QIMR Berghofer

2025-26

STUDENT PROJECTS

QIMR Berghofer

Director's Welcome

QIMR Berghofer is one of the leading medical research institutes in Australia. In 2023 QIMR Berghofer was ranked second in Australia for its success rate with National Health and Medical Research Council (NHMRC) research grants. Our mission is to deliver 'better health through impactful medical research', and we do that by developing new diagnostics, better treatments and more effective strategies to prevent and treat disease. Research at the Institute is channelled through four clinically relevant programs: Cancer Research, Infection and Inflammation, Brain and Mental Health, and Population Health (disease causation, prevention and control).

QIMR Berghofer ("the Institute") is home to more than 1000 scientists, staff and students who consistently generate formidable, high-quality research. In 2023-2024, researchers published 598 unique scientific publications, with more than 53,000 citations, and income from commercial collaborations and contract research of more than $13.7 million.

As a student at the Institute, you will be joining an elite cohort of exceptionally talented scientists from around the globe. You will work alongside leading researchers in state-of-the-art laboratories. You will attend seminars showcasing the latest research findings, and be encouraged to ask questions and help find answers to some of the world's most pressing medical problems. While here, you will be well supported by a professional team who will help you to navigate your chosen academic path. In addition, you will receive mentoring advice and acquire the skills you need to pursue medical research to the highest levels of integrity and scholarship.

At the Institute, we have a long tradition of running a very collegial and cohesive PhD student program. PhD students benefit from a yearly conference where they can showcase their work, experience excellent peer group support and activities, and a much enjoyed awards presentation. The student life at QIMR Berghofer is truly unique and fondly remembered by our alumni.

This booklet gives you an insight into the world that awaits you here. The projects presented within this booklet can often be adapted to suit your particular skills and strengths, so I encourage you to talk to the faculty members about any projects that take your interest and find one that works for you. Lastly, I always advise prospective students to 'shop around'. You are making a big decision, so you want to be sure that you are enthusiastic and inspired by the project you end up pursuing.

I hope you choose QIMR Berghofer as your next home and, if so, I look forward to welcoming you to the Institute for the next step in your academic career.

Professor Fabienne Mackay

Director and CEO

QIMR Berghofer

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Quick facts about QIMR Berghofer

QIMR Berghofer was established in 1945 as "The Queensland Institute of Medical Research" and is celebrating its 80th year in 2025.

598 papers were published (2023-2024).

The QIMR Berghofer student body is very multinational and is strongly supported by a Higher Degrees Committee dedicated to mentoring and guiding students through their candidature.

QIMR Berghofer is a world-leading translational research institute focused on cancer, infections and inflammation, brain and mental health, and population health.

The Institute is home to more than 700 scientists (of which approximately 150 are students) in 71 research laboratories.

The Institute is located at the Herston Health Precinct, which is home to more than 30 health facilities, medical research institutes, universities and organisations.

QIMR Berghofer Student Society

The QIMR Berghofer Student Society is a dynamic organisation that serves as a support system, social hub, and a source of lifelong memories for students at QIMR Berghofer. It provides a network of support where students can connect with peers and mentors who share their research interests and offer academic resources and social support to help them excel in their research endeavours.

The QIMR Berghofer Student Society organises various social events such as lunch barbeques, trivia nights, bake sales, seminar series, annual symposiums and even conference retreats to create opportunities for students to make friends, establish meaningful connections, and foster a sense of community within the scientific community.

Moreover, through engaging events and activities, the QIMR Berghofer Student Society encourages students to create lasting memories that they will cherish throughout their scientific journey, adding a unique dimension to their overall research experience. We are excited for you to join us!

Attendees at the 12th QIMR Berghofer Biennial Postgraduate Student Conference – Mercure Clear Mountain Lodge, Spa & Vineyard, Brisbane Queensland

Why study at QIMR Berghofer?

Studying at QIMR Berghofer provides students with a unique opportunity to have access to diverse clinical and cutting-edge research. Our proximity to the Royal Brisbane and Women's Hospital (RBWH) and the Herston Health Precinct makes us ideal for clinical research collaborations.

In addition to your research training, QIMR Berghofer is committed to your overall professional development. This includes expanding your skills in critical scientific writing, statistics, leadership, communication and protecting your intellectual property. After studying at QIMR Berghofer, your broader skill base will allow you to compete for your future desired career.

Advantages of studying at QIMR Berghofer include:

- Expert supervision from world leaders in their field of research.
- Access to and support from high-quality, purpose-built facilities and technical experts.
- Access to advanced technologies and equipment.
- Exposure to a wide range of interdisciplinary research encompassing everything from population studies to statistics, public health, tropical medicine, immunology and cancer.
- Opportunities for international collaboration and travel.
- Competitive Honours and PhD top-up scholarships.
- Travel support for attending international conferences to promote collaborations and future postdoctoral positions.
- Student mentoring and professional development.
- Dynamic process of review to monitor student progress and ensure timely completion of your degree.
- A regular student seminar program.
- A weekly seminar series presented by researchers, national and international speakers.
- An active student society, symposium and retreat for networking and training.

The QIMR Berghofer student body is a diverse group of Australian and international students involved in a wide range of research endeavours. We are working to make a real difference to health issues affecting Australians and the rest of the world.

Clinician Researcher Academy

The QIMR Berghofer Clinician Researcher Academy ("the Academy") is designed to develop and coordinate research collaborations, career development, professional development, academic training, and mentorship with and for clinician researchers.

Participants at the Academy have access to cutting-edge resources, world-renowned scientists, key networks, and collaborative research opportunities through a range of visitor, affiliate, and student arrangements.

In turn, QIMR Berghofer aims to advance research impact and translation through clinically relevant and clinically informed research, and to promote achievement of our vision of better health and wellbeing through impactful medical research. Our Scientific and Core Services are world-leading and include genome informatics, statistics and research design, research software, programming and high-performance computing, metabolomics, sample processing, sequencing and NATA-accredited flow cytometry, and histology. Our Scientific and Core Services teams provide training in the use of specialist equipment, techniques, and research methodologies.

Our Good Manufacturing Process (GMP) accredited Q-Gen Cell Therapeutics facility has over 20 years of experience in T cell manufacturing supporting the immunotherapy industry and advancing patient outcomes with the manufacture of autologous and allogeneic therapies.

The facility is licensed by the Therapeutics Goods Administration for the manufacture of T cell therapies for clinical trials. The Institute offers a weekly faculty seminar series and regularly hosts national and international experts as guest speakers who share the latest research findings and methods across a range of health and medical research topics. Our clinical higher degree students are supported by a professional team that assist you to navigate the PhD journey and with mentoring advice and skill development to pursue a research career with the highest levels of integrity and scholarship.

Clinical Director:
Professor Elizabeth Powell

Elizabeth.Powell@qimrb.edu.au

qimrb.edu.au/our-research/clinician-researcher-academy

QIMR Berghofer Core Facilities

HISTOLOGY FACILITY

Our Histology Facility is a state-of-the-art service and research laboratory dedicated to advancing histology through expert support and comprehensive services. We provide specialised histology offerings performed by our experienced staff, which include sample preparation, embedding, sectioning and a range of staining techniques, including immunohistochemistry and spatial biology. Our facility is designed to meet the diverse needs of scientists and postgraduate students from the Institute, as well as external and international institutions, creating a collaborative environment that fosters innovation and research excellence.

The strength of our facility lies in our team, known for their extensive expertise in both routine and specialised histological techniques. With specialists in tissue processing, embedding and sectioning, we can adeptly manage a wide variety of sample types and complexities. Our proficiency in antibody optimisation and advanced immunohistochemistry methods, including multiplex staining, allows us to deliver detailed insights into tissue morphology and function, which are essential for both research and diagnostics.

Our commitment to client success goes beyond service provision. Our team is always eager to offer guidance on project planning and development. Whether you need assistance with experimental design, training in specific techniques or troubleshooting existing methodologies, our staff are here to help. We take pride in providing responsive, tailored support that aligns with each client's research objectives.

Central to our mission is a dedication to achieving the highest quality results in a cost-effective manner. We recognise the pressures of research timelines and budget constraints, and we strive to deliver optimal outcomes without sacrificing quality. Our facility is equipped with cutting-edge technology and adheres to rigorous quality control measures, ensuring that all histological preparations meet the highest standards.

SAMPLE PROCESSING

Underpinning outstanding and reproducible science, are consistent and high-quality samples. The quality of these samples is largely dependent on pre-analytical conditions including the timing, collection, storage conditions and sample preparation techniques used. The consistency of producing these samples is paramount in producing consistent and meaningful data.

The Sample Processing service provides expertise and service for the pre-analytical sample handling and preparation of biological samples and is designed to efficiently and economically meet requirements. The service works alongside researchers and clients, to design pre-analytical sample handling solutions for the collection, transportation, storage, aliquoting, blood fractioning and cell isolation (including PBMC preparation and storage), nucleic extraction (DNA and RNA extraction), nucleic sample QC, and PCR of samples.

Capacity for high-throughput processing or single sample processing is accommodated. Our service dovetails a range of the Scientific Services in particular, working closer with the Sequencing Service, to provide a seamless product from sample collection to data.

FLOW CYTOMETRY

Our Flow Cytometry and Fluorescent Activated Cell Sorting (FACS) Facility use lasers and photon detectors to capture vital information about cells, cellular components and other particles. The technology relies heavily on the use of fluorescent probes to detect molecules of interest associated with normal or disease states. The technology is capable of providing data from over 40,000 cells per second and provides our researchers with a vast amount of information.

Flow cytometry is at the forefront of immunology, cancer and infectious disease research, with ever-evolving innovative technology paving the way for scientific advancements. This allows for the rapid detection and identification of distinctive characteristics on individual cells based on light scatter and fluorescence emission.

Immunophenotyping and profiling of different immune cell populations is crucial in immunology research, making flow cytometry an indispensable tool that enables large amounts of complex and comprehensive data to be acquired in a short period of time.

MICROSCOPY

Our Microscopy Facility is equipped with a comprehensive range of instruments for imaging both fixed or living cells and tissue. These include stereo microscopes, slide scanners, compound microscopes, confocal microscopes, intra-vital microscopes, a scanning electron microscope, cyclic immunofluorescence microscopy, spatial molecular imaging, and various analysis stations and software. We are equipped to capture images of cells or tissue stained with colourimetric dyes or fluorescent dyes at various resolutions from macro to super resolution.

