nephron number leads to adult hypertension and chronic kidney disease.

3. High resolution imaging of whole kidneys: in vivo and ex vivo studies

Selected significant publications:


We study how factors such as maternal malnutrition, maternal infection, placental insufficiency and antenatal corticosteroids affect the growth of the baby whilst in the womb. We are also interested in determining how exposure to these factors in pregnancy influences the long-term renal and cardiovascular health of the individual. Additionally, we study the effects of preterm birth, as well as its antecedents and factors associated with neonatal care, on the development of the heart, kidneys and vasculature. We also investigate the consequences of preterm birth on postnatal renal and cardiovascular health in the short-term and long-term. Our research involves studies in human infants, including Indigenous and non-Indigenous infants, as well as studies in animal models.

It is important to determine how these early life insults affect the developing heart, kidneys and blood vessels given that the early life developmental period establishes the lifelong structural architecture (and thus function) of these organs.

Research Projects

These are numerous and directly relate to our research directions described above. Some of our current projects are:

1. The effect of intrauterine growth restriction on the heart and kidneys
2. Effects of antenatal and postnatal steroids on the developing heart and kidneys
3. Preterm birth and/or intrauterine inflammation in the early induction of atherosclerosis
4. Effect of preterm birth on renal and cardiovascular function in Indigenous and non-Indigenous infants and children
From their birth till their destruction, RNAs are always associated with proteins. Deciphering the language of how RNAs interact with specific RNA-binding proteins is a fundamentally important concept in modern molecular cell biology. Our laboratory has two main focuses. First, we are working on understanding how specific mRNAs are selected for post-transcriptional gene regulation during germ cell development. Second, we are investigating the biogenesis and function of a new family of small RNAs (22G endo-siRNAs) and how they help to maintain the genome integrity by modulation the transcriptional program of germ cells. We use a diverse set of experimental approaches, including cell biology, genetics, biochemistry and genomics to study the RNA pathways of the multicellular eukaryotic model organism *C. elegans*.

### Research Projects

1. **Investigate how a conserved protein complex is required for translational repression of many mRNAs and localisation of specific RNA-binding proteins to key sites of post-transcriptional gene regulation in germ cells**

2. **Investigate the biogenesis and function the “22G” family of small RNAs during germ cell development**

3. **Investigating the role of poly(A)-tail in translational silencing (Collaboration with Dr Traude Beilharz)**

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**Selected significant publications:**


The mammalian oocyte is the largest cell in the body and undergoes two highly specialised asymmetric meiotic cell divisions. Coordination of organelle inheritance, polarity and meiotic progression is essential for the production of an oocyte capable of undergoing fertilization and development to term. We use molecular and genetic approaches combined with live cell imaging to investigate the cell biology of these processes in mice and humans. Investigating these questions allows us to understand how oocytes make the transition into a healthy embryo and why it goes wrong in cases such as maternal ageing.

Research Projects

1. Role of mitochondria in controlling meiosis in oocytes
2. Coordinating polarity and cell cycle progression in the meiotic divisions
3. Impact of maternal age and obesity on chromosome dynamics and oocyte quality (in collaboration with Rebecca Robker, University of Adelaide)
The major site of T cell production, the thymus, undergoes significant loss of function by mid-life, caused by the gradual loss of thymic epithelial cells from an early age by an as yet unresolved mechanism. This translates to a declining immune responsiveness to neoantigens and increased susceptibility to infections, cancer and autoimmunity. Of great clinical relevance, it also leads to a reduced capacity for T cell-mediated recovery following cytoablative therapies used in cancer treatments.

We recently identified the organ specific thymic epithelial progenitor cell (TEPC) population in the adult thymus, raising the intriguing possibility that compromised TEPC function is the basis for thymic ageing. In this project, we will use mouse models of ageing, chemotherapy-induced damage and immune regeneration, to explore alterations in TEPC differentiation and function.

Research Projects

1. Thymic epithelial stem cells and the nature of their niche
2. Thymic epithelial stem cells in development and aging
3. Generating ex vivo thymus organoids using defined biomatrices and growth factors
4. Generating functional thymic epithelial cells from pluripotent stem cells
5. Effects of chemotherapy on the thymus and bone marrow
6. Clinically relevant approaches for thymus regeneration, to replenish the T cell repertoire

Selected significant publications:


The endocrine system controls cell-cell communication and coordinates almost all our daily activities. Abnormalities in hormones, receptors and cell signalling pathways underpin many common diseases such as diabetes, high blood pressure and obesity. We are studying the actions of two important steroid hormones, cortisol (a glucocorticoid) and aldosterone (a mineralocorticoid) that are secreted by the adrenal gland and regulate important aspects of systemic physiology and homeostasis, in humans and other mammals. Cortisol has many homeostatic roles in a wide range of tissues both during embryogenesis, particularly the developing lung. Premature babies have underdeveloped lungs and require treatment with synthetic glucocorticoids. Glucocorticoids exert their effects by binding to the intracellular glucocorticoid and mineralocorticoid receptors, GR and MR respectively. Both are members of the nuclear receptor super-family of ligand dependent nuclear transcriptional regulators. Research projects below will utilize a range of molecular, biochemical and genetic techniques in both cell-based and animal systems to investigate these cell signalling pathways and their specific roles.

Research Projects

1. Glucocorticoid-regulated pathways in the pre-term lung and the development of Selective Glucocorticoid Receptor (GR) Modulators (SGRMs)

2. Steroid metabolising enzymes: HSDs and cancer – a novel human enzyme called 11bHSD3

3. Analysis of genomic versus non-genomic effects of the MR in an in vivo dimerization mouse mutant

Selected significant publications:


*joint senior authors.
Our laboratory research interest focuses on how transcription factors (TFs) and epigenetic regulators, along with small RNAs and long non-coding RNAs (lncRNAs) regulate gene expression programs in embryonic stem cells (ESCs), neural stem cells and differentiated cells under normal and pathological conditions, such as, cancers and neurodegenerative diseases. We use various experimental approaches and cutting edge techniques/technologies including – Cell and Molecular Biology, Biochemistry, CRISPRs, CRISPR screens (using sgRNAs to target all the genes in the genome, epigenetic regulators and regulatory elements), ChIPs, ChiP-sequencing, RNA-seq, WGS, ATAC-seq, RRBS, ChIA-PET, 3C, 4C, Hi-C, proteomics, bioinformatics and computational biology to understand the gene regulation under physiological conditions and diseases.

Research Projects

1. Dissect the role of histone demethylases (HDMs) in transcriptional regulatory network in mouse ESCs
2. Investigating substrate specificity and redundancy of HDMs, and their role in controlling gene expression programs in mouse ESCs and development
3. Examining the functions of regulatory elements (Enhancers and Super-enhancers) in ESCs
4. Investigating the role of regulatory elements in human medulloblastoma, a paediatric brain cancer
5. Examining the role of genetic and epigenetic regulation in neural stem cells, brain development and neurodegenerative diseases

Selected significant publications:


The major goal of our is a better understanding of the relationship between diet, cranio-dental morphology, ecology and evolution in modern humans, our closest living relatives (monkeys and apes) and our extinct ancestors. In particular, our research interests mostly focus on functional morphology of the masticatory apparatus in human and non-human primates, and on the importance of the role of diet in human evolution. We use different methods and approaches mostly based on highly sophisticated computer models, ranging from dental wear studies to biomechanics and morphological analyses.

Research Projects

1. Diet and ecology in Plio-Pleistocene African hominins
2. Masticatory function in human and non-human primates
3. Biomechanics of the Neanderthal anterior dentition
4. Emergence of malocclusions in transitional hunter-gatherer societies

Selected significant publications:


Organ size control is a fundamental but poorly understood aspect of life. Our laboratory has played a central role in the discovery and characterisation of a key organ size control network called the Hippo pathway.

We use the extraordinarily powerful model organism Drosophila to discover new Hippo pathway genes and investigate how this pathway controls organ size. To better understand how the Hippo pathway functions we utilise advanced microscopic techniques to monitor pathway activity in real time, in growing organs.

We also investigate the role of the Hippo pathway in human cancer, using cell lines, patient samples and animal models. We have a specific interest in two cancers: melanoma and mesothelioma. By applying our knowledge of Hippo signalling, we aim to discover novel treatments for these diseases.

Research Projects

1. Watching Hippo pathway activity in growing organs, in real time
2. Searching for the complete set of Hippo pathway genes
3. Defining the role of the Hippo pathway in human cancer

Selected significant publications:


In adult testis, there is a population of germline stem cells (spermatogonial stem cells; SSCs) needed for life-long production of spermatozoa and fertility. SSC maintenance is dependent on crosstalk between cell-intrinsic factors and growth factors produced from a stem cell niche. We have identified key transcription factors and growth factor signalling pathways involved in self-renewal and differentiation of SSCs. Through use of mouse models, we aim to define critical pathways regulating SSC function.

Projects will focus on characterizing mechanisms of SSC regulation with particular emphasis on components of transcription factor networks and their downstream targets. This work will involve use of mouse models, isolation and in vitro culture of SSCs, flow cytometry and cell/molecular biological techniques. These studies can have particular relevance to the stem cell and fertility fields.

Research Projects

1. Transcriptional networks controlling germline stem cell fate
2. Signalling pathways regulating germline stem cell maintenance

Selected significant publications:


Female fertility and reproductive health are influenced by the number and quality of eggs stored in the ovaries in structures known as primordial follicles. Established in the ovaries before birth, the supply of primordial follicles is progressively depleted throughout life due to the natural aging process. The ovarian reserve of primordial follicles may also become prematurely depleted following exposure to DNA damaging anticancer treatments, leading to loss of fertility and early menopause. We are working to understand the regulation of primordial follicle number and quality in order to improve the health and fertility of women during aging and following anti-cancer treatment.

Research Projects

1. Uncovering the molecular mechanisms that determine the length of the female fertile lifespan

2. Characterising ovarian damage caused by anticancer treatment

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Selected significant publications:


The Kile lab has a longstanding interest in the development, survival and function of blood cells. Using molecular approaches combined with state-of-the-art imaging technologies, we seek to understand the regulation of key processes like apoptosis at steady state, and in disease settings such as leukemia and inflammatory disease.

Research Projects

1. Apoptosis, mitochondrial damage and the innate immune response

2. The role of senescence, death and clearance in blood cell homeostasis

3. Caspases, infection and cancer

Selected significant publications:


Steps involved in Finite Element Analysis: model creation, model simulation and model validation (Panagiotopoulou et al., 2017)

Locomotor pressures and their links to pathologies in elephants.
Our group aims to decipher fundamental mechanisms that control brain
developmental and function. C. elegans has a small and well-defined nervous system
that we use as a model to study neuronal development and function at single-neuron
resolution. Sophisticated molecular genetic techniques, ease of observation and
detailed anatomical, genetic and molecular information make the worm an excellent
experimental model.