We provide assistance and training on all instruments and software in the facility and can provide full service for some services if required.

Our Microscopy Facility is proudly supported by the Australian Cancer Research Foundation (ACRF) and operates microscopes in the ACRF Centre for Comprehensive Biomedical Imaging.

We also proudly support and interact with the:

- Australian Microscopy and Microanalysis Society (AMMS);
- Light Microscopy Australia (LMA);
- Microscopy Australia (MA);
- ACRF Cancer Biology Imaging Facility and the ACRF Cancer Ultrastructure and Function Facility at the Institute for Molecular Bioscience (IMB);
- Centre for Microscopy and Microanalysis (CMM) – University of Queensland (UQ);
- Microscopy Facility at Translational Research Institute (TRI);
- Microscopy Facility at the Queensland University of Technology (QUT);
- Advanced Microscopy Facility at the Queensland Brain Institute (QBI).

ANALYTICAL FACILITY

Our Genetic Analysis and Sequencing Facility includes Next-Generation and Capillary Sequencing, using several sequencing platforms and supporting auxiliary instruments. DNA Sequencing and Next-Generation sequencing are used in molecular biology to study genomes, transcriptomes and the proteins they encode.

Information obtained through sequencing allows researchers to identify phenotypes in cancers, diseases and complex disorders by changes in genes and gene associations. This data has the potential to help identify potential drug targets and vaccine candidates and influence patient outcomes in clinical applications.

Our sequencing services employ capillary sequencing and both long read and short read Next-Generation sequencers to deliver consistent high quality genomics data.

METABOLOMICS

Metabolomics can provide an overview of the metabolic status and global biochemical events associated with a cellular or biological system, and in medical research in particular, provide mechanistic understanding of the biochemical and metabolic changes that occur during the onset, progression, or as a consequence of disease.

Metabolites include the nutrients we obtain from food, the lipids found in cell walls, the bases that make up DNA/RNA, and the amino acids that are coded for by genes and are subsequently assembled to form proteins. Metabolites are the small molecule compounds that are the substrates, intermediates, and end products of the multitude of metabolic pathways required for life.

PROTEOMICS

Our Proteomics Facility uses liquid chromatography–mass spectrometry (LC-MS) to analyse samples from a variety of medical research projects and to measure the proteome. These highly sensitive instruments can provide impressive depth for proteomic analysis of complex samples.

Proteomics is the study of proteins in biological systems, encompassing their structures, functions, and interactions. While genomic data can provide a basic template for the proteins in a system, proteomics is required to truly evaluate protein expression and how it changes in response to various stimuli.

It is well established that transcriptomic sequencing expression levels do not always correlate to experimentally observed protein expression levels. As proteins are responsible for carrying out most of the activities within a cell, it is imperative to study them directly in order to properly understand how cells function, and how these functions can be dysregulated, to cause disease states.

Proteomics offers medical researchers an array of vital information on cellular processes to better understand their disease states of interest and how to treat them.

QIMR Berghofer Services

Q-Gen
Cell Therapeutics

genomiQa
PRECISION ANALYTICS

Q-GEN CELL THERAPEUTICS

As one of the largest cell manufacturers in Australia, we leverage our extensive expertise and state-of-the-art technologies to deliver high-quality products. Our team of highly skilled professionals work tirelessly to deliver exceptional customer service and technical support, ensuring that our clients receive tailored solutions that meet their unique requirements.

With specialist teams in manufacturing, quality control, quality assurance, supply chain, equipment engineering and regulatory compliance, we can assist in all aspects of your clinical trial project. Our dedicated project management support and an unwavering commitment to cell therapy development ensures Q-Gen is your preferred manufacturing partner.

GENOMIQA

GenomiQa is a start-up company that has grown out of QIMR Berghofer. We offer hospitals, clinicians, researchers, and biopharma companies high-quality analysis of data from whole genome sequencing. Founders, Dr Nic Waddell and John Pearson, have more than 35 years' combined experience in genomics and bioinformatics. These areas of expertise blend powerfully within GenomiQa's products and services, which are designed to support personalised treatment and better outcomes for patients.

We bring precision analytics to routine clinical practice. In practice, this offers:

- More accurate diagnostics;
- Better decision support for clinicians;
- Precision drug development.

Medical Research Opportunities

Join one of the largest medical research institutes in Australia.
The options for students to be part of QIMR Berghofer are:

A Research Higher Degree Student at QIMR Berghofer (PhD, MPhil, Masters Coursework or Honours)

We have a wide range of student projects, and many can be tailored to a student's research interests. Some projects have the flexibility required for clinical students.

B Clinical Research Rotation – Royal Brisbane and Women's Hospital

The clinical research rotation for Junior/Senior House Officers is a unique opportunity to gain insight and skills in research methodology, study design, data analysis and evidence-based medicine, while contributing to meaningful projects that can improve patient care and outcomes.

C Vacation Research Program

Through The University of Queensland, Queensland University of Technology, and Australian Catholic University, we offer vacation research experience. These are small projects carried out over a 4-8 week period during the university summer (November-February) breaks giving students research experience and some financial support.

D Volunteer Program

Students who have an interest in medical research and would like to gain some experience can apply to be a research volunteer. This is not associated with any university course. These unpaid placements run for a limited period of time and acceptance is at the discretion of QIMR Berghofer.

General info: qimrb.edu.au

University students webpage: qimrb.edu.au/education/for-university-students/

Projects webpage: qimrb.edu.au/student-projects/

Further enquiries: GraduateEducation@qimrb.edu.au

Quick Admissions Guide for Students

1. Check you are eligible for the degree you are interested in undertaking. This is specific to the university you are enrolling in.
2. Check the QIMR Berghofer website and identify a Student Project or Research Laboratory that matches your research interests.
3. Contact the QIMR Berghofer scientist via email providing the following information:
   i) Whether you want to undertake Honours, MPhil, or PhD study.
   ii) Discuss your research interests and any previous research experience.
   iii) Provide your academic CV and university transcript.
4. Arrange to meet in person or have a Teams/Zoom interview. If a supervisor accepts you as a student, then continue the rest of the steps below.
5. Enrol through an Australian university. *
6. Complete the admission process to QIMR Berghofer. An approval notification will be sent to you via email.
7. International students must also have an appropriate visa from the Australian Department of Home Affairs. #
8. Provide evidence of full admission/enrolment to an Australian university and scholarship (if applicable).

Congratulations, you are ready to begin your candidature!

PLEASE NOTE: This is only a brief guide and it is your responsibility to familiarise yourself with the details or requirements for each step.

**IMPORTANT: Apply for admission to QIMR Berghofer and your chosen university at the same time. Many university departments will not approve your application until you have at least provisional approval from QIMR Berghofer.*

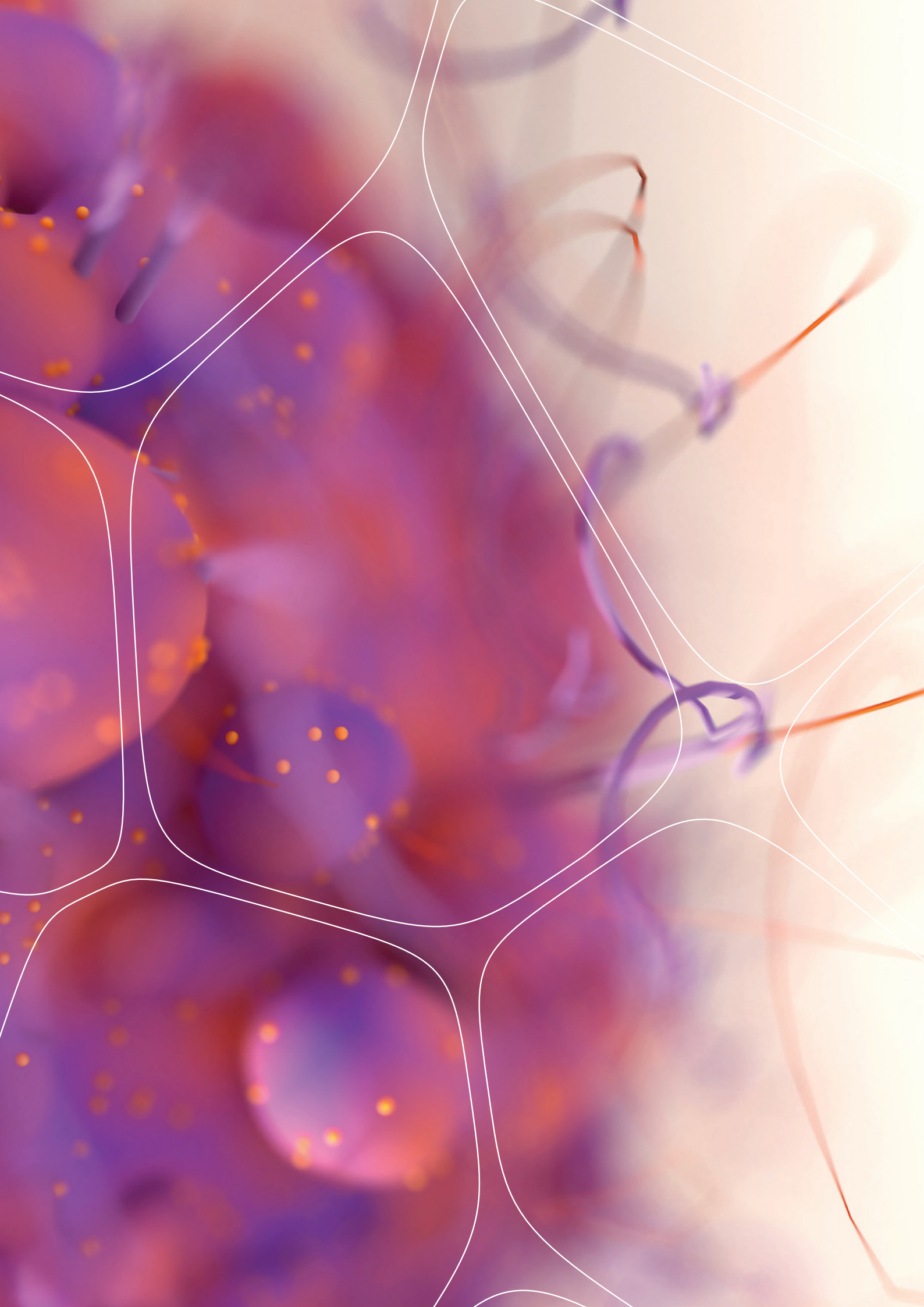
 # This process may take up to 12 weeks to finalise, and this should be taken into consideration when determining your start date.