Research Projects
1. Control of metabolism through brain-intestinal communication
2. Elucidating molecular mechanisms that control axon outgrowth
   and guidance

Selected significant publications:
1. Juozaityte V, Pladevall-Morera D, Podolska A, Norgaard S, Neumann B,
   Pocock R. 2017. The ETS-5 transcription factor regulates activity states in
   Caenorhabditis elegans by controlling satiety. Proc Natl Acad Sci USA 114:
   E1651-E1658
2. Gramstrup Petersen J, Rojo Romanos T, Juozaityte V, Redo Riveiro A, Hums I,
5. Pocock R and Hobert O. 2008. Oxygen levels affect axon guidance and neuronal
Our laboratory is interested in the transcriptional and epigenetic mechanisms that govern cell identity, in particular pluripotency and the reprogramming of somatic cells into induced pluripotent stem (iPS) cells. Being able to reprogram any specific mature cellular program into a pluripotent state and from there back into any other particular cellular program provides a unique tool to dissect the molecular events that permit the conversion of one cell type to another. The reprogramming technology and iPS cells can be applied to generate animal and cellular models for the study of various diseases as well as in future cellular replacement therapies. Understanding the epigenetic changes occurring during these processes is necessary to ultimately use iPS cell technology for therapeutic purposes.

We use mouse models and a combination of different molecular, biochemical, cellular techniques and genome wide approaches to dissect the nature and dynamics of such events.

Research Projects

1. The kinetics and universality of the epigenetic and genomic changes occurring during reprogramming

2. The composition and assembly kinetics of transcriptional regulation complexes at pluripotency genes

3. How the cell of origin influences the in vitro and in vivo plasticity potential of cells generated during the reprogramming process

Selected significant publications:


Kidney disease is a widespread and debilitating health issue facing millions of people worldwide. The progression to end-stage renal disease is now a critical health issue where the incidence is rising rapidly at a rate of around 6-8% per year. Our research focuses on the development of stem cell-based therapies and/or growth factors that may repair damaged kidney tissues and reverse the development of scarring, thereby reducing the need for kidney dialysis or organ transplantation.

Research Projects

1. Pluripotent stem cells from patients with kidney disease
2. Using mesenchymal stem cells to protect against kidney fibrosis
3. Promoting organ growth and maturation in premature babies

Selected significant publications:


Selected significant publications:


Our group studies how the embryo develops with a view to understanding the developmental basis for congenital diseases and those caused by a compromised fetal environment. In particular, we are interested in understanding the developmental mechanism known as “branching morphogenesis”, which is employed by a large number of organs to establish the tissue architecture required to facilitate exchange of nutrients, gases or waste in the adult organ. The branched airways of the lung and the urine collecting system of the kidney are examples of the end products of this remarkable process. By accurately quantifying how this happens in model organisms, we aim to determine, in an appropriately rigorous manner, how genetic changes and environmental factors can shape organ structure. This is important for understanding the developmental origins of congenital diseases and in assessing whether and how the “normal” variations observed in the structure of organs between different individuals are influenced by their experiences and exposures as an embryo.

Research Projects

1. Understanding normal and abnormal kidney development
2. Dissecting the molecular basis of congenital kidney diseases

Selected significant publications:


* joint first, ^ joint communicating
Dr Richard Berry
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The specificity of the immune system is determined by cell surface receptors that recognise molecules of self- and/or viral origin. Understanding these interactions at the molecular level can provide profound insights into the basic processes underpinning immunity and how these may be modulated to treat infection or disease. My research is focused on two broad areas within this theme;

1. understanding the mechanistic basis of immune receptor triggering, with a particular focus on the T-cell receptor-CD3 signalling apparatus, and
2. investigating how natural killer cell receptors function in both healthy and virally infected organisms.

To achieve these aims we use a wide range of structural and biophysical techniques including X-ray crystallography, cryo-EM and small angle X-ray scattering.

Research Projects
1. The structural basis for signalling via the T-cell receptor-CD3 complex
2. Natural Killer cell receptor structure and function
3. Subversion of innate immunity by viral immune-evasins

Representation of the cytomegalovirus encoded m157 immunoevasin (pink) engaging the stalk of the activating Ly49H receptor (blue).

Structure of the pre-T-cell receptor super-dimer.

Selected significant publications:


www.monash.edu/discovery-institute
A. Proteases in immune defence. Cytotoxic lymphocytes kill infected or cancer cells by releasing proteases (granzymes) which enter the target cell via the pore-forming protein, perforin (Fig). Granzyme B kills cells due to its ability to activate caspases, and is one of the most cytotoxic proteases known. Other granzymes, and related proteases such as cathepsin G, activate cytokine signalling.

B. Regulation of proteases by serpins. Serpins trap and inactivate proteases. Some intracellular serpins protect cells against their own proteases e.g. Serpinb9 protects cytotoxic lymphocytes against granzyme B. Serpin deficiency or misfolding results in blood clots, immune dysfunction, lung and liver disease, cancer or dementia. SerpinA1 misfolding leads to liver and lung disease. We have shown that Serpinb6 deficiency causes inner ear degeneration and hearing loss.

C. Perforin-like molecules in immunity. MPEG1 is an ancient protein related to perforin, and it is found in phagocytes of organisms ranging from sponges to humans. Its molecular role is entirely unknown, but it is suggested to perforate phagocytosed microbes.

Research Projects
1. Cathepsin G
2. Serpins and cell death
3. MPEG1

Selected significant publications:
Viral infection is a significant cause of global mortality and economic burden. Did you know the Spanish influenza outbreak of 1918 killed more than 40 million people? Or that hepatitis B is the most common infectious disease in the world, causing 600,000 deaths each year? The success of a virus is partly determined by how well it can evade the host innate immune response. Well-known RNA viruses like influenza A and the hepatitis C implement immune evasion strategies. Unfortunately however, these immune evasion mechanisms are often poorly understood and hampered by our limited understanding of how anti-viral immunity is activated by innate immune receptors such RIG-I. We also have a poor understanding of how post-translational modifications, such as ubiquitination, modulate signalling. We use X-ray crystallography combined with in vitro and in vivo functional assays to understand 1) how anti-viral immunity is coordinated by host-proteins 2) viral immune evasion mechanisms. This information will enable us to devise new ways to combat viral infection. Our studies also have indirect impacts for cancer research as some of our targets are implicated in cell cycle regulation and tumor growth.

Research Projects
1. Understanding anti-viral immunity
2. Viral immune evasion mechanisms

Selected significant publications:

* denotes joint senior author.
A. Understanding mechanisms of colistin resistance in *Acinetobacter baumannii*. *Acinetobacter baumannii* has been identified as one of the top three dangerous Gram-negative hospital pathogens as it can cause a range of life-threatening infections and many strains are now resistant to almost all current antibiotics. Colistin is used as a last-line therapy against MDR *A. baumannii*, but infections caused by colistin-resistant strains are an emerging problem.

B. Defining the mechanisms of *Pasteurella multocida* pathogenesis and identifying novel virulence regulators. *Pasteurella multocida* is a Gram-negative bacterial pathogen that causes a number of different diseases in cattle, pigs and poultry, resulting in serious economic losses worldwide in food production industries. We are interested in understanding the molecular mechanisms of pathogenesis in this bacterium with an aim to developing new, more effective and widely applicable vaccines or antimicrobial drugs.

**Research Projects**

1. Determine the precise mechanisms of colistin resistance
2. Construct an *A. baumannii hfq* mutant and characterise its phenotype
3. Identify important regulatory sRNA molecules and determine the genes which they control
4.Mutate predicted virulence regulators and assess their effect on *P. multocida* gene expression and virulence

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Selected significant publications:


We combine x-ray crystallography and biophysics with molecular simulation to study the structure, folding and dynamics of proteins, with a particular focus on the design and engineering of proteins for medical and biotechnological application. Our team is a unique and exciting mix of experimentalists and computational biologists using modeling and simulation to make predictions that can be tested in the lab.

Research Projects

1. Designing potent protease inhibitors as potential anti-cancer agents
2. Using computational and experimental methods to design and evolve novel proteins
3. The evolution of protein dynamics

Design, engineering and evolution of Adnectins. Implications of GAD65 autoactivation for neurotransmitter biosynthesis and autoantigenicity.

Selected significant publications:


Our group focuses on studying dendritic cells (DC) by analysing the cell surface receptors they express with the view that these receptors contribute to specialised functions. Ultimately the knowledge that we acquire is directed at generating better and safer vaccines. Our research approach is exemplified by our work with Clec9A: we have identified a molecule critical to the function of a certain DC subset and then exploited this molecule as a means to deliver cargo to DC and thereby creating better vaccines. We have also discovered a receptor that plays an important role in recognising certain types of DNA. Since modified oligonucleotides (DNA) are used as adjuvants in vaccines, it is important to understand how this receptor (DEC-205) interacts with DNA and what the consequences of this interaction are. Importantly, by maximising the efficiency with which DEC-205 captures DNA, we can design DNA with superior adjuvant properties.

Research Projects

1. Characterising the immunostimulatory properties of CpG
2. Identifying CpG oligonucleotides that promote CD8 T cell responses
3. Properties of inducing potent immune responses
Research in our laboratory focuses on understanding the ways in which parasites of red blood cells cause disease and death in humans or animals.

A. Studies on malaria: Malaria causes severe morbidity, mortality and socio-economic hardship particularly in Africa, South America and Asia. The disease is caused by protozoan parasites of the genus Plasmodium, with at least five species known to infect humans. Symptoms, including fever, chills, headaches and anaemia, are attributable to replication of parasites within red blood cells (RBCs) and vary in severity depending on the parasite species and the immune status of the host. In the case of falciparum malaria, serious complications can arise due to sequestration of parasitised RBCs (pRBCs) in the microvasculature of the brain or the placenta resulting in cerebral malaria and pregnancy associated malaria respectively.

B. Studies on babesia: Babesia bovis is an important haemoproteozoon parasite of cattle that shows striking similarities with human malaria parasites. The disease is of major national and international importance and imposes huge economic burdens on the beef and dairy industries. A better understanding of the basic biology of these parasites and the relationship between parasites and their host is required for the development of anti-parasitic vaccines, drugs and new therapeutic regimens for this important disease. We are also interested in learning more about the basic biology of this parasite since it offers a unique opportunity to answer important questions about malaria infection that are not currently possible to perform in humans.

Research Projects

1. Characterisation of malaria PHIST-domain proteins
2. Understanding the function of unique \( P. falciparum \) FIKK kinases
3. Characterisation of novel Babesia bovis exported parasite proteins
4. Identification of the Babesia bovis ridge protein

Selected significant publications:


Model of immature particles of vaccinia virus. The X-ray crystal structure of the scaffolding protein D13 was used to model the honeycomb lattice wrapped around the surface of an immature virion-like particle. These particles, shown in the background, were produced in vitro by tethering D13 to artificial lipid bilayer membranes and imaged by cryo-EM.

The spherical and honeycombed architecture of poxvirus immature virions is atypical and departs from the compact icosahedral shells found in many DNA viruses [3].

This figure shows the structure of a virus that causes the beak and feather disease in critically endangered birds, including the orange-bellied parrot. The outer protein shell and inner DNA-containing cage were modeled using a combination of X-ray crystallography at the Australian Synchrotron and cryo Electron Microscopy at the Ramaciotti centre, Monash University [1].
My group focus on antibiotic discovery: specifically, how to make new antibiotics to overcome the severe threat posed to modern medicine by antimicrobial resistance (e.g. MRSA). To do this, we adopt a multi-disciplinary approach with a focus on the glycopeptide antibiotics (GPAs), which include the last resort clinical drugs vancomycin and teicoplanin. As these are highly complex molecules, as a society we depend on biosynthesis for their production. Thus, generating new variants of GPAs relies on our ability to understand and exploit the natural biosynthesis machinery, which centres on a fascinating enzymatic peptide assembly line known as a non-ribosomal peptide synthetase (NRPS) and the cyclisation of this NRPS precursor peptide into a rigid, active antibiotic through the action of Cytochrome P450 monooxygenases. My group investigates these enzymatic systems using a combination of approaches (chemical synthesis, structural biology, biochemistry, enzymatic catalysis & protein engineering) in order to reengineer these and produce new, more effective antibiotics and to exploit these enzymes as biocatalysts. Furthermore, my group is using our expertise with GPAs to identify new cellular targets for novel antimicrobial therapies as well as developing novel approaches to treat deadly antibiotic-resistant bacterial pathogens such as MRSA. pathogens..

Research Projects

1. Exploiting biocatalysis and chemical synthesis to generate new antibiotics

2. Redesigning antibiotic biosynthesis to enable production of modified antibiotics

3. Overcoming antimicrobial resistance by exploiting novel strategies to kill superbugs

Selected significant publications:


The immune system has 2 essential types of thymus-derived (T) cells: i. Conventional T cells (T-conv) promote inflammation to rid the body of pathogens and tumours, and ii. Regulatory T cells (T-reg) suppress inflammation.

Charles Darwin referred to competition between individuals and species as a "struggle for existence". T-conv and T-reg cells also compete against each other for resources. A feature of a safe immune system is that T-reg cells outcompete T-conv cells in the steady state. A key limiting resource is antigen, to which a T cell binds via its unique T-cell receptor (TCR). Self-proteins dominate the body’s antigen landscape in the steady state. We aim to understand mechanisms that focus T-reg cells on key self-proteins. We hope that detailed insight into the T-reg/self-protein axis will improve diagnostic accuracy and therapeutic efficacy in autoimmune diseases and cancers.

Research Projects

1. **Thymocyte Deletion: Which Cells Kill?**

The thymus works like a filter for our immune system: it allows useful cells to enter the body and disposes of the rest. We study how the thymus contributes to a safe and effective immune system. We also study how mistakes in the thymus lead to autoimmune diseases.
My laboratory has worked on the development of Cryo-Electron Tomography and Subtomogram averaging on large scale in order to study various stages of the replication cycle in HIV-1 as well as on the development of hardware and software solutions for Correlative Light and Electron Microscopy (CLEM). Currently we are focusing on the development of hardware and software to extend the use of cryo-CLEM to in situ structural biology and biochemistry. The goal of our research is to bring full automation and high throughput in the sample preparation, data collection and analyses for cryo-Electron Microscopy performed directly in cells or in embryos at early stages of development.

Selected significant publications:


Our laboratory uses a model of chronic viral infection to understand how viruses interfere with host immune responses. Our studies have contributed to understanding the immunological pathways invoked in response to viral infection, the pathophysiology of the resulting disease and the strategies needed to improve clinical outcomes. We have developed a number of unique models that allow us to gain significant insights about the infection per se, as well as how it contributes to the development of autoimmunity and post-transplant disease.

Our research involves the analysis of immune responses, principally in vivo, with the overall aim of determining how these responses are generated and maintained so that they can be harnessed therapeutically.

Our Major Research Interests are:

- Chronic viral infections
- Transplantation
- Autoimmunity
- Immunotherapy

Research Projects

1. Understand the immune requirements for controlling chronic viral infection
2. Define the role of viral infection in the aetiology of autoimmune disease and its complications
3. Improve the outcome of cytomegalovirus infection following bone marrow transplantation

Selected significant publications:


The overarching goal of our lab is to identify factors that shape the emergence and evolution of rapidly evolving pathogens such as Influenza, Ebola, and Zika. To achieve this goal we conduct (1) virus surveillance in animal, humans, and the environment, (2) characterize virus genomes and virus-host interactions using next-generation sequencing methods, and (3) apply computational methods to integrate the sequence data with clinical, epidemiological and immunological data that are generated from disease surveillance and laboratory experiments. Our primary organism of study is influenza, due to its rapidly evolving small malleable genomes, although we have ongoing projects in gastroenteric pathogens such as Rotavirus and Enterovirus 71 and vector-borne pathogens such as Dengue.

Research Projects

1. Evolution and transmission mechanisms of Influenza virus
2. Phylodynamics of vector borne (e.g. dengue), respiratory (influenza) and gastroenteric (rotavirus) viruses
3. Mechanisms of host-jumps of emerging infectious diseases

Host ecology of influenza A viruses, indicating major hosts and pathway of emergence of pandemic viruses such as the 1918 Spanish Flu pandemic and the 2009 Swine Flu pandemic.

Selected significant publications:


Pore forming toxins (PFTs) are fascinating proteins that have the ability to breach cell membranes by forming pores in the lipid bilayer. These pores can be either lytic to the target cell, e.g. by osmotic flux, or the pores can mediate the translocation of proteins (typically toxins) into the cytoplasm of the target cell. They are found in all kingdoms of life, especially pathogenic bacteria. Our research looks at the structure and evolution of pore forming toxins such as the MAC, fungal toxins and aerolysin.

Our research also explores the role of pore forming proteins in animal development, their development to target and kill cancer cells.

Research Projects

1. Structural and immunological studies of the Membrane Attack Complex
2. MPEG: Understanding how macrophage use pore forming toxins
3. Developing a fungal pore forming toxins as a pest control agent

Pleurotolysin, a hole punching protein from the carnivorous oyster mushroom. The background is the negative stain TEM image. The rainbow object is the model based on single particle cryo-electron microscopy.

Selected significant publications:


Viruses are part of day-to-day encounters that the immune system needs to deal with. How the immune system “sees”, recognises and eliminates viral infection is not fully understood. Indeed, viruses are able to mutate in order to escape the immune system surveillance. If we were to develop better vaccine and drugs, or even vaccine against viruses like HIV, it is essential to understand the mechanism of viral recognition and viral escape prior to this.

Research Projects

1. Structural investigation into T cell response to Influenza virus
2. Structural investigation into T cell response to HIV

Selected significant publications:


The differentiation of hematopoietic stem cells into lymphocytes in the bone marrow and thymus is governed by interactions with non-lymphoid stromal cells. Stromal cell dysregulation with age perturbs immune cell development, causing clinical problems in transplant and cancer settings. Infusion of mesenchymal stem/stromal cells is being used in clinical trials to treat a range of inflammatory diseases, yet major questions remain about their mode of action. Our lab seeks to address these questions and understand the basis for age-related immune defects, with a view to treatments that can reverse this process.

Research Projects

1. The mechanisms underlying the broad therapeutic effects of infused mesenchymal stem/stromal cells.
2. Stromal-immune cell interactions in cell therapy.
3. The impact of ageing on mesenchymal stem/stromal cell function.

Selected significant publications:


Immune ‘checkpoint’ inhibitors can increase the activity of tumour-resident cytotoxic lymphocytes and have revolutionised cancer treatment. Current therapies block inhibitory pathways in tumour-infiltrating CD8+ T cells and recent studies have shown similar programs in other effector populations such as natural killer (NK) cells. Natural killer (NK) cells possess an innate ability to detect and kill malignant cells, as such NK cell activity is inversely correlated to cancer incidence, NK cell infiltration in tumours predicts cancer patient survival and NK cells specifically prevent cancer metastasis. However, the mechanisms underpinning how NK cells specifically recognise transformed cells and how tumours escape NK cell control, remain undefined. Our laboratory studies how NK cell development, homeostasis and function is regulated by transcription factors, growth factors, receptors and signalling molecules. The goal of these studies is to understand how to therapeutically harness NK cell anti-tumour immunity in cancer.

Research Projects

1. Negative regulation of NK cell effector functions
2. Cell death pathways in NK cells
3. Role of NK cells in driving tumour inflammation

Selected significant publications:


Human health and longevity is dependent on the ability of the immune system to clear the multitude of different foreign pathogens encountered over the life of the host. Our research studies the ability of the immune system to clear pathogens and form immunity through production of antibody and B cell memory. These projects will use both immunological assays and molecular biology techniques to study how the immune system forms long-lived immunity.

Research Projects

1. Transcriptional regulation of antibody diversity
2. Epigenetic regulation of immune memory
3. Chronic infectious diseases

Selected significant publications:


The word “stroma” is Greek for mattress, and “stromal cells” were originally understood as cells in organs that provided structural support and not much else. In recent years our understanding of stromal cells, and the immunologically-specialised roles these cells play has simply exploded, and they are now one of Immunology’s most far-reaching and fascinating areas of study.

Our research program is focused on fibroblast-like stromal cells found in secondary lymphoid organs and tumours. These cells create the structure on which leukocytes crawl and interact. We and others have shown that fibroblasts in lymph nodes are fundamental to healthy immune function, through interactions with T cells, B cells, dendritic cells and macrophages, directly supporting cell survival, function and migration.

The laboratory studies key mechanisms of action, aiming to target these cells directly with therapeutic effect. We are also now focusing on exploring how these cells manipulate the immune response against cancer, a topic at the forefront of cancer immunology.

The research program utilises primary human tissues as well as mouse models, cutting-edge flow cytometry, cell culture, immunofluorescence, RNA-Seq and live cell imaging.

**Research Projects**

1. Exploring the profibrotic actions of CCL18 in the cardiovascular system

2. Role of the inflammasome in the pathogenesis of pulmonary hypertension

3. Using human amnion stem cells to improve stroke outcome

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Selected significant publications:


Nuclear transport is central to processes such as signal transduction, oncogenesis and differentiation, where changes in transcription within the nucleus are effected by transcription factors which access the nucleus through the cellular nuclear transport system. This is also critical in viral infection, where viruses hijack host transport mechanisms to effect nuclear targeting of critical viral proteins, as well as to prevent the host anti-viral response.

Our work focusses on cancer and viruses of medical significance such as Dengue, to define the role of nuclear transport in disease, and how this can be exploited for therapeutic intervention through novel antiviral/anti-cancer agents.

Research Projects

1. **Host-Virus Interactions in Lethal Infection; Therapeutic Targets**
2. **Antiviral Agents against Lethal Viruses**
3. **Nuclear Transport in Cancer; Therapeutic Strategies**
4. **Nuclear Transport in Stress; Survival and Death**

Cell gone viral: Infection by respiratory virus (green) perturbs cell morphology, including mitochondria (red). Blue is DAPI (cell nucleus).
Helicobacter pylori (Hp) is a prototype of a cancer-inducing pathogen. This motile, rod-shaped Gram negative bacterium colonises persistently in the human stomach, causing chronic gastritis and gastric cancer in susceptible individuals. Virulent Hp expresses a Type IV secretion system (T4SS), a major virulence factor which functions as macromolecular machine gun that “shoots” virulence proteins and peptidoglycan molecules into the host cells. Recently, we discovered that a novel adhesin of Hp, CagL, is expressed on the surface of T4SS and is able to dock onto integrin receptors on human gastric epithelial cells, turn on integrins and simultaneously trigger the secretion of other virulence molecules into the stomach cells. Once intracellular, the Hp virulence factors including CagA and peptidoglycan then interact with specific host signalling molecules to trigger activation of host tyrosine kinases, nuclear factor kappa B (NFκB) and/or downstream proinflammatory responses such as the secretion of cytokines. Meanwhile, the vacuolating toxin secreted by Hp dysregulates normal host cell functions, causes severe cytotoxicity and disrupts the gastric epithelium. The molecular basis of how Helicobacter infection progresses into cancers however remains largely a mystery. Our lab is interested in using a multi-disciplinary approach to understand the pathogenesis of Helicobacter-associated malignancies.