General info: qimrb.edu.au

University students webpage: qimrb.edu.au/education/for-university-students/

Projects webpage: qimrb.edu.au/student-projects/

Further enquiries: GraduateEducation@qimrb.edu.au



Cancer Research Program

At QIMR Berghofer, our leading cancer researchers are developing new techniques that will help us to understand, prevent, detect, and treat cancer, a leading cause of death in Australia.

Cancer cases are expected to grow to 185,000 per year over the next decade as Australia's population ages. It is the second most common cause of death, exceeded only by cardiovascular disease.

Our researchers are working on a number of projects that include:

- Prevention: identifying specific modifiable environmental and genetic factors that reduce a person's risk of developing cancer.
- Detection: developing better screening tests, so that cancer can be detected earlier.
- Treat: identifying better treatments for cancer and conduct clinical trials to test for effectiveness.

Although overall cancer survival rates have improved in the past 20 years, several types of cancer have poor five-year survival rates. These include ovarian, brain, oesophageal, lung, pancreas and colorectal cancer. Our research at the Institute is aimed at developing a better understanding of who is at risk of particular types of cancer and how treatment options can be tailored and more effective.

Our researchers continue to pioneer novel strategies and treatments across a broad range of cancers to help save lives and improve the quality of treatment.

B-lymphocytes in Autoimmunity and Malignancies

Director and CEO, Group Leader: Professor Fabienne Mackay

Fabienne.Mackay@qimrb.edu.au

qimrb.edu.au/researchers-and-labs/b-lymphocytes-in-autoimmunity-and-malignancies

The B-lymphocytes in Autoimmunity and Malignancies Laboratory studies the immunobiology of B-lymphocytes, particularly the B cell survival factors BAFF and APRIL and their receptors BAFF-R, TACI and BCMA.

Professor Fabienne Mackay has shown that excess BAFF leads to autoimmunity in mice and is associated with human autoimmunity, in particular systemic lupus erythematosus (SLE). This has encouraged the development of Belimumab, a therapeutic BAFF-blocking antibody that has been approved for use in SLE in the clinic. The laboratory's effort has been extended to understand how dietary interventions lower the risk of developing SLE and how diet/dietary metabolites can be used as therapeutic modalities.

Another research area of the laboratory is chronic lymphocytic leukaemia (CLL), a blood cancer caused by the clonal expansion of mature B cells. Patients with CLL show severe systemic immunodeficiency that results in death in a quarter of CLL patients, despite therapeutic intervention. Our laboratory has shown that CLL cells rely on BAFF/APRIL to suppress the immune system through IL-10 production.

We aim to identify novel therapeutic targets that will be able to restore patient immune function in CLL and halt CLL progression. Hence, the laboratory is developing a therapeutic antibody against CLL which would not compromise the host's protective immunity.

In an attempt to identify a novel therapeutic target for CLL, we have identified that a fat-rich diet halts CLL progression. We are now investigating the cellular and molecular mechanism underlying this protection against CLL.

Fuelling the fight—How diet shapes the immune response to leukaemia background.

Co-Supervisor: Dr Yong Sheng

Yong.Sheng@qimrb.edu.au

This project is suitable for a PhD student, or Honours followed by PhD student.

Chronic lymphocytic leukaemia (CLL) is a type of blood and bone marrow cancer that progresses slowly over time. It is one of the most common types of leukaemia in adults and typically occurs during or after middle age. While many patients experience a form of CLL that grows slowly and stays stable for years without treatment, some patients develop more aggressive forms of the disease. CLL leads to an overproduction of abnormal immune cells called B lymphocytes, which can weaken the body's ability to fight infections and attack cancer cells. Infections are one of the main causes of death in CLL patients, and current treatments often further weaken the immune system. Additionally, many patients become resistant or intolerant to treatment, making it harder to manage the disease. There is a pressing need for new treatments that can help restore immune system function in CLL patients.

In our recent research using a patient-derived xenograft (PDX) model of CLL, we discovered that feeding mice a ketogenic diet accelerates CLL progression via a T-cell-mediated mechanism. However, the clinical relevance of these findings and the underlying molecular mechanisms induced by the ketogenic diet remain unexplored. It is possible that certain metabolites resulting from the diet could have a pro-leukaemic effect, presenting new hypotheses for investigation. This project will utilise a PDX model of CLL, where human CLL cells are injected into immunodeficient mice lacking T, B, and NK cells. This allows us to study the behaviour of human CLLs and T cells in a living animal. The mice will be fed different diets, and we will track how the disease progresses using various laboratory techniques.

AIMS

The primary goal of this project is to investigate the impact of the ketogenic diet on CLL progression, with a focus on understanding the metabolic changes that drive the disease. Specifically, we will address the key following:

- Investigate the effects of different dietary fats on immune cell function in CLL, comparing the ketogenic diet with other high-fat or low-fat diets to identify specific dietary components that influence T-cell responses.

- Assess the reversibility of ketogenic diet-induced T-cell exhaustion by transitioning mice off the ketogenic diet and evaluating whether T-cell functionality can be restored.
- Characterise the epigenetic changes in T cells induced by the ketogenic diet and determine whether these changes contribute to T-cell exhaustion and reduced anti-tumour immunity.
- Evaluate the role of the kynurenine pathway and AHR activation in the ketogenic diet-induced T-cell dysfunction and identify potential metabolic intermediates as therapeutic targets.
- Conduct a pharmacological screen of small-molecule inhibitors that target metabolic enzymes activated by the ketogenic diet to identify compounds that can restore T-cell function and inhibit CLL progression.

Identifying inhibitors that target these metabolic changes could provide a foundation for developing new treatments for CLL that work in a completely different way from current therapies, with fewer side effects. This research will give the student working on this project hands-on experience with cutting-edge techniques, such as working with mouse models, cell cultures, and analysing data from flow cytometry and metabolomics. The findings could also open up opportunities for collaboration with companies developing new cancer treatments.

PROJECT POTENTIAL

This project could lead to the development of new, first-in-class treatments for CLL that focus on altering metabolism. This would be a game-changer for patients whose CLL no longer responds to existing treatments, providing an entirely new option for managing the disease.

Discovering novel immunoregulatory molecules underlying the pathogenesis of systemic lupus erythematosus.

Co-Supervisor:
Dr M Arifur Rahman

Arifur.Rahman@qimrb.edu.au

This project is suitable for an Honours, Masters, or PhD student.

The B-lymphocytes in Autoimmunity and Malignancies Laboratory investigates the immunobiology of B-lymphocytes, particularly the B cell survival factors BAFF and APRIL, and their receptors BAFF-R, TACI and BCMA. Professor Mackay has shown that excess BAFF leads to autoimmunity in mice and is associated with human autoimmunity, in particular systemic lupus erythematosus (SLE).

The BAFF receptor TACI is highly expressed on memory B cells in SLE patients, and BAFF-TACI interactions lead to elevated autoantibody production which drives disease pathology. The genetic deletion of TACI has been shown to protect against SLE, but the underlying mechanism remains largely unknown.

AIMS

- Investigate the cellular mechanism by which TACI signalling leads to exaggerated autoantibody production in SLE.
- Investigate how altered gut microbiota (through the regulation of immunoglobulin A production by TACI) and metabolites are associated with SLE disease severity.
- Use a new mouse model of lupus overexpressing human BAFF to be combined to a model expressing human TACI.
- Compare targeting TACI versus belimumab treatment (a lupus treatment blocking BAFF).

This project will use a range of immunological techniques (mouse models of disease, flow cytometry, confocal microscopy, ELISA), metagenomic sequencing, microbiome analysis and metabolomics to characterise the immunological mechanisms of action. We will validate the research findings using clinical samples.

PROJECT POTENTIAL

Current therapies for human lupus are strongly immune-suppressive and/or toxic. The limitations of these treatments were especially evident during the COVID-19 pandemic, which has seen a disproportionate number of patients with SLE developing a severe/fatal COVID-19 infection. There is a need for new therapies able to stop autoimmunity without compromising vital immune defences.

Investigating the role of purinergic receptor signalling in the onset and progression of systemic lupus erythematosus.

Co-Supervisor: Dr M Arifur Rahman

Arifur.Rahman@qimrb.edu.au

This project is suitable for an Honours, Masters, or PhD student.

Many important metabolites that signal via purinergic receptors (molecules in the plasma membrane) are obtained from food or synthesised by the body. BAFF is a B cell survival factor, and the overexpression of BAFF in BAFF-transgenic (BAFF-Tg) mice causes the expansion of autoreactive pathogenic B cells leading to systemic lupus erythematosus (SLE). Research has shown that BAFF-Tg mice are deficient in a range of these metabolites.

We have demonstrated that BAFF-Tg mice fed a high-

fibre diet express a high level of a particular metabolite, which is associated with a reduction in autoreactive B cell numbers and protection from SLE. Supplementation also protects the BAFF-Tg mice against SLE. However, the cellular and molecular mechanism by which the metabolite protects against SLE is not known. We have generated mice deficient in the purinergic receptor (PR) associated with the metabolite for use in this project.

AIMS

- Investigate the requirement of a purinergic receptor in the high-fibre diet-mediated protection against SLE.
- Investigate if metabolite- purinergic receptor signalling is critical for the protection against SLE.
- Characterise a novel metabolite therapy for SLE.

This project will use a range of immunological techniques (mouse models of experimental SLE, flow cytometry, confocal microscopy, ELISA), metagenomic sequencing, microbiome analysis and metabolomics to characterise the immunological mechanisms of action. We will validate the research findings using clinical samples.

PROJECT POTENTIAL

To develop an entirely new treatment avenue for lupus and explore a novel set of metabolites and signalling pathways with significant clinical potential.

Investigating the role of the chemokine receptor ACKR3 in immune signalling and disease.

Co-Supervisor: Dr M Arifur Rahman

Arifur.Rahman@qimrb.edu.au

This project is suitable for an Honours, Masters or PhD student.