Research Projects

1. The molecular mechanisms by which Helicobacter pylori causes stomach cancer

Selected significant publications:


CD8+ T cell immunity is critical for the effective elimination of viruses. Our research utilizes advanced cellular and molecular approaches to interrogate the key determinants of effective CD8+ T cell responses to virus infection; namely those controlling CD8+ T cell recognition of virus, anti-viral CD8+ T cell magnitude, and T cell effector function. Understanding these determinants confer optimal immunity also allows us to perform targeted analyses of CD8+ T cell dysfunction, such as that observed with advanced age.

Research Projects

1. Cellular and molecular analysis of ageing in CD8+ T cells
2. The influence of thymic selection on virus-specific CD8+ T cell populations
3. Unravelling antiviral CTL response determinants

Despite pathogen complexity, CD8+ T cell responses often fall into immunodominance hierarchies, where epitopes that routinely elicit relatively large responses are termed immunodominant and those that elicit smaller responses are termed subdominant. Such hierarchies are highly reproducible between individuals in both humans and mouse models.

Our work aims to identify key epigenetic and metabolic determinants of age-related dysfunction, with the ultimate aim of discovering druggable molecular targets to restore function in the elderly.

Selected significant publications:

Our research focus is understanding how the sentinels of the immune system, the dendritic cells (DC), sense and respond to "danger" in their environment, and to use this knowledge for improving vaccines and immunotherapies. DC have an array of receptors designed to detect pathogen-associated and damage-associated molecular patterns. These receptors enable DC to sense invading pathogens or other danger (e.g., damaged or dead cells) and to direct the type of protective immune response required. Importantly, there are multiple DC subsets which are tailored for different functions. DC subsets can recognise different pathogens and damage signals, and respond accordingly. Our focus is to determine the receptors that enable the DC to sense and respond to such signals, and their role in inducing immune responses.

Research Projects

1. **The dendritic cell receptor Clec9A: dead cell recognition and immune modulation**

2. **Molecular mechanisms that underpin dendritic cell cross-presentation**

3. **The regulatory receptor Clec12A and its control of inflammatory diseases**

Selected significant publications:


Cardiovascular and cerebrovascular diseases are the global leading cause (>30%) of death. The plasminogen activation (PA) system plays a dual role: removal of thrombotic occlusions and promotion of haemorrhagic reactions. We investigate the molecular interactions between components of the PA system and the mechanism of activation and inhibition via structure and function studies. We apply these knowledge to the development of better and more efficient strategies, such as the use of specific monoclonal antibodies, to modulate the activity of the system. Successful outcomes would be of great benefit to the outcome of clinical conditions such as tissue injuries, clotting disorders, bleeding, inflammatory disease, in bacterial or viral infections and in cancer metastasis.

Research Projects

1. **Structural characterization of monoclonal antibodies which mediated down regulation of cancer progression**

2. **Finding new strategies for the treatment of traumatic injuries**

**Small Molecule Inhibitors to Plasmin Derived from Tranexamic Acid (TXA)**

Selected significant publications:


While most studies in adaptive immunity have focused on peptide-mediated immunity, my research aims to explore the unchartered territory of lipid- and metabolite-mediated immunity. This aspect of immunity represents a new frontier in immunity. Indeed, there is a number of pressing fundamental questions that I wish to address through my research program and that include: (i) What is the extent of the chemical diversity of immunogenic non-peptidic antigens (Ags)? Are there more atypical Ags to be discovered in mammalian and non-mammalian species? (ii) How are these lipid and metabolite Ags presented and recognized? (iii) What are the molecular mechanisms that underpin the recognition event and the signalling outcomes? (iv) How did non-classical MHC molecules evolve to fulfill their molecular functions within a specific species? By applying a multi-disciplinary and highly innovative approaches that include comparative immunology, chemistry, structural biology, cell immunology, advanced atomic and molecular imaging, my research program aims to provide comprehensive and fundamental insights into molecular recognition of non-peptidic Ags, and gain an evolutionary perspective on the structure and function of MHC-like Ag-presenting molecules.

Research Projects

1. To investigate the CD1 family and lipids-mediated immunity.
2. To investigate the MR1 family and metabolites-mediated immunity.
3. To explore the field of comparative immunology (Structure and function of MHC-like molecules in evolutionary distinct species, e.g. Marsupials, frogs, and bats).

Selected significant publications:

Antibiotics are a cornerstone of modern medicine and over the last century have significantly decreased mortality worldwide. Unfortunately, resistance to these ‘magic bullets’ has become one of the greatest threats to human health that the world faces, now and in the coming decades. If proactive solutions are not found to prevent widespread antibiotic resistance, it is estimated that by 2050 ~10 million people per year will die of infections. The World Health Organization (WHO) has urged all government sectors and society to act on antimicrobial resistance (AMR). On 27 February 2017, multidrug-resistant K. pneumoniae, P. aeruginosa and A. baumannii were identified by WHO as the highest priority pathogens, which require urgent attention for the discovery of novel antibiotics. Over the last decade, ‘old’ polymyxins are increasingly used as the last defence against these Gram-negative ‘superbugs’. My research in the systems pharmacology of polymyxins and drug discovery has made a significant contribution to the global commitment to combat antibiotic resistance in Gram-negative pathogens.

Research Projects
As no new antibiotics will be available for Gram-negative ‘superbugs’ in the near future, it is crucial to optimise the clinical use of polymyxins and develop novel, safer polymyxins. My major research programs are:

1. Optimising clinical use of polymyxins and their synergistic combinations using pharmacokinetics/pharmacodynamics/toxicodynamics (PK/PD/TD) and systems pharmacology
3. Development of virtual bacterial cells using systems pharmacology and computational biology
4. Discovery of new-generation polymyxins against multidrug-resistant P. aeruginosa, A. baumannii and K. pneumoniae

Selected significant publications:

Antimicrobial resistance (AMR) is a global problem in human health, and a key element to this problem is the evolution of antibiotic-resistant bacterial pathogens. These bacteria depend on surface exposed proteins to interact with human tissues, bind to medical devices such as catheters, and to evade the immune system. As a result, the process of cell surface protein assembly is an Achilles’s heel for bacterial pathogens, and one that we are working to attack. We have been working to understand in molecular detail how bacterial outer membrane proteins are assembled. We mapped the evolution and topological features of the outer membrane protein assembly machinery, solved the structure of key catalytic components, discovered new components in this pathway and have succeeded in an understanding of this process of outer membrane assembly. Using super-resolution microscopy and cryo-electron microscopy we image bacterial cells for nanoscale details of the bacterial cell surface: to open it up to drug treatment, to understand how bacteriophage attack and kill superbugs, and to detail the protein secretion responses of these superbugs. We are now initiating high-throughput genetic screens to better understand the factors that enable the regulation, and spread, of antibiotic resistance in bacterial pathogens.

Research Projects

High-throughput genetic screens to:

1. Cryo-electron microscopy of bacterial protein secretion machines
2. Nanoscale imaging of bacterial cell surfaces
3. Bacteriophage as agents against antimicrobial resistance
4. Regulation of outer membrane protein assembly in bacterial pathogens

Selected significant publications:


Selected significant publications:


Our laboratory is focussed on gut pathogens, particularly those involved in antibiotic-associated diarrhoea, and we examine how these pathogens interact with the host and cause disease through the use of animal infection models. We use novel ways to genetically modify bacterial pathogens (including *Clostridium difficile*) of both human and animal origin. We are using this approach to understand how these micro-organisms harness regulatory and virulence factors to cause disease. We are also developing immunotherapeutics and small molecules to prevent and treat infections by the hospital superbug *Clostridium difficile*. Lateral DNA transfer between bacterial pathogens is also a major study area, associated with antibiotic resistance or virulence gene transfer in the context of gut pathogens and antibiotic-associated diarrhoeal disease.

**Research Projects**

1. **Understanding the host immune response to *Clostridium difficile* infection**

2. **Functional and genetic analysis of hospital antibiotic-associated diarrhoeal pathogens**

3. **Analysis of toxin secretion in the large clostridial toxin (LCT) producing clostridia**

Transmission electron microscopy on a section of a *Clostridium difficile* spore within a vegetative cell (Dr Yogi Srikhanta).
Diet determines gut microbiota composition, and bacterial metabolites underlie numerous “western lifestyle” diseases.

Selected significant publications:


Our laboratory focuses on understanding mechanisms of cell migration, and cytokines and chemokines for immune responses. Our research has relevance to applied outcomes for immunological diseases, including new monoclonal antibody treatments for inflammation, fibrosis and cancer. Recently we have uncovered molecules and receptors responsible for gut homeostasis, supporting a ‘diet hypothesis’ to explain the increased incidence of inflammatory diseases in western countries.

Research Projects

1. GPR65, a receptor that explains asthma, IBD and allergy
2. Medicinal food diet to manipulate the microbiome and treat western lifestyle diseases
3. The ‘Nutrition-microbiome-physiology axis’ and mechanisms- epigenetics and GPCRs
Dr Eliana Marino
Juvenile Diabetes Research Foundation (JDRF) Fellow
Head, Immunology and Diabetes Laboratory
Monash Biomedicine Discovery Institute
Infection and Immunity Program

Selected significant publications:


The notion that diet and/or the gut microflora influences immunity and autoimmunity have not been taken in deep consideration, in part because precise molecular pathways had not been identified. Studies of inflammatory bowel disease and experimental colitis in mice have suggested that short-chain fatty acids (SCFAs), which are produced by gut bacteria during fibre fermentation in the gut, can have anti-inflammatory effects on the development of many inflammatory diseases. Our lab investigates the relationship between the immune system, the intestinal microflora and diet that cause inflammation and autoimmunity. Thus, we are trying to understand how microbial SCFAs regulate gut homeostasis, affect regulatory T cell (Treg) biology and subsequently affect inflammatory responses associated with autoimmune diabetes, insulin resistance, proteinuria and the incidence of obesity.

Research Projects

1. Effects of food and microbial SCFAs on inflammation: what are we eating?

The University of Melbourne

Dr Eliana Mariniño
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OTHER PROGRAM AFFILIATIONS

Cardiovascular Disease
Metabolism, Diabetes and Obesity
HCMV is a β-herpesvirus that infects over 60% of the adult population. HCMV is a significant cause of morbidity and mortality in immuno-compromised individuals such as organ transplant recipients. However, the largest burden of disease occurs from intrauterine HCMV transmission during pregnancy. Occurring in 1% of pregnancies worldwide, HCMV can cause permanent hearing loss, vision impairment, and mental retardation. There is no vaccine currently available, and discovery of new antivirals is urgently required. Importantly, the process by which infectious virus is packaged and released is not well understood, and this presents a novel molecular loci to develop antiviral therapeutics.

Research in our laboratory uses cutting-edge proteomics together with virology, molecular biology, microscopy, and bioinformatics to investigate the molecular mechanisms used by viruses to replicate and assemble infectious virions.

Research Projects

1. Dissecting the viral assembly complex induced by Human Cytomegalovirus
2. Hijacking of host exosome pathways for Human Cytomegalovirus egress
3. Exploring the biological functions of the novel lipoamidase SIRT4

Selected significant publications:

2. Gopal SK, Greening DW, Zhu HJ, Simpson RJ, Mathias RA. 2016. Transformed MDCK cells secrete elevated MMP1 that generates LAMA5 fragments promoting endothelial cell angiogenesis. Sci Rep. 6, 28321
Our laboratory is interested in characterising new drug targets. We are primarily interested in the development of new drugs to control infectious diseases. Our lab has a strong research focus in the design of novel anti-malarial drugs as well as other parasitic and bacterial diseases. Primarily we are a structural microbiology laboratory using techniques in molecular biology, X-ray crystallography, biochemistry and biophysics to analyse drug targets of interest. We use this mechanistic information to design inhibitors or analogues with potential applications in human medicine. Our laboratory has close connections with both the Department of Microbiology and the Monash Institute of Pharmaceutical Sciences (in Parkville).

Research Projects

1. Developing New Antimalarial Drugs
2. Development of Phage Lysins as Novel Antimicrobials
3. Development of New Drug Targets for Malaria

Selected significant publications:


Our group is investigating a number of issues that relate to eye diseases which may have an immune or inflammatory basis to their pathogenesis. In addition, the group also studies eye development and aging. The World Health Organization estimates that over 45 M people are blind and 314 M people are visually impaired. The Ocular Immunology group has a number of active projects that are aimed at understanding common blinding diseases such as corneal infection, retinopathy of prematurity, and age-related macular degeneration. The research group sees itself as part of a larger global effort to understand these conditions - if we can help place one small piece in the larger jigsaw puzzle of medical research that will help future treatment of these conditions then we will have succeeded.

Research Projects

1. Are there antigen presenting cells in the normal brain parenchyma and retina?
2. Novel treatment protocols for human retinopathy of prematurity using a clinically relevant mouse model
3. Investigating perivascular macrophages in the ocular microenvironment

Selected significant publications:

Throughout life exposure to a myriad of pathogens moulds our immune system to establish a repertoire of specific memory T cells that maintain immune-surveillance and can be rapidly recruited to combat secondary challenges from previously encountered pathogens. The T-cell immune reactivity is dependent on the exquisite interaction between the T-cell receptor (TCR) and the self-major histocompatibility complex (MHC) displaying pathogen-derived peptides. Key interactions between the TCR/MHC/peptide complex are not only imperative for pathogenic control/clearance but also pertinent to many human disorders (i.e. autoimmunity, allergy, cancer) and therapies for end-stage disease (i.e. transplantation). My research interests explore how the antigen-specific T cell repertoire, shaped by pathogenic exposure to form a historical template, is able to influence future immune responses through TCR cross-reactivity towards unrelated human leukocyte antigen (HLA) allomorphs. Indeed, TCR cross-reactivity may underpin or contribute to immune mechanisms that drive susceptibility to numerous human disorders via inappropriate T cell responses.

Research Projects

1. Understand the role of TCR cross-reactivity in human disease
2. Utilising immunoproteomics to determine allopeptides
Viruses pose one of the grand challenges to human and animal health globally and within Australia. Viral disease progression is critically dependent on the formation of specific interaction networks between viral proteins and host cell factors, which enable viral subversion of important processes such as antiviral immunity and cell survival.

We use advanced cellular/molecular biology approaches to elucidate these interactions at the molecular level, and to define their functions in diseases caused by highly lethal human viruses including rabies, Australian bat lyssavirus, Nipah, Hendra, and Ebola, as well as a number of agriculturally significant and potentially zoonotic animal viruses. The overarching aim of the research is to identify novel targets and strategies for the development of new vaccines and therapeutics for currently incurable viral diseases.

Research Projects

1. Elucidating the Rabies Virus P protein Axis
2. Nucleolar targeting by RNA viruses
3. Viral reprogramming of host cell signalling
4. Super-resolution analysis of the virus-host interface
5. Using Viruses to Cure Neurological Diseases

Selected significant publications:


Cell images from high resolution confocal microscopic analysis, showing virus-host interactions within nucleoli (upper panel) and at the microtubule cytoskeleton (lower panel).
The rapid spread of antimicrobial resistance against current front line drugs requires a new approach to treat infectious diseases. Rather than killing the pathogen directly, we focus on host factors that promote infections. This enables us to re-purpose already existing drugs to fight off common infections. By applying this approach, we have now shown that killing infected cells prevents lethal infections (Speir et al, Nature Micro, 2016).

Identifying new host targets requires a better understanding of the host-pathogen interaction. To do so, we have established live-cell imaging to follow in high resolution how host cells and microbes adapt during infections. Our vision is to identify novel interactions and test their role in disease by utilizing molecular and biochemical approaches. In collaboration with other researchers at the BDI Antimicrobial Resistance Group, we are now developing new host-directed treatment options to combat superbugs.

Research Projects

1. Imaging of host-microbe interactions
2. Targeting host cell death factors to prevent infections
3. Genetic and chemical screens to identify new host factors

Imaging pathogen macrophage interactions: (A) Electron microscopy shows that many bacterial pathogens, including the Neisseria superbug, the causative agent of Meningitis and Gonorrhoea, produce outer membrane vesicles (OMV). (B) These vesicles (stained red) contain several virulence factors that are targeted to various organelles in macrophages, including mitochondria (stained in green). (C) By using super resolution microscopy, genetic and biochemical assays we have now identified how bacteria hijack host cell death pathways to evade innate immunity.

Selected significant publications:


* Co-corresponding author
# Co-first author
Dendritic cells are sentinels of the immune system that produce cytokines and interferons upon sensing danger. They are also professional antigen presenting cells, thereby connecting the innate and adaptive immune systems. Our laboratory investigates how pathogens and their products and/or self-nucleic acids activate dendritic cells. We aim to decipher how this activation influences the function of dendritic cells. We investigate how this process may differ in different body locations, at different ages and in different disease settings. Major aims are to understand the role of dendritic cells in bone marrow malignancies and in autoimmune diseases such as Lupus.

Research Projects

1. The role of checkpoint inhibitors in dendritic cell activation
2. The role of bone marrow dendritic cells in the transition of myelodysplasia to leukemia
3. The contribution of interferon-lambda to disease in lupus
4. The response of dendritic cells to antibiotic-resistant strains of Staphylococcus aureus
5. The interaction of dendritic cells with malaria parasites

Selected significant publications:


Our research program focuses on the mechanisms of pathogenesis of important hospital-acquired pathogens. More specifically, *Acinetobacter baumannii*, an emerging Gram-negative bacterium, *Staphylococcus aureus*, a Gram-positive bacterium, and *Candida albicans*, the most common human fungal pathogen. We combine bacterial and fungal genetic techniques with exciting in vivo infection model systems (mammalian and non-mammalian [*Caenorhabditis elegans* and Zebrafish]) to characterise the role of novel genes in virulence and antimicrobial resistance. Our over-arching goal is to identify new targets that may be amenable for future drug development, with a focus on microbial virulence, persistence and adaptation.

**Research Projects**

1. **Impact of antibiotic resistance on immune recognition of *Staphylococcus aureus***
2. **Impact of antibiotic resistance upon virulence and persistence in *Staphylococcus aureus***
3. **Characterising novel virulence mechanisms and the regulation of virulence in the emerging hospital-acquired pathogen; *Acinetobacter baumannii***
4. **Virulence of the most common human fungal pathogen; *Candida albicans***

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**Selected significant publications:**


Fluorescent protein technology has revolutionised the way in which we carry out experiments in the life sciences, and few areas of biological research remain untouched by the technology. Fluorescent proteins such as the green fluorescent protein (GFP) cloned from the jellyfish Aequorea victoria, have been engineered to produce proteins with different fluorescent properties (for example see picture) useful for sensing a vast range of events in living cells. GFP is just one member of the protein superfamily found in marine organisms. Although each member folds to form the same 11-stranded b-barrel a variety of different chromophores (the light emitting component buried inside the barrel) together with the complex network of interactions between the chromophore and the surrounding amino acid side-chains (the protein matrix) determine the myriad range of optical properties.

Our aim is twofold: (a) understand the complex and subtle relationship between FP structure and optical properties, and (b) use newly acquired knowledge to design and engineer new FPs for novel biotechnology applications. In particular we are exploring their use in the fields of autophagy research, super-resolution microscopy and optogenetics. In the new and exciting field of optogenetics light-sensitive probes are used together with focussed light to switch processes ‘on’ and ‘off’ in living cells, tissues and intact organisms.

Research Projects

1. Engineering and characterization of FPs with useful optical properties
2. Developing probes for optogenetics
3. Developing probes and using FP for super-resolution microscopy
4. Autophagy of mitochondria (mitophagy)
5. Autophagy of the nucleus (nucleophagy)
6. Developing new biosensors for accelerating autophagy research

Selected significant publications:

Our laboratory specialises in targeted and global quantitative proteomics of complex biological samples, with a specific focus on identifying targets of the immune response and host-pathogen interactions. The laboratory has an outstanding track record in delivering high end outcomes including recent publications in highly regarding peer reviewed journals including Nature, Nature Immunol, Nat Struc Mol Biol, PNAS, J Exp Med, Immunity, Elife, Mol Cell Proteomics, Proteomics and J Proteomics Res. We combine cutting edge proteomics with human immunology, molecular virology, structural and functional immunology to address a wide variety of questions related to fundamental immunology, translational medicine, vaccination and immunotherapy.

Research Projects

1. Understanding the relationship between cellular stress and antigen presentation (type 1 diabetes and infectious disease)
2. Allergic responses to drugs: new mechanisms and targeted interventions
3. Understanding host-virus interactions and the design of novel anti-virals (HIV, Ebolavirus, influenza)
4. What causes autoimmune disease (diabetes, arthritis, psoriasis)?
5. Cancer immunology – neoepitopes, check point blockade and the anti-tumour immune response
Over the past decades, advances in our understanding of the immune system have led to the development of more effective, specific and safe approaches for the management of inflammatory associated disorders. In this context, monoclonal antibodies (mAbs) offer unprecedented opportunities to drug development because of their ability to target almost any cell surface or secreted molecule with remarkable specificity and safety. Our objective is to develop new classes of therapeutic mAbs against G protein-coupled receptors (GPCRs) using cutting edge technologies in mAbs development, engineering and pre-clinical validation. We have demonstrated that targeting specific GPCRs was an innovative approach for the treatment of various inflammatory and autoimmune disorders. Our goal is to move academic science into translation. We are currently involved in commercially oriented projects in collaboration with pharmaceutical companies, including Pfizer, Corvus Pharma, and Novo-Nordisk.

Research Projects

1. Development of therapeutic antibodies against difficult targets such as GPCRs
2. Optimization of monoclonal antibodies using humanization; Fc engineering and affinity maturation technologies
3. Development of bispecific antibodies for the treatment of autoimmune diseases
4. Therapeutic assessment of monoclonal antibodies using human knock-in mouse disease models

Selected significant publications:

Research in our laboratory is centred on the molecular genetics of pathogenic anaerobic bacteria, asking three fundamental mechanistic questions.

- How do pathogenic anaerobes, particularly Clostridium perfringens and Dichelobacter nodosus, cause disease in humans and animals?
- How is the expression of virulence genes regulated in these bacteria?
- How do virulence and antibiotic resistance genes move from one bacterium to another?