Chemokines are a class of signalling molecules that are important for maintaining homeostasis and the inflammatory responses of cells. Chemokine receptors respond to these molecules by signalling to cells to proliferate or move. In addition to these classical chemokine receptors, there are also atypical chemokine receptors, which are poorly understood.

The atypical chemokine receptor ACKR3 (also named CXCR7) has been implicated in cancer survival and metastasis and is also protective against fibrosis. ACKR3 can bind to the chemokines CXCL11 and CXCL12, as well as other non-chemokine signalling molecules. ACKR3 has been proposed as a key receptor to target developing therapeutics for cancer and fibrosis, however there is a significant gap in the current knowledge about the role of this receptor in normal physiology and immune signalling.

Our research group has begun characterising the role of ACKR3 and the cell populations that express it.

This project will further explore how ACKR3 regulates immune cell function at steady-state, following immunisation, and in diseases like lupus and cancer.

AIMS

- Determining the cell types that express ACKR3 and investigate the role that ACKR3 plays.
- Analyse mice that lack ACKR3 on specific cell types of interest.
- Define the role of ACKR3 in immunity, such as the T cell-dependant and T cell-independent immune responses.
- Investigate the role of ACKR3 on self-reactive B cells.

Through these studies, students will gain significant expertise in mouse models of disease, cell culture, flow cytometry, immunohistochemistry and other laboratory techniques.

PROJECT POTENTIAL

To pioneer knowledge in a neglected area of immunology, validate these findings with human immune cells and publish a high impact, world-first discovery. This project has the potential to uncover aspects of autoimmunity never contemplated before.

Can diet influence immune tolerance?

Co-Supervisor: Dr M Arifur Rahman

Arifur.Rahman@qimrb.edu.au

This project is suitable for an Honours or Masters student.

The B-lymphocytes in Autoimmunity and Malignancies Laboratory has a model of B cell immune tolerance, known as SW_{HEL}. The SW_{HEL} model is a cross between mice with B cells that express a B cell receptor (BCR) specific for the experimental antigen Hen Egg Lysozyme (HEL), and mice that express membrane HEL. In the resulting offspring, the HEL becomes the self-antigen and developing SW_{HEL} B cells in the bone marrow are self-reactive B cells. The resulting SW_{HEL} B cells are eliminated in the bone marrow through a process of negative selection in response to their BCR binding HEL.

These SW_{HEL} mice can be crossed with mice expressing a soluble version of HEL, secreted in the blood. In the resulting offspring, the self-antigen is circulating and binding of the SW_{HEL} BCR to soluble HEL is not as strong. With a weaker SW_{HEL} BCR interaction to soluble HEL, SW_{HEL} self-reactive B cells can survive in the bone marrow but are negatively selected in the periphery or are anergised (neutralised and unable to be activated by HEL).

This project will explore the hypothesis, "can diet (eg. high fat) prevent negative selection and therefore promote autoimmunity?" To explore this, the above two models of B cell tolerance described will be fed with

various diets and the impact of diet on the emergence of self-reactive B cells and their activation status will be investigated.

AIMS

- Determine whether diet can affect the emergence of self-reactive B cells.
- Explore whether diet can interfere with negative selection and promote autoimmunity.
- Dissect molecular mechanisms of immune tolerance affected by dietary intervention for the purpose of developing novel therapies promoting immune tolerance.

The work involves animal models, flow cytometry, ELISA, histology and a number of omics methods.

PROJECT POTENTIAL

No research group to date has explored the role of diet in this model. This approach is very novel and could potentially lead to alternative therapeutic approaches for autoimmune diseases with huge clinical impact.

Functional Cancer Genomics and Functional Genetics

Senior Group Leader: Professor Stacey Edwards

Stacey.Edwards@qimrb.edu.au

qimrb.edu.au/researchers-and-labs/functional-cancer-genomics

The Functional Cancer Genomics Group is focused on identifying new therapeutic targets for breast and ovarian cancer.

We are particularly interested in those targets that have genetic evidence linking a DNA variant to risk of the cancers. Most risk variants fall in noncoding regions of the genome and are enriched in DNA regulatory elements such as enhancers, which can be located hundreds of kilobases away from their target genes.

The noncoding genome also serves as a template for the transcription of long noncoding RNAs (lncRNAs), which often show cell-type-specific expression and function, making them exceptional drug targets.

We integrate genetic information with a diverse range of sophisticated molecular approaches to identify and evaluate protein-coding genes and lncRNAs that are driving cancer development.

Program Director (Cancer Research), Senior Group Leader: Professor Juliet French

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qimrb.edu.au/researchers-and-labs/functional-genetics

The Functional Genetics Laboratory combines genetics and functional genomics to pinpoint the key genes and pathways implicated in the development of both breast and ovarian cancers.

We are interested in understanding how inherited and/or acquired genetic variants located in noncoding DNA contribute to cancer development. More particularly, we investigate regions that are either transcribed into functional RNAs such as long noncoding RNAs (lncRNAs) or those that act as DNA regulatory elements such as enhancers.

Identifying the lncRNAs affected by noncoding genetic variants and the protein coding genes they regulate is necessary to identify therapeutic opportunities for primary and secondary cancer prevention. These can be achieved by identifying novel targets or using existing therapies that can be repurposed for the prevention or treatment of either breast and ovarian cancers.

Evaluation of new long-noncoding RNAs driving breast or ovarian cancer development.

This project is suitable for an Honours or PhD student.

BACKGROUND

It is now clear the majority of the human genome is transcribed from both DNA strands but only 2% encodes protein. Much of this transcription is derived from DNA sequences that do not encode functional proteins. The majority of these transcripts are long non-coding RNAs (lncRNAs) defined as being >200 bp in length. While it is generally accepted lncRNA transcription is functionally significant, the scope and function of lncRNAs in cancer is still not well understood.

Genome wide association studies (GWAS) have identified thousands of common variants associated with an increased risk of breast and ovarian cancers. Large-scale genome sequencing projects have also identified regions of the genome that are frequently mutated in breast and ovarian cancers. Importantly, the majority of these disease-associated variants and mutations lie within intergenic regions and introns of protein-coding genes, suggesting that undiscovered RNA transcripts such as lncRNAs, may play a direct role in cancer development. We have recently used different RNA sequencing and bioinformatic approaches to identify hundreds of new breast and ovarian cancer-related lncRNAs.

AIM

We have recently used RNA sequencing and bioinformatic approaches to identify hundreds of new cancer-related lncRNAs. We now want to understand how these lncRNAs modulate breast and ovarian cancer development.

METHODS

Projects will use multiple in vitro approaches to determine how the variants and mutations alter lncRNA function, including CRISPR-based lncRNA editing and reporter assays. We will link lncRNAs to their target protein-coding genes using HiChIP chromatin assays and CROP-seq experiments. We expect that some of the lncRNAs will have cancer-related biological functions. We will therefore overexpress or silence lncRNAs in breast and ovarian cancer cells and examine their effects on cell growth, response to DNA damage, apoptosis, migration and tumour formation.

We will also assess the function of lncRNAs in tumour formation using an explant assays in mice. The discovery of novel regulatory lncRNAs influencing cancer development may reveal entirely new avenues for breast and ovarian cancer therapeutics.

Students will have access to unique expertise and reagents, and will acquire skills in tissue culture, CRISPR-based methods, RNA and DNA manipulation, confocal microscopy, FACS analyses and other molecular biology techniques.

Molecular Oncology

Team Head: Associate Professor Olga Kondrashova

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qimrb.edu.au/researchers-and-labs/molecular-oncology

The Molecular Oncology Laboratory utilise advanced bioinformatic and machine learning methodologies to analyse a variety of cancer data types, including genomic, transcriptomic and DNA methylation data. This analysis allows us to understand how different cancers respond to treatments and influence patient outcomes.

A large part of our work involves studying pre-clinical cancer models to ensure their accurate representation of human disease, thereby enabling the discovery of treatment strategies and biomarkers that can be translated into clinic.

Our research spans multiple solid cancer types, including ovarian, endometrial, breast and lung cancer. Our work is highly collaborative. We partner with several clinical and molecular cancer laboratories to facilitate the most translatable research.

Re-sensitising treatment resistant metastatic ovarian cancer.

Primary Supervisor: Associate Professor Jacinta Simmons

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This project is suitable for an Honours or Masters student.

High grade serous ovarian cancer is most often detected after it has moved away from the ovaries and fallopian tubes, where it is harder to treat and almost always becomes resistant to current treatments. Standard therapy relies on tumour cells being unable to accurately repair DNA damage due to mutations in common DNA damage response genes. Resistance to treatment occurs when tumour cells gain further mutations to bypass or repair mutated genes to re-enable accurate DNA repair.

The project will employ CRISPR screening, cell, and molecular biology techniques to investigate mechanisms of resistance and identify novel strategies for re-sensitising ovarian cancer to therapy.

Translational Cancer Immunotherapy

Group Leader: Associate Professor Siok Tey

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The Translational Cancer Immunotherapy Laboratory investigates the means by which the immune response can be harnessed to control cancer. Our team of biomedical and clinical scientists have a strong focus in translating basic science knowledge into new therapies that can be taken to clinical trial.

Bone marrow transplantation is the most established form of cancer immunotherapy and has been a longstanding interest of our laboratory. Its curative potential resides in the donor T cells, which are very effective in recognising and eradicating cancer cells. However, these T cells can also attack vital tissues, and the resulting organ damage. This is known as graft-versus-host disease (GVHD), and is a major source of transplant-related morbidity and mortality.

Our research seeks to enhance the anti-tumour response and attenuate GVHD through T cell engineering. These include the use of "safety switches"

to enable T cells to be deleted in the setting of GVHD and the use of regulatory T cells (Tregs) to attenuate GVHD.

Our above experience in T cell engineering has led to our current research focus in Chimeric Antigen Receptor (CAR) T cell therapy. CAR T cells are gene-modified immune cells (T cells) that can recognise specific surface proteins on tumour cells. They can be very effective in killing these tumour cells and can cure up to 50% of certain blood cancers. Our laboratory is developing new CARs with the aims of making them more effective and accessible. These include CAR T cells directed at blood cancers and childhood cancers. In collaboration with the Royal Brisbane and Women's Hospital, we are one of only a few groups in Australia with the capacity to make clinical grade CAR T cells on campus and take them to clinical trial.