**Research Projects**

1. Host-pathogen interactions in Clostridial myonecrosis
2. Regulation of toxin production in Clostridium perfringens
3. The conjugative toxin plasmids of Clostridium perfringens
4. Pathogenesis and genomics of the ovine footrot pathogen, Dichelobacter nodosus

Selected significant publications:


The academic research program within this laboratory is concerned with defining the key molecular interactions underlying receptor recognition events that are the primary determinants of innate and adaptive immunity.

The laboratory’s research has provided an understanding of the basis of peptide, metabolite and lipid presentation, T-cell triggering, aberrant T-cell reactivity, monomorphic and polymorphic Natural Killer (NK) receptor recognition. The team’s research on anti-viral immunity has provided an understanding of the factors that shape MHC-restriction (e.g., Immunity, 2003, 2016; Nature Immunol, 2005, 2007, 2015). Moreover, we have demonstrated how the pre-TCR, a receptor crucial for T-cell development, functions by autonomous dimerization (Nature, 2010). In relation to aberrant T-cell reactivity, our team has provided insight into alloreactivity (Immunity, 2009), Celiac Disease (Immunity, 2012; NSMB, 2014) and HLA-linked drug hypersensitivities (Nature, 2012, NSMB 2014). Regarding innate and innate-like recognition, the team has shed light into how Natural Killer cell receptors interact with their cognate ligands (Nature 2011; J. Exp. Med. 2008 & 2016; Nature Immunol 2010, 2011, 2012, 2015; Nature Comms. 2016). Most recently, our team identified the long sought after ligand for MAIT cells, namely showing that MAIT cells are activated by metabolites of vitamin B (Nature 2012, 2014; Nat Commun 2012; Nat Immunol 2010, 2011, 2012, 2015, 2016; Nature Comms. 2016). Many current team members have contributed to the discovery that the DR1 molecule present these T cells are held at bay and can be overthrown. Nature. 545, 243-247 (2017). [Illustrator: Vanette Tran]

In Goodpasture’s disease when the molecule DR15 is present it can select and instruct T cells to attack the body. But when people also have the protective DR1 molecule present these T cells are held at bay and can be overthrown. Nature. 545, 243-247 (2017). [Illustrator: Vanette Tran]

Selected significant publications:


# denotes joint senior author
The research focus of our group is structural biology of virulence factors of the carcinogenic bacterium Helicobacter pylori. (I) H. pylori must be able to swim by means of its flagella in order to infect the human host and persist for years in the gastric mucosa. We study the mechanism of force generation in H. pylori flagellar motor and the structure and function of the key motility and chemotaxis proteins. (II) Development of gastric cancer in infected individuals is facilitated by exposure of gastric cells to H. pylori protein CagA. We investigate the mechanism of CagA-mediated gastric cell transformation. (III) The eradication rates achieved with the standard therapy have been declining and now fall in approximately 20%-30% of the patients, mainly due to antibiotic resistance. We investigate structure and function of the essential H. pylori proteins that have not yet experienced selective pressure in the clinical setting. The structural insights gained through this work will provide strategies for rational design of novel therapeutics.

Research Projects

1. Carbonic anhydrase inhibitors as new anti-H. pylori agents (Collaboration with Dr Terry Kowk-Schulein & Professor C. Supuran (Univ. of Florence))

2. How does H. pylori sense environmental cues? (Collaboration with Professor K. Ottemann (Univ. of California))

Selected significant publications:


A/Professor Jiangning Song
Senior Research Fellow
Head, Structural Bioinformatics Laboratory

Structural bioinformatics is the branch of bioinformatics concerned with the analysis and prediction of the three-dimensional structure of biological macromolecules on a genomic scale by developing computational methods. Machine-learning techniques have recently provided cost-effective solutions to challenging problems that were previously considered difficult to address. Our research focus is to develop heterogeneous biological feature-integrated approaches and tools based on machine learning and data mining to further our understanding of biological systems. We are motivated to investigate, develop and apply cutting-edge bioinformatics methodologies to understand and address a range of open and challenging problems in genomics, molecular biology and systems biology. The developed bioinformatics algorithms and tools can be used as powerful means to facilitate high-throughput screening (HTS), guide rational drug design and address emerging challenges in precision pharmacology. To date, bioinformatics tools we developed include Cascleave, Cascleave 2.0, APIS, PROSPER, hCKSAAP_UbSite, Crysalis, Procleave, Periscope, GlycoMine, PROSPER 2.0, Bastion4 and DeepCleave.

Research Projects

1. Computational modelling and experimental validation of types III, IV and VI secretion effector proteins in Gram-negative pathogens
2. Reconstruction of structural interaction networks at the host-pathogen synapse
3. Comparative genome-scale metabolic modelling of Klebsiella pneumonia
4. Predicting the effects of noncoding variants de novo in the human personal genome
5. A machine-learning-based method to link protein post-translational modification stoichiometry and functional phenotype

Selected significant publications:


Inflammation is the response of a tissue and its microvascular system to injury or infection. A hallmark of inflammation is the accumulation of leukocytes (white blood cells), which remove pathogens and necrotic tissue by phagocytosis and proteolytic degradation. However, excessive leukocyte recruitment or activity leads to the release of toxic substances and degradation of healthy tissue, i.e. inflammatory disease.

Leukocyte recruitment in inflammation is controlled by the expression and secretion of small proteins called chemokines at the site of inflammation and by the subsequent interaction of those chemokines with chemokine receptors located on the surfaces of circulating leukocytes. A detailed understanding of chemokine-receptor interactions is required in order to rationally develop novel therapeutic agents against inflammatory diseases. Our group is investigating several important aspects of chemokine and chemokine receptor biochemistry with the overall goals of better understanding and ultimately controlling their biological functions.

Research Projects

1. Biased receptor agonism by chemokines
2. Structural basis of chemokine recognition
3. Tick evasins – Natural chemokine antagonists
Selected significant publications:


# Indicates correspondence

Microbial pathogens kill millions of people every year, and the rise of antimicrobial resistance (AMR) is of huge concern to global health. We might soon run out of treatment options for many deadly pathogens, including bacteria and fungi that infect the most vulnerable patients, such as those undergoing cancer chemotherapy or organ transplants. Our standard approaches to drug discovery are inefficient, and the microbes can rapidly develop resistance to any new drug. My team, together with the AMR Group at the BDI, are focused on novel approaches to anti-infective treatments:

i. We are studying how the nutritional and metabolic status of the patient could be manipulated to boost immune responses thereby clearing infections.

ii. We exploit the concept of drug re-purposing to identify antifungal therapeutics with novel mechanisms of action.

Our approach is interdisciplinary, with molecular and cell biology, ex vivo and in vivo models of infection (immune cells, animal models), imaging, and the “omics” approaches of Systems Biology. We collaborate with engineers and clinicians to design improved therapeutic and diagnostic strategies for deadly hospital infections.

Research Projects

1. Understanding host-pathogen interactions in innate immunity.
2. Metabolic interactions between microbes and immune cells that drive infection.
4. Characterisation of novel antimicrobial compounds with novel mechanisms of action and improved efficacy.

The image is adapted from Fig 2 in Uwamahoro et al mBio 2014, v5: e00005.
Mapping genome wide deposition of histone protein modifications during virus-specific T cell differentia-
tion. Shown is mapped ChIP-seq data for two histone modifications, H3K4me3 (red) and H3K27me3 (blue).

Our laboratory aims to identify novel transcriptional and epigenetic pathways and regulatory elements that regulate virus-specific killer T cell differentiation, function and the establishment of immunological memory. Such analysis will lead to the identification of molecular immune correlates of protective immunity that will serve to better understand how optimal immunity is generated. Further, this information will contribute to improvement of immunotherapies for infection (vaccines), autoimmune disease and cancer therapy. We use a multidisciplinary approach that includes the application of multiple next generation sequencing applications (RNA-seq, ChIP-seq, ATAC-seq, and HiC), small molecule inhibitor treatment of epigenetic and transcriptional regulators, novel transgenic and gene deficient mouse models, viral models of immunity and advanced bioinformatics.

Research Projects

1. The role of chromatin remodellers in determining chromatin architecture during virus-specific T cell responses

2. Mapping genome wide targets and mechanisms of action of killer T cell specific transcription factors

Selected significant publications:


Our work is principally focused on events central to infection and immunity. Specifically we work on deducing the structural arrangement of Killer-Cell Immunoglobulin-like Receptors (KIR) and their ligands and detail the molecular mode of interaction generating their complexes. This has important implications in disease and transplant outcomes. We also investigate immune reactions to specific drugs. This work is intended to lead to the better design and screening of new therapeutics.

**Research Projects**

1. **Structural and functional investigation of KIR receptors**

2. **What causes drug hypersensitivity?**

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**Selected significant publications:**


Protein RNA binding events play major roles in infection and innate immunity. Examples of these include the regulation of translation of viral genetic material and the detection of viral infection. Poliovirus is one of the best studied and offers an ideal archetypal picornavirus for investigation. Translation of its RNA requires the exploitation of a number of host cell proteins that bind to specific structures in the 5’ non-coding region, the internal ribosomal entry site (IRES), that allow the ribosome to dock leading to viral protein synthesis. We are investigating the molecular mechanisms that underpin the binding of host proteins to the IRES which provides a platform for the ribosome to bind. Ultimately, we plan to develop molecules that will inhibit these essential viral RNA host protein interactions.

RIG-I is a cytosolic protein that upon binding to viral dsRNA undergoes a conformational rearrangement that initiates a signalling cascade that ultimately leads to production of interferon. Recently small RNA stem loops have been discovered that can activate RIG-I. We are studying the activation of RIG-I by these RNAs to understanding the basis of activation which may lead to therapeutic interventions.

Research Projects

1. RNA translation - Poliovirus
2. RIG-I recognition of viral RNA

Selected significant publications:


We use structural and molecular biology to investigate protein function and dysfunction in immunity, haemostasis, cell signaling and developmental biology. Support for the laboratory includes an ARC Federation Fellowship, NHMRC and ARC grants, an ARC Centre of Excellence in Advanced Molecular Imaging together with funding from the Wellcome Trust. Generally projects involve any or all of the following techniques: X-ray crystallography, small angle x-ray scattering, electron microscopy, bioinformatics, molecular and cell biology, enzymology and protein chemistry.

Research Projects:

1. **Perforin in immunity & cancer** (Collaboration with Professor Joe Trapani, Peter MacCallum Cancer Centre; Professor Ray Norton, MIPS)
2. **Fibrinolysis in diabetes** (Collaboration with Professor J Shaw, Bakers IDI)
3. **GABA functions in disease** (Collaboration with Dr K Tuck, Chemistry Department, Monash University)
4. **Understanding the structural basis for bacterial conjugation** (Collaboration with Professor J Rood, Microbiology Department, Monash University)
The overarching goal of research in our lab is to define the cellular and molecular mechanisms that control immunity and inflammation at mucosal sites such as the intestine and the lung. The various subsets of immune and non-immune cells at mucosal sites are present in a tightly controlled equilibrium that when perturbed by infection, chemicals or genetic predisposition, results in dysregulated inflammation and diseases including asthma and allergy, inflammatory bowel diseases (IBDs), food allergies and cancer. Understanding the molecular and cellular principles underlying mucosal inflammation represents a potential target for identifying novel therapeutics for the treatment of these diseases.

Research Projects

1. Epigenetic regulation of mucosal immunity and inflammation
2. Retinoic acid, Hic1 and intestinal immune homeostasis
3. Methylation is the new phosphorylation: Dynamic regulation of signal transduction by methylation

Selected significant publications:


Metabolism, Diabetes and Obesity Program
Group Leaders
We examine how the brain senses hormone and nutrient information in different metabolic states and how the brain integrates this information to encode physiological and behavioural changes that maintain energy homeostasis. The work is critical to help identify the causes of obesity, anorexia and type-2 diabetes.

We are examining how metabolic states such as fasting or starvation influence other brain systems, such as anxiety and stress, motivation and memory. Clearly maintaining energy homeostasis is not only good for body weight, but also for mental health. Similarly changes in mental health can affect food intake and body weight. We are working to identify interconnected neural pathways linking metabolism to mood, motivation and neuroprotection.

Research Projects

1. How does emotional, cognitive and motivational information from the cerebral cortex influence hypothalamic control of energy homeostasis
2. How does endocrine feedback during negative energy balance coordinate and integrate metabolism with stress, anxiety, motivation and memory; the role of ghrelin and ghrelin receptors
3. How does the brain sense changes in metabolic state in order to control energy homeostasis; implications for obesity and type 2 diabetes

Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) provide a unique way to remotely control specific neuronal populations. Localised DREADD expression only in arcuate nucleus NPY neurons.

DREADD activation with an exogenous ligand increases cFos, a marker of neuronal activation (red nuclei) expression only in NPY (green) neurons.

Selected significant publications:

Our laboratory focuses on developing new therapies for obesity, diabetes and metabolic disorders. Our research has mapped the neural circuits in the brain that sense nutrients, glucose, and fat to control appetite and body weight. That map of the brain helped us develop therapeutics for the treatment of obesity. We are now interested to determine if similar pathways can regulate blood glucose levels. Our lab is also looking at how obesity causes heart disease and how to reverse obesity-induced heart disease risks.

Research Project:

1. How does leptin increase blood pressure?
2. What causes hypertension in pregnancy?
3. How does the brain regulate glucose disposal by the body?
4. Does the brain regulate glucose secretion by the liver?
5. Can we identify, and modify, new pathways that regulate body weight or blood glucose?
6. Screening for new diabetes targets.
Members of the transforming growth factor-β (TGF-β) protein superfamily play key roles in the regulation of cellular growth and differentiation. These proteins have documented roles in embryogenesis and reproduction, as well as wound healing, immune function, fibrosis and tumour progression. Our group has a long-term interest in understanding the mechanisms that govern the regulation of individual members of the TGF-β family and their impact on biological activity.

Research Projects
1. **Targeting activin to combat life-threatening cancer cachexia**
2. **Therapeutic potential of TGF-β proteins for the diagnosis and treatment of female infertility**
3. **Inhibins as therapeutics for osteoporosis and sarcopenia**

Selected significant publications:


Our laboratory focuses on understanding how body weight is regulated. We have a particular interest in understanding how energy expenditure occurs within mammals. Our work primarily focuses on thermogenesis, which is a specialised process where the body expends energy in the form of heat. Our work aims to understand how the brain regulates thermogenesis. We have a number of unique and novel models that allow us to characterise the control of body weight, food intake and energy expenditure. The metabolic neuroendocrine group has a particular interest in understanding how the following impact on energy homeostasis and weight control:

1. Control of thermogenesis in humans.
2. Stress, stress responsiveness and obesity.
3. Exercise.

Research Projects

1. Sex differences in the control of thermogenesis
2. Stress, weight loss and predisposition to obesity
3. Role of thermogenesis in weight regulation in humans

Selected significant publications:


The primary focus of the laboratory is brown fat biology, particularly its innervation. Given the consensus that activation of the β-adrenoceptor on brown or “brown – like” beige fat cells by noradrenaline is a critical element in the effective functional recruitment of energy expenditure in these tissues, we have focussed on the details of the central neural circuits involved. This theme is being pursued in the first four of the funded projects listed below.

In addition, there are two other major projects in the lab which have unexpected overlap with our focus on brown fat biology. One is the use of our rodent model of the adjustable gastric band which is being used to define mechanisms underpinning the efficacy of the procedure, particularly in relation to the use of adjunctive pharmacotherapies with the band. The second is a functional dissection of midbrain reward pathways, using Cav-Cre viruses and DREADD technologies, to define the contribution of these pathways to the mediation of voluntary starvation in a rodent model of anorexia nervosa.

**Research Projects**

1. “Smart Food” – The fulcrum in the energy balance equation
2. Determining the impact of the nutrient milieu in the CNS on thermogenic tone using obese prone and obese resistant rodents
3. Central neural regulation of brown fat function – glucose sensing
4. Central neural regulation of brown or beige fat function
5. The use of a rodent model of the AGB to define the mechanisms underlying increased efficacy of the AGB when combined with pharmacotherapies
6. Reward pathways and their involvement in the etiology of anorexia nervosa

**Selected significant publications:**

The tight regulation of metabolic control is important for organismal function and wellbeing. The pathways by which certain ingested nutrients coordinate proper function, and particularly how certain nutrient signalling pathways talk to each other when nutrient balance is altered, is poorly understood. We adopt an integrated systems approach to further the understanding of adaptive/maladaptive metabolism and the molecular mechanisms involved therein, with the eventual aim to discover new therapies for diseases with a metabolic basis such as obesity, diabetes, and perhaps cancer. Our particular interest lies in the complex interaction between nutrients, hormones, and signalling pathways which connect these to ultimately coordinate systemic metabolic control.

Research Projects

1. Nutrient-hormonal-signalling nodes controlling metabolic homeostasis
2. Stress-signalling pathways in adaptive metabolic control
3. Inter-organ metabolic cross-talk in health and disease

Selected significant publications:


Mitochondria are the powerhouses of our cells. They are also important in other processes including apoptosis, innate immunity and in neurological diseases including Parkinson’s. Disorders of mitochondrial energy generation cause degenerative diseases and often lead to infant death. Mitochondria are generally found as a reticulated network radiating from the nucleus with individual mitochondria undergoing fission and fusion for proper distribution, quality control, and stress responses. Our lab investigates biochemical and cell biological processes related to these areas. Research projects are designed to ensure each student encounters a range of techniques and along with weekly lab meetings, will give them expertise for future scientific and non-scientific careers. Example of projects are below.

**Research Projects**

1. **CRISPR/Cas9 approaches to understand human mitochondrial protein function and disease**

2. **Mitochondrial dynamics & neurodegeneration**

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**Selected significant publications:**


The primary research focus of the Integrated Physiology Lab is on the development of obesity-associated diseases such as diabetes and cardiovascular diseases. We use mouse models of disease states in order to probe the mechanisms underlying obesity-associated disease development. We use world leading research techniques in order to answer fundamental questions such as “what is a healthy diet? can I be overweight and healthy?” “as a woman am I at increased risk of developing an obesity-associated disease”. 2019 represents a particularly exciting year in the Integrated Physiology Lab as we are embarking upon a novel research stream; investigating the effects of air pollution on the cardiovascular, respiratory and metabolic health.

Research Projects

1. **Delineating the role of the melanocortin system in metabolic vs cardiac control**

2. **The effect of particulate matter on metabolic and glycaemic control**

3. **The effects of air pollution, particulate matter on the cardiovascular system.**

Selected significant publications:


Brain areas dedicated to controlling food intake and body weight include aspects of the hypothalamus, key centres for sensing, integrating and formulating appropriate behavioural responses to changes in energy status and the hedonic, reward-based neural circuits. One nutrient that is controlled and maintained within narrow limits is glucose. Glucose levels are maintained by a network of interacting peripheral and central glucose-sensing systems. Consequently understanding the fundamental mechanisms by which function-specific glucose-sensing neurons and networks detect, respond and formulate appropriate output and if and how they are subject to dysfunction in obesity and diabetes is critical to developing future intervention strategies. We employ an electrophysiological approach to identify mechanisms by which function-specific neurones and circuits detect changes in energy status to co-ordinate appropriate behavioural responses and how they change depending on the energy status of the organism.

Research Projects

1. **Glucose-sensing neurones in the brain: how do they do it?**

2. **Motivation and reward: glucose, ghrelin and the mechanisms regulating the dopaminergic neural circuits of the ventral tegmental area**

**Selected significant publications:**


A cell’s ability to respond to its extracellular environment involves a complex and highly organised series of events referred to as cellular signalling. Our laboratory focuses on a group of enzymes known as Protein Tyrosine Phosphatases (PTPs) that regulate tyrosine phosphorylation-dependent cellular signalling. We use cutting edge biochemical, cell biological and imaging approaches as well as knockout mice and Drosophila genetics to delineate the roles of PTPs in varied human diseases. A key focus of the laboratory is on understanding the roles of PTPs in the control of energy expenditure and glucose homeostasis.

Research Projects

1. The central nervous system (CNS) control of energy expenditure and glucose homeostasis in obesity
2. Molecular mechanisms by which obesity drives the development of fatty liver disease
3. Obesity and the gut microbiome
4. Obesity and cancer; cancer metabolism

Nonalcoholic steatohepatitis and liver fibrosis in mutant mice fed a high fat diet.
Metallo-peptidases cleave amino acids from either the N- and C-termini of peptide hormones to either generate or degrade bioactive peptides. These enzymes play important roles in the body and alterations in their activities can impact on a diverse range of physiological processes in both healthy and diseased states. Our research is focussed on insulin-regulated aminopeptidase (IRAP) particularly in diseased states. Our findings have revealed previously unsuspected roles for IRAP particularly its involvement in memory processing, glucose homeostasis, cardiovascular function and water and electrolyte balance. We have a drug development program targeting IRAP and have identified specific inhibitors that await development into clinically effective drug therapies.

Research Projects

1. Role of IRAP in the pathogenesis of Alzheimer's Disease
2. IRAP contributes to the neuro-inflammatory response in ischemic damage
3. Does IRAP regulate glucose and fat metabolism?

Selected significant publications:


Selected significant publications:


Work in our laboratory has contributed extensively to the field of neuroendocrinology and currently have 3 main divisions:

- Reproduction: effects of gut peptides on the brain; role of kisspeptin and gonadotropin inhibitory hormone on reproductive function; vaccination in early life for life-long sterility.
- Metabolic neuroendocrinology: predisposition to obesity; relationship between stress and metabolic function.
- Heat stress: effects on body tissues, gut and brain function.

We utilise sheep models, which allow a range of studies not easily undertaken in small laboratory species. We have developed a number of novel neuroendocrine methodologies that allow analysis ranging from the whole animal down to the single cell and subcellular function. These techniques facilitate national and international collaborations, with grant funding from Australian and offshore sources. In addition, our laboratory undertakes a range of contract research projects.

Research Projects

Research in the Neuroendocrinology Lab currently focuses on the following areas:

1. Central regulation of reproduction by kisspeptin and gonadotropin inhibitory hormone
2. Estrogen signalling in neuroendocrine systems
3. Control of food intake and energy expenditure by leptin and novel regulatory factors
4. Optogenetic control of kisspeptin function
5. Neonatal sterility vaccination, using a novel approach
6. Heat stress in various genetic models
Selected significant publications:


Research Projects

1. Understanding the pathophysiology causing a variety of sleep disorders.

2. Determining simplified ways to measure the causes of sleep apnoea.

3. Assessing how respiratory control changes during sleep.


5. Assessing the bi-directional relationship between sleep apnoea and insomnia as well as post-traumatic stress disorder (PTSD).
Chronic pain is a major global health burden, affecting nearly 20% of the Australian population. This condition results in hypersensitivity to sensory input so non-painful stimuli can become painful. Analgesics that are currently in use provide relief in a small proportion of chronic pain patients and there is a great need for more effective therapeutics.