CAR T cells – redirecting T cells for cancer immunotherapy.

This project is suitable for Honours, Masters, and PhD students.

BACKGROUND

Chimeric Antigen Receptors (CARs) are genetically engineered molecules that can redirect T cells to recognise particular antigens, such as those expressed by cancer cells. T cells that are transduced by CAR targeting CD19 have been effective in treating B cell cancers, e.g. B-cell leukaemia and lymphoma, where conventional treatments have failed.

This exciting technology is one of the major breakthroughs in cancer therapy this decade. However, not all patients respond, and not all responses are durable and there is limited success to date in CAR T cells targeting solid cancers.

This project involves developing and testing new concepts in CAR T cell engineering to make them more effective, safer and more able to target solid cancers. Our laboratory is involved in pre-clinical development, through to research translation and early phase clinical trials. There is also an opportunity for students to be involved in clinical correlative research to better understand the immunobiological determinants of clinical response and toxicity.

AIMS

The overarching aim of this project is to develop safer and more effective CAR T cell therapies for blood cancers and solid cancers, and take these to early phase clinical trials.

This is achieved through several interrelated projects with the following aims:

- Investigate how CAR T cell function can be modulated by changing individual components within the CAR transgene.
- Optimise methods for the clinical scale manufacture of CAR T cells as a precursor to future clinical trials.
- Examine the longitudinal fate of CAR T cells and the bystander immune compartment in patients undergoing CAR T cell therapy.

APPROACH

We use a range of immunology, molecular biology and cell therapy approaches to achieve these aims. Not all projects will involve all these approaches. Immunology techniques include cell culture, multiparametric flow cytometry (including spectral cytometry), live-cell imaging and a range of in vitro immunological assays (e.g. ELISA, cytokine bead array). Some projects will involve in vivo experiments using mouse models, and some projects will involve analysis of clinical samples. Molecular techniques include CAR gene design and cloning, and CRISPR/Cas9 gene knock-out. Cell therapy technology includes generation of viral vectors, small-to-large scale cell processing, including the use of clean room suites within the Good Manufacturing Practice (GMP) facility.

PROJECT POTENTIAL

The project is suitable for biomedical scientists and clinicians who are interested in wetlab research.

Students will have the opportunity to work on different phases of the development of a novel cell and gene therapeutic. All students will have the opportunity to work on the pre-clinical development and testing of novel CARs. Masters or PhD students may have the opportunity to work on clinical scale-up and technology transfer to GMP facility. PhD students may also have the opportunity to take a technology through to early phase clinical trial.

Understanding the immunobiology of bone marrow transplantation.

Co-Supervisor:
Dr Andrea Henden

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This project is suitable for an Honours or Master student.

BACKGROUND

Bone Marrow Transplant (BMT) offers cure to patients with aggressive blood cancers. Its efficacy lies in the ability of the newly transplanted immune system to recognise and destroy recipient malignant cells as foreign, a phenomena known as graft-versus-malignancy (GVM). However, if healthy cells and tissues are targeted, the complication of graft-versus-host disease (GVHD) occurs.

Post-transplant, all patients are managed with immunosuppression to control the balance between GVM and GVHD, however immunosuppression brings risk of infection and poor response to vaccines. Each of these complications are mediated by immune control, and new therapies to manipulate immunity post-transplant are required.

AIMS

- Examine the impact of the gastrointestinal microbiome on T cell function and GVHD.
- Examine the fate of T cell and non-T cell immune populations after BMT and the impact of viral infection and cytokines on immune reconstitution.

METHOD

- Immunophenotyping including flow cytometry and spectral cytometry.
- Measurement of soluble immune mediators.
- Correlation with clinical outcome data.

Cancer Genetic Susceptibility

Team Head:
Associate Professor Tracy O'Mara

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The Cancer Genetic Susceptibility Laboratory primarily studies the role of genetics in endometrial cancer risk and development. Our team leads large-scale genetic studies for endometrial cancer and uses these data to answer a variety of research questions falling under three main themes: prevention, prediction and treatment.

From risk variants to genes: Understanding endometrial cancer susceptibility.

Co-Supervisor:
Associate Professor Dylan Glubb

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This project can be adapted in scope for an Honours or PhD student.

BACKGROUND

Along with our international Endometrial Cancer Association Consortium collaborators, we have identified a number of endometrial cancer risk regions in the genome.

Although we have identified potentially causal risk variants, the target genes at most regions remain unknown. To address this, we have profiled the regulatory landscape of these loci using gene expression, chromatin accessibility, chromatin looping, and single-cell multiomics data from endometrial cell lines, organoid models, and tumour samples. These datasets will allow us to identify and prioritise candidate susceptibility genes for functional validation.

AIM

Identify high confidence gene targets of endometrial cancer risk variants and assess their effects on relevant phenotypes in endometrial cancer models.

PROJECT POTENTIAL

Through the identification of high confidence gene targets at endometrial cancer risk regions, we will gain a deeper understanding of endometrial cancer aetiology and identify potential targets for endometrial cancer therapy.

Genetic epidemiology of endometrial cancer.

This project is suitable for Honours, Masters, and Doctorate students.

BACKGROUND

Endometrial cancer is the most commonly diagnosed invasive gynaecological cancer in developed countries. In contrast with many cancers, the incidence and mortality of endometrial cancer is steadily increasing, largely due to increasing rates of obesity, the strongest risk factor for this disease.

Through leadership of the Endometrial Cancer Association Consortium (ECAC), our laboratory runs the largest genetic study of endometrial cancer. To date, we have identified 16 genetic regions associated with endometrial cancer predisposition by genome-wide association study (GWAS), which account for ~25% of the genetic heritability attributable to common genetic variants (O'Mara *et al*, Nat Commun 2018).

Incorporation of existing GWAS data with newly acquired GWAS datasets from international collaborators will identify further genetic regions associated with endometrial cancer risk. Additionally, we have approved access to large, well-phenotyped international datasets (e.g., UK Biobank, N = 500,000). This allows us unparalleled ability to examine the genetics of endometrial cancer, as well as explore its relationship with risk factors, such as obesity.

AIMS

- To identify new genetic risk regions for endometrial cancer, by performing the largest GWAS meta-analysis for this disease.

- To use computational approaches to identify and explore risk factors of endometrial cancer.
- To use genetic data to construct and test risk prediction models for endometrial cancer.

APPROACH

This project will use standard GWAS pipelines to identify genetic variants associated with endometrial cancer risk, including imputation, QC and association testing. Post-GWAS analyses to explore novel regions could also be performed (e.g. eQTL analyses, integration with functional genomic datasets).

The relationship between endometrial cancer and potential/known risk factors will be performed using approaches such as genetic correlation (LD Score Regression) and Mendelian randomisation. Endometrial cancer risk prediction models will be constructed using polygenic risk scores in combination with endometrial cancer environmental risk factors and tested for efficacy in independent datasets.

Transplantation Immunology

Team Head:
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Stem cell transplantation is considered the "gold standard" procedure for the treatment of blood cancers (including leukaemia, lymphoma and myeloma) in both adults and children. Globally, over 9,000 patients per year undergo this high-risk, life-saving therapy.

However, graft-versus-host disease (GVHD) occurs in 50-70% of patients, of which 20% will develop severe GVHD that is untreatable. Unfortunately, additional complications such as infection and cancer relapse are common.

Research conducted by the Transplantation Immunology Laboratory focuses on improving our understanding of the pathophysiology of complications following stem cell transplantation. Using unique pre-clinical models combined with innovative technologies, the group aims to define the immunological mechanisms that underpin these complex disease processes, with the view of translating the basic research findings into clinical practice.

Harnessing the gut microbiome to improve stem cell transplantation.

Aspects of this project would be suitable for an Honours, Masters, MPhil, MD and PhD student. Email the supervisor to discuss suitability.

BACKGROUND

Haematopoietic stem cell transplantation (HSCT) is considered the gold standard procedure for the treatment of high-risk blood cancers. However, graft-versus-host disease (GVHD) remains a barrier to the success of this life-saving immunotherapy. GVHD occurs in 50-70% of transplanted patients, of which 20% will develop severe GVHD which is unresponsive to therapy and is eventually fatal. Thus there is an urgent need for new treatments.

Systemic exposure to gut microbes (and their derivatives) which are normally sequestered in the lumen, are initiated by chemotherapy/radiation treatment prior to transplant and can have profound effects on GVHD severity. Antibiotic-based approaches to deplete the microbiome and prevent acute GVHD have been partially successful, however increasing antibiotic resistance and the realisation that many bacteria have important anti-inflammatory properties severely limits this approach.

AIM

This project aims to improve our fundamental understanding of microbial-host interactions that regulate protective and pathogenic mechanisms after transplant.

Understanding infectious respiratory complications after stem cell transplantation.

Aspects of this project would be suitable for an Honours, Masters, MPhil, MD and PhD student. Email the supervisor to discuss suitability.

BACKGROUND

Respiratory viral infections are a major global public health problem. RSV-induced bronchiolitis and pneumonia are the leading cause of hospitalisation in infants and young children worldwide, while in adult allogeneic hematopoietic stem cell transplant (HSCT) recipients the incidence of progression from upper to lower respiratory tract infection is 40-60%, with mortality rates as high as 80%. With the lack of efficacious antivirals, new treatment options are needed.

Given the paucity of mechanistic data to guide clinical studies or define the basis of disease, we established a murine model of RSV infection after SCT using pneumonia virus of mice (PVM), the murine homologue of human RSV, to address the knowledge gaps in the field.

AIM

This project aims to investigate fundamental immunological mechanisms which underlie the RSV-mediated post-transplant complication.

PROJECT POTENTIAL

This research will lead to the delineation of critical mechanisms that underpin fatal pneumonitis, and the identification of potential therapeutic targets to ameliorate RSV-driven HSCT transplant mortality.

Identifying novel MAIT cell expansion strategies to mitigate graft-versus-host disease.

Aspects of this project would be suitable for an Honours, Masters, MPhil, MD and PhD student. Email the supervisor to discuss suitability.

BACKGROUND

Respiratory viral infections are a major global public health problem. RSV-induced bronchiolitis and pneumonia are the leading cause of hospitalisation in infants and young children worldwide, while in adult allogeneic hematopoietic stem cell transplant (HSCT) recipients the incidence of progression from upper to lower respiratory tract infection is 40-60%, with mortality rates as high as 80%.