Our lab investigates changes in neuron signalling that happen in pain circuits during the development of chronic pain. Some of these changes can be targeted therapeutically, so the aim of our work is to identify pathological changes and find ways to modify them for the treatment of pain. To understand pain circuitry and to characterize potential analgesics, we use patch-clamp electrophysiology, optogenetics and calcium imagining in brain and spinal cord tissue from animal models. We also use immunohistochemistry and confocal imaging, behavioural assays and genetic profiling.

Research Projects
1. Decoding dysfunctional spinal cord circuitry in chronic pain.
2. Identifying Novel Molecular Targets for Treating Chronic Pain.

Selected significant publications:
Dr Sanjaya Kuruppu
Head, Kuruppu Research Group

Monash Biomedicine Discovery Institute
Neuroscience Program

Development of novel drugs from animal venoms is a major focus of our current research. We have developed an ideal drug candidate that targets one of the main pathological features of Alzheimer’s disease. Preclinical trials on this molecule are currently underway funded by the National Foundation for Medical Research and Innovation. Other major focus of our group is the role of the endothelin system in cardiovascular and renal disease. Together with researchers in engineering, our laboratory is aiming to develop a device similar to a glucometer with capacity to measure endothelin levels in circulation to detect renal disease early.

Research Projects

1. Examining the effect of venom derived molecule(s) as novel drug leads for Alzheimer’s disease
2. Examining the role of the endothelin system in cardiovascular and renal disease with a particular emphasis on characterising endothelins as biomarkers
3. Characterisation of toxins in animal venoms as potential lead compounds targeting cardiovascular disease

Selected significant publications:


Parkinson’s disease (PD) is one of the most common of the neurodegenerative disorders, affecting 1-2% of the population worldwide. Multiple lines of evidence place mitochondrial dysfunction as a central player in the pathogenesis of sporadic PD, and studies of genes associated with familial PD demonstrate convergent pathways involving oxidative stress and mitochondrial dysfunction. Two proteins commonly mutated in familial PD, PINK1 and Parkin, play a key role in maintaining mitochondrial integrity by identifying damaged mitochondria and degrading them through a selective form of autophagy termed mitophagy. Our lab investigates the molecular mechanisms of PINK1/Parkin mitophagy and how it works with mitochondrial repair pathways to maintain healthy mitochondria. Furthermore, given the fundamental importance of autophagy to cellular viability, our research also aims to understand the factors and processes that drive autophagy.

Research Projects

1. PINK1/Parkin mitophagy
2. Mitochondrial quality control
3. Autophagy mechanisms

Transmission electron microscopy was used to generate a 3D reconstruction of a damaged mitochondrion (red), engulfed by an autophagosome (green), surrounded by the endoplasmic reticulum (blue) during PINK1/Parkin mitophagy.

Selected significant publications:


Our research seeks to understand the biology of age-related functional decline in the nervous system. Progressive neurological dysfunction with age adversely affects the quality of life in older adults and presents serious financial challenges to public health, but the cellular and molecular mechanisms underlying the functional decline in the nervous system with age are yet to be fully elucidated. Because age-related motor and sensory dysfunction are prominent phenomena observed in nearly every species, these phenomena lend themselves to research of age-related progression of neurological dysfunction. Given its short lifespan, powerful genetics, simple nervous system, and evolutionarily conserved molecular mechanisms in ageing, *C. elegans* serves as a convenient platform for the research of age-related deficits in the nervous system at different levels, from genes, neurons to behaviours. Our previous research demonstrated not only that these worms have multiple sensory modalities, but also that they are subject to age-related motor system functional decline. Extrapolating from these findings, our short-term goal is to demonstrate how aging triggers the functional deterioration in both the somatosensory and olfactory system. Ultimately, we aim to identify novel therapeutic targets of various age-related neurological disorders by discovering new genes involved in functional aging as well as develop pharmacological interventions for various age-related neurological diseases.

**Research Projects**

1. The molecular mechanisms of Sensory perception
2. Behavioural encoding neural circuits
3. Functional ageing in the nervous system

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**Selected significant publications:**


Our group focuses on the field of visual neuroscience, we investigate how activity in specific areas of the brain (e.g. The Middle Temporal Area, MT in Figure) contributes to the perception of motion. We take advantage of the visual and auditory systems to study higher order function.

Historically, sensory systems have provided some of the most robust insights into brain function. Different parts of the brain represent information from the different senses (see Figure), but what happens when one of these areas is damaged? We now study how the activity of different parts of the brain changes after damage to another using V1 lesion as a model. Activity in area MT may be responsible for residual vision after damage to the most important visual area. We will extend this paradigm to study the neural basis of how training with simple perceptual tasks can improve visual function after V1 damage.

While we have a good idea on the function of visual and auditory areas, little is known about how these areas interact to give a unified percept, e.g. to locate a moving car. We seek to find out how neurons allow us to do this, investigating the ways in which information that is initially represented in V1 and A1 are combined. Multisensory integration becomes particularly important to people with sensory deficits, such as those with Cochlear implants and hearing aids.

Research Projects

1. Neural plasticity underlying visual motion perception after damage to the primary visual cortex (V1)
2. Neural mechanisms underlying training-induced recovery from V1 damage
3. Neural mechanisms of audiovisual integration

Selected significant publications:

In a changing environment we need to select the most appropriate behaviour-guiding rules to achieve our goals. We would like to study the neural substrate and underlying mechanisms of such cognitive flexibility. We have implemented various techniques such as lesion-behavioural study, single-cell recording and non-invasive brain stimulation in humans and also in animal models to address these questions. Establishing animal models of cognitive tests for recruiting higher cognitive functions such as abstract rule implementation and executive functions has opened new chapters in investigating the neural basis of cognitive processes which previously was considered as exclusive faculties of human brain function. Techniques used in our laboratory include behavioural and electrophysiology studies in animal models and psychophysical and brain stimulation studies in humans.

Research Projects

1. Understanding the role prefrontal cortex in executive control of goal-directed behaviour

2. Understanding the role of anterior cingulate cortex in cognitive flexibility

Selected significant publications:


Most of us rely on our sense of vision to navigate and interact with the world around us. The ease with which we do so, however, belies the challenging computational problems solved routinely by the brain. Our aim is to understand how neurons represent visual space for the purpose of goal-directed behaviours, such as reaching and walking. We record neural activity in visual cortex while subjects perform perceptual and motor tasks. We then combine the data with modelling and computer simulations to infer causal links between neural computations, perception, and behaviour.

Research Projects
1. Eye movements and the neural representation of visual space.
2. Rapid plasticity in sensory systems - linking neuronal adaptation and perception.
3. Neural computations for predictive coding in visual cortex.
4. Hierarchical information processing in the primate visual cortex.
5. Plasticity of perceptual space under sensorimotor interactions.

Selected significant publications:
The overarching goal of our laboratory is to understand how our nervous systems remain intact and functional over our lifetimes. A hallmark of neurodegenerative disorders such as motor neuron, Alzheimer’s, Parkinson’s, and Charcot-Marie-Tooth diseases is degeneration of the nervous system. We lack a complete understanding of the molecules and mechanisms employed by neurons to preserve their complex structures over time, which has hampered the development of effective therapies. To understand the fundamental molecular mechanisms regulating axonal degeneration we use the nematode *C. elegans* as a model system due to its simplified and exceptionally well-characterised nervous system.

We also study how the nervous system can be repaired after it has been damaged. Injuries to the nervous system, such as spinal cord injuries, can inflict lifelong disabilities due to ineffective repair of the damaged nerve fibres. We focus on highly effective repair mechanisms in *C. elegans* in order to define how the nervous system can repair itself and re-establish function.

**Research Projects**

1. **Cellular and molecular mechanisms of axonal regeneration**
2. **Modelling Charcot-Marie-Tooth disease in C. elegans**
3. **Uncovering novel genes involved in degeneration of the nervous system**

Green and red fluorescent proteins allow visualisation of specific subsets of neurons in the nematode *C. elegans*.  

Selected significant publications:


We study how the activity of small populations of sensory neurons underlies conscious visual perception and the control of eye movements. We employ a diverse range of methods including studies of human and animal behaviour, extracellular neuronal recordings using multi-electrode arrays and computational modelling. We are particularly interested in two main questions:

1. How does sustained exposure to a visual stimulus affect neuronal encoding and perception of subsequently seen stimuli?

2. How does the activity of small population of sensory neurons encode visual motion, and how can we decode this population activity to predict perception and behaviour?

Research Projects

1. The neural correlates of perceptual backward masking
2. Is visual cortex self-aware?
3. How do sensory neurons incorporate dynamic stimulus statistics?

Selected significant publications:


Selected significant publications:


Our laboratory is interested in the organization and connections of areas related to sensory processing in the primate brain. Using a variety of neuroanatomical, electrophysiological, and imaging techniques, we are asking questions about how the brain creates an accurate picture of the external world based on input from the senses and stored information about past experiences.

Research Projects

1. Large-scale map of connections of the marmoset cerebral cortex
2. Functional organisation of the primate visual cortex
3. Neural computations involved in vision
4. Understanding how the brain controls the arms during reaching for objects

Selected significant publications:


The development of neural prostheses is emerging as an exciting new frontier, bridging cutting edge engineering techniques with neuroscience research. Our lab is working to improve and develop a wide range of neural prostheses, including Brain Machine Interfaces for upper limb control, bionic eyes, and cochlear implants. We are particularly interested in developing new technologies such as stentrodes, and utilizing novel neuroscience approaches like the local field potential to improve the efficacy of devices. On the basic neuroscience side, we study the role of the local field potentials in communication across brain areas and potential roles in multi-effector decision making, reward learning and movement planning.

Research Projects

1. Cortical vision prostheses to restore sight to the blind
2. Brain machine interfaces for high dimensional reaching control
3. Understanding how brain oscillations aid in coordinating long-range cortical communication

The Monash Vision Group cortical vision prosthesis, which consists of an array of penetrating microelectrodes connected through a ceramic casing to electronics that are capable of delivering electrical stimulation and receiving wireless power and control signals.
Neurogenesis is a fundamental process of generating new neurons, which integrate into existing circuits. Neurogenesis is important for learning and memory, ageing and neurodegenerative disorders. Both intrinsic and extrinsic mechanisms regulate neurogenesis. miRNAs are short noncoding RNAs that regulate gene expression at the posttranscriptional level that appears to be involved in multiple steps of neurogenesis. However, it is not clear how these miRNAs are modulated during neurogenesis. Our laboratory aims to identify promoters of miRNAs, such as mir663, that mediate pathways specially regulated neurogenesis.

Research Projects

1. TAGing APP constrains Neurogenesis: Pathological Role of miR-663 Regulated Genes in Alzheimer’s Disease.

2. To develop natural alternative solutions, with an emphasis on those that target reduced antibiotic usage, for the benefit of both animals and humans.
Monash University has been recognised for its enduring work in gender equity and for fostering an inclusive workplace culture with this citation from the Workplace Gender Equality Agency.

CONTACT US
Whether you want to research, invest, study or partner with us, we’d be delighted to hear from you.

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