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AIM

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PROJECT POTENTIAL

This research will lead to the delineation of critical mechanisms that underpin fatal pneumonitis, and the identification of potential therapeutic targets to ameliorate RSV-driven HSCT transplant mortality.

In situ immune cell profiling using spatial transcriptomics in gastrointestinal graft-versus-host disease.

Aspects of this project would be suitable for an Honours, Masters, MPhil, MD and PhD student. Email the supervisor to discuss suitability.

BACKGROUND

Acute gastrointestinal graft-versus-host disease (GVHD) is a common, life-threatening complication following allogeneic haematopoietic stem cell transplantation. Gut GVHD occurs when donor-derived T cells traffic to host GI tract tissue in response to cytokine release during conditioning chemotherapy, resulting in T cell mediated apoptosis of GI tract mucosa.

Early identification of patients at greatest risk of gut GVHD would allow for trials of early escalation of immune-suppressing treatment to prevent gut GVHD onset or ameliorate its severity. Currently, there is a lack of predictive tools for the early detection of acute gut GVHD. Although blood based biomarkers are relatively easily obtained, they are often less informative compared with tissue-based biomarkers.

AIM

This project aims to examine the feasibility of applying spatial transcriptomics in the diagnosis and prognostication of acute gut GVHD.

PROJECT POTENTIAL

This research will generate tissue specific cellular transcriptomic signatures that may serve as potential biomarkers to improve early acute gut GVHD diagnosis and prognostication.

Cancer Neuroscience

Team Head: Dr Lachlan Harris

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At the core of the Cancer Neuroscience Laboratory is a focus on researching cellular quiescence, a reversible hibernation-like state, adopted by brain cancer cells to evade chemotherapy and radiotherapy. By targeting these quiescent cells, we might overcome treatment resistance and improve outcomes for people with glioblastoma.

To identify novel therapeutic approaches to target quiescence, the laboratory also focuses on understanding how quiescence is regulated in normal neural stem cells in the memory centres of our brains.

- Brain cancer – targeting treatment resistant, quiescent cancer stem cell populations through direct targeting, reactivation or suppression strategies.
- Modelling – determining the most effective approaches (direct targeting, reactivation, suppression) to target treatment resistant, quiescent cancer stem cell populations.
- Metabolism – its impact on quiescent brain cancer stem cells and normal adult neural stem cell populations.

- Healthy adult neural stem cell quiescence – identifying novel regulators, with a focus on calcium binding proteins.
- Dysfunction of adult neural stem cell quiescence during the aging process, and its possible role in cognitive disorders such as depression and anxiety.

Should I stay, or should I go? How brain stem cells decide to leave quiescence.

This project is suitable for an Honours or PhD student - multiple projects available.

BACKGROUND

Quiescence is a type of reversible cell-cycle arrest displayed by many resident tissue stem cell populations, which helps to ensure we have a lifelong population of stem cells to maintain tissue homeostasis, respond to injury and other stimuli. One region where these stem cells exist is in the brain. In mice, a major model organism, there are two main stem cell niches in the adult brain. These are the subgranular zone of the hippocampus and the subventricular zone lining the lateral ventricles of the forebrain. When quiescent neural stem cells in these regions activate, they generate neurons that function in memory, spatial navigation and odour discrimination. Similar neural stem cell populations with similar functions exist in the human brain.

AIM

This project aims to uncover novel molecular regulators of brain stem cell quiescence.

METHOD

One prism through which this will be explored, is by interrogating how brain stem cells enter deeper quiescence during the aging process. The project will employ a range of techniques using aged wildtype mice, genetically modified mice and primary neural stem cell cultures derived from the hippocampus and subventricular zone of postnatal/adult mice.

OUTCOMES

The outcomes of this project are expected to shed light on how quiescence is regulated. The genes/cellular processes we identify as being important in quiescence can then be explored in the context of diseases where adult neurogenesis is disrupted, for example during aging and major depressive disorder. Likewise, these findings will also be of interest to brain cancer research, where quiescence is frequently co-opted by cancer stem cells to evade therapies. Specifically, this project will: 1) establish the role of a novel group of calcium-binding proteins in deciphering activation/proliferation cues using in vitro and in vivo models. 2) determine if decreased expression of these proteins explains why quiescence deepens during aging and 3) determine if these proteins are functionally important in the progression of brain cancers, with a specific focus on quiescence and treatment resistance.

Improving survival for adult brain cancer patients by targeting 'sleeping' cancer stem cells.

This project is suitable for Honours or PhD students - multiple projects available.

Glioblastoma (GBM) is the most common malignant primary brain tumour in adults and is inevitably fatal, with a median survival of just 15-months after diagnosis. Standard treatment involves surgical resection, postoperative radiation and chemotherapy. Unfortunately, significant populations of resistant glioma stem cells remain after chemotherapy, these cells regrow the tumour, and patients ultimately succumb to the illness. Glioma stem cells resist treatment in part because they are in a state of cellular sleep, known as quiescence. The quiescence of glioma stem cells means they divide very rarely, whereas current chemotherapy preferentially targets fast-dividing tumour cells. A common strategy in cancer research is to combine chemotherapy with drugs that slow tumour growth. However, this approach often increases the resistance of tumours as it forces more cells into quiescence. The innovative research program Dr Harris is developing is to target quiescent GSCs by leveraging unique features of quiescence and turning them into therapeutic vulnerabilities.

Astrosenescence: The role of senescence and cell cycle disruption in space travel.

Supervisor:
Dr Eoin O'Sullivan

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BACKGROUND

Spaceflight presents unique stressors, including microgravity and cosmic radiation, which may accelerate cellular aging processes such as senescence. Cellular senescence is characterised by permanent cell cycle arrest, secretion of pro-inflammatory factors, and DNA damage. Understanding how spaceflight impacts cellular senescence could provide crucial insights for long-term human space exploration, including strategies to counteract tissue degeneration.

AIM

To identify and validate the presence of cellular senescence and associated pathways in mice and human tissues exposed to spaceflight, using single-cell and bulk RNA sequencing data.

OBJECTIVES

- Data collection: Obtain and process single-cell and bulk RNA-Seq datasets of mice and human tissues subjected to spaceflight from NASA or SpaceX missions.
- Senescence and cell cycle signature optimisation identification: Using in house expertise, as well as established signatures.
- Validation of senescence pathways: Investigate senescent pathway activity, such as DNA damage responses, telomeric RNA, and altered metabolic profiles, across different tissues.
- Heterogeneity in senescence: Explore the heterogeneity of senescent cells using single-cell RNA sequencing, identifying which cell types are most affected by spaceflight conditions.
- Technologies:
  - Single-Cell and Single Nucleus RNA-Seq
  - Bulk RNA-Seq
  - Spatial RNA-Seq

EXPECTED OUTCOMES

- A validated set of senescence markers and pathways activated by spaceflight in both single-cell and bulk datasets.
- Insights into the prevalence and characteristics of senescent cells in different tissue types after spaceflight exposure.
- Foundation for future work investigating interventions to mitigate senescence-related tissue damage during space missions.

Available for semester 1, 2 and summer.

Students placed overseas who want to conduct a project remotely are welcome.

The ideal candidate should have an interest in single cell and bulk RNA-Seq workflows and will be able to programme in R/Python.

Leukaemia Research

Group Leader:
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The Leukaemia Research Laboratory is researching myeloid blood cancers that include acute myeloid leukaemia (AML), myelodysplastic syndrome (MDS) and myeloproliferative neoplasms (MPN) as part of its translational leukaemia research work.

These very aggressive and rapidly fatal blood cancers are among the most common types of cancer affecting Australians. The laboratory's efforts concentrate on understanding how leukaemia stem cells in AML and MPN are able to regenerate leukaemia (or cause relapse in patients), even after cytotoxic chemotherapy.

Research has focused on generating robust models of leukaemia and dissecting the pathways of self-renewal in leukaemia stem cells and normal blood stem cells.

The group aims to tailor treatments for individual patients, identify new drug pathways and explore repurposing existing drugs to target resistant leukaemia types.

The role of additional mutations in treatment response and disease progression in MPN.

Co-Supervisor:
Dr Megan Bywater

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This project can be adapted in scope for an Honours, Masters, or PhD student.

MPNs are a group of disorders characterised by the excess production of mature myeloid cells. MPNs are driven by the constitutive activation of the JAK-STAT signalling pathway as a consequence of mutations in either JAK2, MPL or CALR in haematopoietic stem cells (HSC). Pioneering work from our laboratory has demonstratedthe efficacy of interferon alpha (IFNα) in the preferential targeting of MPN stem cells. In addition to these MPN-driver mutations, patients often present with additional mutations that can alter disease presentation. It is currently unclear if and how the presence of additional mutations may alter treatment outcomes in MPN, particularly in response to IFNα, and what mutation combinations are sufficient to drive transformation to leukaemia.

In this project, we will use our well-established murine model of mutant Jak2-driven MPN in combination with CRISPR engineering technology to generate additional mutation combinations observed in the human disease. By treating these genetically engineered mice with IFNa we will determine what additional mutations or mutation combinations confer resistance to therapy and how. By ageing these mice and monitoring their disease phenotype long-term, we will determine what mutation combinations result in the emergence of leukaemia. These studies will primarily employ mouse procedural work, primary cell culture, flow cytometry and basic molecular biology. Mechanistic studies are likely to include the use of high content sequencing technologies like RNAseq and ATACseq at a bulk, and possibly single cell, level.

The role of the immune system in disease evolution and treatment response in AML.

This project can be adapted in scope for an Honours, Masters, or PhD student.

Acute myeloid leukaemia (AML) is an aggressive blood cancer characterised by the excessive production of immature myeloid elements. AML is a genetically heterogeneous disease in that it is known to be driven by an extensive list of somatic mutations and chromosomal re-arrangements. We have demonstrated that the endogenous immune system is only capable of mounting a sufficiently powerful anti-AML immune response in specific molecular subtypes of AML. Through these studies, we have demonstrated that mutations that drive the constitutive activation of Nras result in the upregulation of antigen presentation machinery and immunostimulatory ligands. Of great interest is that the overexpression of the oncogene MYC is sufficient to inhibit multiple aspects of this pro-immunogenic mutant Nras-driven phenotype. Futhermore, we have also demonstrated that treatment of AML with the commonly used therapy Azacitidine results in the upregulation of immunogenic ligands on the AML and changes in the composition of the immune microenvironment.

In this project, we will use established models of mutant Nras-driven AML to determine how changes in MYC activity alter the expression of immunogenic ligands and if it also changes the composition of the immune microenvironment. We will also determine the dependency of Azacitidine treatment efficacy on the presence of a competent immune system, and how this relates to transcriptional and epigenetic changes that occur in the AML in response to treatment.

These studies will primarily employ mouse procedural work, primary cell culture, flow cytometry and basic molecular biology. Mechanistic studies are likely to include the use of high content sequencing technologies like RNAseq, ATACseq and EMseq.

Role of MYC in leukaemic cell differentiation.

Co-Supervisor:
Dr Jasmin Straube

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This project can be adapted in scope for an Honours, Masters or PhD student with a bioinformatics background.

MYC is a pleotropic transcription factor with a key role in controlling cell proliferation. Deregulation of MYC through amplification or genomic rearrangement is the oncogenic driver in many cancers of different tissue origin. Novel therapies that inhibit downstream effects of MYC activation have great efficacy and improve clinical outcome. In acute myeloid leukemia (AML) compared to other cancers, MYC is not subject to genomic amplification or rearrangement. However, it is highly expressed in majority of AMLs. We recently identified a novel role of MYC as regulator of the antigen presenting machinery but other than, little is known about its role in AML disease progression and therapy resistance.

The objective of this project is to study the effect of MYC expression in AML with different oncogenic drivers. The project involves the use of single cell RNA-sequencing data of human AML patients to characterise the role of MYC expression in different stages of leukaemic cells. You will use dimension reduction, machine learning and novel RNA velocity estimation techniques to integrate data from AML with different genetic backgrounds.

The results of the projects will aid to understand the combined effect of MYC expression and different oncogenic drivers on cell phenotype and differentiation and to rationalise MYC downstream effect inhibition as a treatment for AML.

What determines leukaemic stem cell maintenance and resistance to chemotherapy?

Can be adapted in scope for an Honours, Masters, or PhD with a bioinformatics background.

Acute myeloid leukemia is a highly aggressive disease with the majority of patients still relapsing even after achieving remission from chemotherapy. It is hypothesised that relapse arises from residual leukaemic stem cells that are resistant to chemotherapy. To date transcriptional analysis of AML has focused on whole bone marrow or peripheral blood samples, which is mainly composed of leukaemic blasts, masking the

transcriptional program of leukaemic stem cells. Data generated from AML samples using single cell RNA sequencing will enable the analysis of the leukaemic stem cell transcriptome.

The aim of this project is to analyse single cell RNA sequencing data of AML to determine potential mechanisms of resistance in leukaemic stem cells. These findings will be correlated with previously identified genome-wide CRISPR screen hits that conferred chemotherapy resistance in AML cell lines and other datasets of relapsed/refractory AML. In addition, you will characterise leukaemic stem cells compared with leukaemic blasts. You will use dimension reduction and machine learning approaches to integrate data of AMLs with different genetic background and prognosis. Findings from this project will inform further investigation of pathways involved in chemotherapy resistance and therapeutic strategies targeting chemoresistant leukaemic stem cells.

Genome Variation and Regulation in Disease

Team Head: Associate Professor Jonathan Beesley

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qimrb.edu.au/researchers-and-labs/genome-variation-and-regulation-in-disease

The team in the Genome Variation and Regulation in Disease Laboratory are interested in how human genetics contributes to disease and how they can use these discoveries to find better treatments.

Researchers integrate large-scale genetic and functional genomics data to guide computational analyses and laboratory experiments. The team are using a diverse array of approaches including pooled functional genetic screens, multiplex reporter assays, and genome editing to pinpoint the causal genetic changes, their target genes and pathways, and the cell types in which they act.

Identifying the causal genes at cancer risk loci.

This project is suitable for an PhD or Honours student.

The laboratory is involved in genome-wide association studies (GWAS) to identify common variations underlying the risk of breast and ovarian cancers. The current challenge is in the functional interpretation of genetic association data. With this aim, we use a variety of computational approaches to define potential molecular mechanisms at GWAS loci and to generate specific hypotheses to guide further experimental work.

Specific areas of interest include:

- Analysis of high throughput sequencing data, such as ATAC-seq and HiChIP from primary breast samples and cultured cells.
- Integration of genetic and functional genomics data to predict target genes at GWAS loci.
- Mining of public epigenomic datasets such as those from the ENCODE and ROADMAP Consortia.
- Identification of candidates for drug repositioning.
- Analysis of CRISPR screen data.

The project would suit a bioinformatics student with an interest in gene regulation. Students would work closely with dry and wet laboratory scientists to identify cancer genes and pathways, which might represent targets for future drug development.

Cancer Metabolism

Group Leader: Associate Professor Nils Halberg

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qimrb.edu.au/researchers-and-labs/cancer-metabolism

These projects can be adapted in scope for an Honours or PhD student.

The Cancer Metabolism Laboratory is keenly interested in how the physiological state of a person affects cancers.

Over a person's lifetime, somatic cells will accumulate spontaneously occurring gene mutations, the majority of which do not cause disease. The global incidence of cancer has more than doubled over the past 30 years – primarily due to increasing living standards, modern lifestyles, and an aging population.

The common denominator for these is alterations to the physiological homeostasis of the individual at risk rather than a change in mutational burden. This strongly implies that the interaction of physiological conditions with cells harbouring oncogenic mutations governs cancer risk.

The Cancer Metabolism Laboratory utilises systems biology technologies to both clinical biobank and mouse models to dissect the molecular drivers of the intersect between physiology and tumorigenesis.

Mechanistic understanding of how obesity causes cancer.

Obesity increases the risk of developing thirteen types of cancer that normal weight individuals may not develop, despite harbouring the same cancer risk loci. Globally, overweight/obesity may account for 544,300 cancer cases every year and is currently implicated in 15-20% of cancer-related mortalities. This places obesity second only to smoking as the most prevalent preventable cause of cancer.

Research Project 1: What are the properties of cancer cells adapted to aberrant physiological environments?

We have previously demonstrated that obesity is not associated with additional oncogenic genetic alterations that could explain the increased cancer risk. Instead, we demonstrate that cancer cells undergo adaptive epigenetic remodelling and gain tumour initiating properties when exposed to prolonged periods of obese conditions. This interaction between metabolic, epigenetic, and tumorigenic events currently represents significant knowledge gaps.

AIMS

- Uncover the relationship between systemic metabolic challenge as induced by physiological stressors and intracellular metabolite dynamics in cancer cells.
- Identification of the metabolites that are sufficient to drive tumour initiation – and how this is achieved.
- Determine how metabolite-driven epigenetic changes can display loci specificity.
- Discover the epigenetic, transcriptional and translational machinery required to that link physiological stressor to tumour initiation.

Key methodologies for this project are in vivo CRISPR loss- and gain-of-function screens, single cell transcriptomics and epigenomics, in vivo tumour modelling and metabolomic tracer studies.

Research Project 2: How do physiological stressors affect the tumor ecosystem?

We know that stem cells are intrinsically connected to the cellular niche in which they reside and that these cellular interactions are particularly important and instructive for stem cell plasticity. In this project, we ask if an obese environment instructs the cancer stem cell niche to govern cancer cell dedifferentiation and enhanced stemness features.

AIMS

- To develop a comprehensive cellular spatial map of the cancer stem cell niche in obese and non-obese cancer patients.
- To comparatively extract obesity-dependent deregulated cell abundancies and cellular interactions within such niches.
- To mechanistically dissect the causal importance of the obesity-dependent niche composition.

The key methodologies for this project are spatial interrogation of the tumour microenvironments (sequencing and proteome-based), in vivo tumour modelling and antibody-based therapeutics.

Research Project 3: How does physiological stressors affect somatic fully differentiated cells of the body?

This project address two areas that we believe are currently severely understudied: 1) How does the obese phenotype affect male and female germ cells and thereby the intergenerational metabolic health and 2) How does a history of obesity affect future possibilities of cancer risk (epigenetic memory).

AIMS

- Uncover the relationship between systemic metabolic challenge the epigenetic landscape of both male and female germ cells.
- Demonstrate how efficiently the obese phenotype is transferred between generations in mice.
- Conduct generational cancer studies.

Key methodologies for this project are single cell transcriptomics and epigenomics, metabolomics, mouse in vitro fertilisation and advanced mouse cancer models (genetic and viral based).

Medical Genomics

Senior Group Leader:
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The Medical Genomics Team analyses next generation sequence data to address clinical challenges in a variety of diseases. The approaches we take include:

- Characterising cancer genomes with short and long read sequencing;
- Classification of tumours into significant subtypes;
- Identification of mutational processes that underlie tumour development;
- Determining genomic and transcriptomic features associated with immune response.

Ultimately, we aim to take steps towards 'personalised medicine' to enable the diagnosis, management and treatment of patients.

Sid Faithfull Brain Cancer

Group Leader:
Professor Bryan Day

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Our direct focus is to investigate the biological processes critical for the development of these intractable tumours, commercialise our research findings and bring our novel antibody therapies to clinical trial to improve the lives of brain cancer patients.

The Sid Faithfull Brain Cancer Laboratory focuses on glioblastoma (GBM) which is the most common and aggressive form of adult brain cancer. GBM kills approximately 1,900 people per year in Australia. Survival rates are very poor with a median survival of approximately 15 months. Meaningful advancements in patient treatment and survival have not changed for decades. New and better treatment therapies are urgently needed.

The laboratory also studies a number of paediatric brain cancers including medulloblastoma and an incurable form of brain stem glioma called Diffuse Midline Glioma (DMG), previously known as Diffuse Intrinsic Pontine Glioma (DIPG). Our goal is to design therapies that specifically treat the tumour site while keeping the healthy developing brain intact in these young patients.

Targeting novel receptors in GBM.

Co-Supervisor:
Dr Rochelle D'Souza

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This project can be adapted in scope for an Honours or PhD student.

BACKGROUND

We have generated well-characterised monoclonal antibodies (mAbs) against two receptor proteins that are present on two discrete cell populations and propose to use these simultaneously to effectively target this devastating disease. By targeting two proteins specifically expressed on the tumour and not normal brain, we aim to reduce toxicity while effectively killing most of the tumour. We have conjugated the mAbs with a drug to make antibody drug conjugates (ADCs) and aim to test their killing efficacy in vitro.

AIM

To validate dual targeting using ADCs as an effective therapeutic strategy for GBM in vitro.

APPROACH

- In vitro killing assays to determine GBM cell killing and IC50;
- Apoptosis/cell death assays;
- Flow cytometry and western blotting;
- Immunofluorescence and confocal microscopy.

OUTCOME

Validation of novel ADCs that have anti-cancer effects in primary GBM cell line models which would then serve as a base for further validation in animal models. This would pave the way for translation into the clinic to improve outcomes for patients with GBM.

Cancer Drug Mechanisms

Group Leader and Chair of Higher Degrees Committee:
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qimrb.edu.au/researchers-and-labs/drug-discovery-cancer-drug-mechanisms-group

The Cancer Drug Mechanisms Laboratory combines expertise in cell biology with understanding of drug mechanisms to treat cancers and other chronic diseases.

The laboratory's cancer biology work currently focuses on understanding the development and progression of cancers of the skin and oral cavity.

Specifically, the laboratory is investigating the molecular mechanisms involved in the progression and metastasis of melanoma, head and neck cancer, as well as cutaneous squamous cell carcinoma. These mechanisms also affect drug resistance of cancers.

The identification and understanding of pathways in these cancers is crucial prior to the design or identification of suitable treatments. The group also uses its cell biology knowledge to assist in the development process for novel agents targeting cancer and other chronic disorders.

Developing small molecule inhibitors to target treatment refractory melanoma.

This project is suitable for an Honours, Masters, MPhil, or PhD student.

BACKGROUND

Cutaneous melanoma is a neoplasm of melanocytes, the pigment producing cells in the skin, and is the most aggressive and lethal form of skin cancer. The incidence of melanoma has increased dramatically over the past three decades, including in Australia where it is now the fourth most commonly diagnosed cancer.

It is estimated that over 16,800 Australians will be diagnosed with melanoma in 2025 and over 1,300 people will die. Metastatic dissemination of melanoma is a serious complication for the successful treatment of the disease, and represents the most common cause of death for melanoma patients.

We have identified a transcriptional program in melanoma tumour cells that triggers dissemination of melanoma cells and allows survival. The program simulates chronic interferon-γ exposure, and also results in extracellular matrix alterations. These changes have been observed in melanoma patients that are resistant to standard of care therapy. We have now linked the driver of this signature, the transcription factor BRN2, with worse patient outcome following this therapy. It is possible to directly target BRN2 binding to DNA using small molecule inhibitors. Targeting BRN2 directly increases specificity, as it is not widely expressed in normal adult tissue.

AIM

This project aims to develop novel small molecule inhibitors of BRN2 for single agent or combination therapy of patients with therapy refractory melanoma.

PROJECT POTENTIAL

Generation of novel BRN2 targeting agents could benefit melanoma patients, as well as additional cancer types where the transcription factor is highly expressed including glioblastoma and neuroendocrine prostate cancer.

Molecular Immunology

Group Leader:
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The Molecular Immunology Laboratory works on the immunology of infectious diseases such as malaria, as well as cancer and autoimmunity. In 2016, the laboratory discovered programmed cell death1 ligand 2 (PD-L2) was contrary to dogma, not a "brake" on the immune system, but actually an essential activator of immunity.

In 2023, the laboratory's spin-out company, Fovero Therapeutics, developed novel immunotherapies for cancer and autoimmunity as well as diagnostics for these diseases. Fovero Therapeutics is focused on developing immunotherapies for cancers with the greatest unmet need such as MSS+ colon cancer and triple negative breast cancer.

Dissecting immune responses against cancer.

This project is suitable for an Honours, Masters, MPhil, MD, or PhD student.

The Molecular Immunology Laboratory works on the immunology of malaria, cancer and autoimmunity. In 2016, the laboratory discovered Programmed cell death1 Ligand 2 (PD-L2) was contrary to dogma, not a "brake" on the immune system, but actually an essential activator of immunity. The laboratory has since then used this finding to develop multiple immunotherapies and diagnostics for the treatment of cancer and autoimmunity. The products developed from research are now developed for human treatment by the Institute's spin-out biotech company Fovero Therapeutics. The laboratory continues to undertake basic research and have projects that would suit an Honours or PhD student.

BACKGROUND

The laboratory has discovered and developed a novel immunotherapy for colon cancer with outstanding protection. We now want to understand the mechanism of protection and if it applies to other cancers.

AIM

To dissect immune responses against cancer with the aim of developing novel immunotherapies.

PROJECT POTENTIAL

To have on impact on cancer care.

Post-treatment Cancer Immunobiology

Group Leader:
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In the light of therapy-induced or organ-specific cues in the cancer macroenvironment, the Post-treatment Cancer Immunobiology Laboratory leverages genetically modified mice and clinical samples for cellular- and-molecular immunology-based high-throughput analyses, thus delving into the mechanisms of how the acquired inflammation and epigenetic regulation impose therapy response or resistance.

In particular, they are looking at how post-treatment inflammation reshapes the function of anti-tumour T cells and other underrepresented immune populations, aimed to explore whether the underlying molecular traits can apply to tailoring T cell-based immunotherapy and new drug development.

Epigenetic manipulation of DC-donated mitochondria boosts T cell anti-tumour immunity.

This project is suitable for an Honours, Masters, MPhil, MD, or PhD student.

BACKGROUND

Optimising mitochondrial fitness is crucial for both endogenous anti-tumour T cells and engineered T cell therapy products. Dendritic cells (DCs) play a pivotal role in orchestrating T cell immune responses; however, it is unclear whether DCs can modulate T cell mitochondrial function and whether this cellular interaction can be harnessed in T cell therapy. Notably, intercellular mitochondria transfer represents an emerging mechanism in cancer immunobiology, with the potential to enhance T cell therapy efficacy. We preliminarily observed DC-donated mitochondria in co-stimulated CD8 T cells in vitro and hypothesise that this phenomenon also exists in vivo. Since mitochondrial DNA (mtDNA) plays a key role in metabolic fitness, we will investigate its epigenetic regulation following mitochondria transfer. Our preliminary data suggests that aberrant expression of the mtDNA methyltransferase METTL4 impairs DC co-stimulation of CD8 T cells. Therefore, we aim to explore how mtDNA methylation and transcription are regulated in mitochondria-transferred T cells and whether METTL4 depletion can rewire this process to reserve T cell stemness and responsiveness.

AIMS

- Demonstrate the importance of DC mitochondria donation in T cell anti-tumour immunity;
- Explore whether 6mA methylation selectively restricts donor mtDNA transcription in mitochondria-transferred CD8 T cells;
- Identify how 6mA methyltransferase METTL4 impedes DC-induced CD8 T cell fitness;
- Enhance adoptive T cell therapy by targeting the METTL4-6mA machinery.

METHOD

- In vitro T cell activation/exhaustion systems;
- In vitro and in vivo mitochondrial reporter systems;
- Chemoimmunotherapy models;
- Adoptive T cell therapy models.

PROJECT POTENTIAL

The mitochondria transfer phenomenon is paradigm-shifting our understanding of cancer immunobiology. With DC-T cell communication interpreted at the intercellular mtDNA level, this study will update and translate our knowledge about how T cells acquire mitochondrial fitness and treatment responsiveness. By combining mitochondrial supercharging with epigenetic reprogramming, we may develop better T cell therapy products against a wide range of cancers and treatment responsiveness. By combining mitochondrial supercharging with epigenetic reprogramming, we may develop better T cell therapy products against a wide range of cancers.

Too much of a good thing: how post-immunotherapy inflammation compromises tumour immunity in the liver.

This project is suitable for an Honours, Masters, MPhil, MD, or PhD student.

BACKGROUND

Innovative immunotherapy drugs such as immune checkpoint inhibitors (ICIs) have replaced the first-line treatment for many cancers, however, their therapeutic effects on primary and secondary liver cancers are limited. Clinician researchers including myself have noticed that unwanted locoregional inflammation may lead to disease progression and therapy resistance in the liver. My research has identified a group of liver "inflammation checkpoints" that can diminish cancer-promoting inflammation and enhance anti-tumour immunity. I have also developed liver inflammation-targeted strategies to improve immunotherapy efficacy and resolve conventional therapy resistance. This project will take advantage of my years of clinical expertise in ICI resistance and my research experience

in cancer-promoting inflammation, emphasising how CD8 T cells are regulated by ICI-induced liver-specific inflammation.

AIM

This project aims to investigate the post-ICI CD8 T cell trajectory in the liver and understand how intrahepatic inflammatory signals impose on T cell function. By identifying and leveraging new immune populations and molecular targets, we intend to design relevant combination strategies to orchestrate anti-tumour immunity in the liver.

APPROACH

Based on genetically modified mice and clinical samples, we will investigate the post-treatment cancer microenvironment using single-cell sequencing and multiplex immunohistochemistry. Different mouse strains will be used for tumour inoculation and drug administration. Mouse or human tissues will also be acquired for in vitro culture systems. In addition to high-throughput flow cytometry and other immunological analyses, molecular & cellular biology experiments and multi-omics methods will be applied to mechanistic exploration.

PROJECT POTENTIAL

This project will reveal a phase-and-context-dependent regulation of CD8 T cell anti-tumour immunity, potentially breaking the liver-specific barriers to immunotherapy response.

Conjoint Gastroenterology

Honorary Group Leader:
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The Conjoint Gastroenterology Laboratory studies the molecular genetic alterations that underlie the progression of benign bowel polyps to bowel cancer.

It has a particular interest in serrated polyps that were previously thought to have no malignant potential but are now recognised to be the precursors of approximately 20% of bowel cancers. This work has led to profound changes in the practice of colonoscopy so that it now better protects against bowel cancer.

The laboratory has now developed an animal model of the serrated pathway and are testing chemoprevention strategies. The bowel cancers that arise through the serrated pathway often carry an oncogenic BRAF mutation and develop DNA methylation, silencing important genes such as mismatch repair genes. These characteristics are important in predicting prognosis and response to chemotherapy and this is also a focus of our research programme.

Collaboration with gastroenterologists, surgeons, pathologists and oncologists is a key aspect of the laboratory's research.

Gene Regulation and Translational Medicine

Senior Group Leader:
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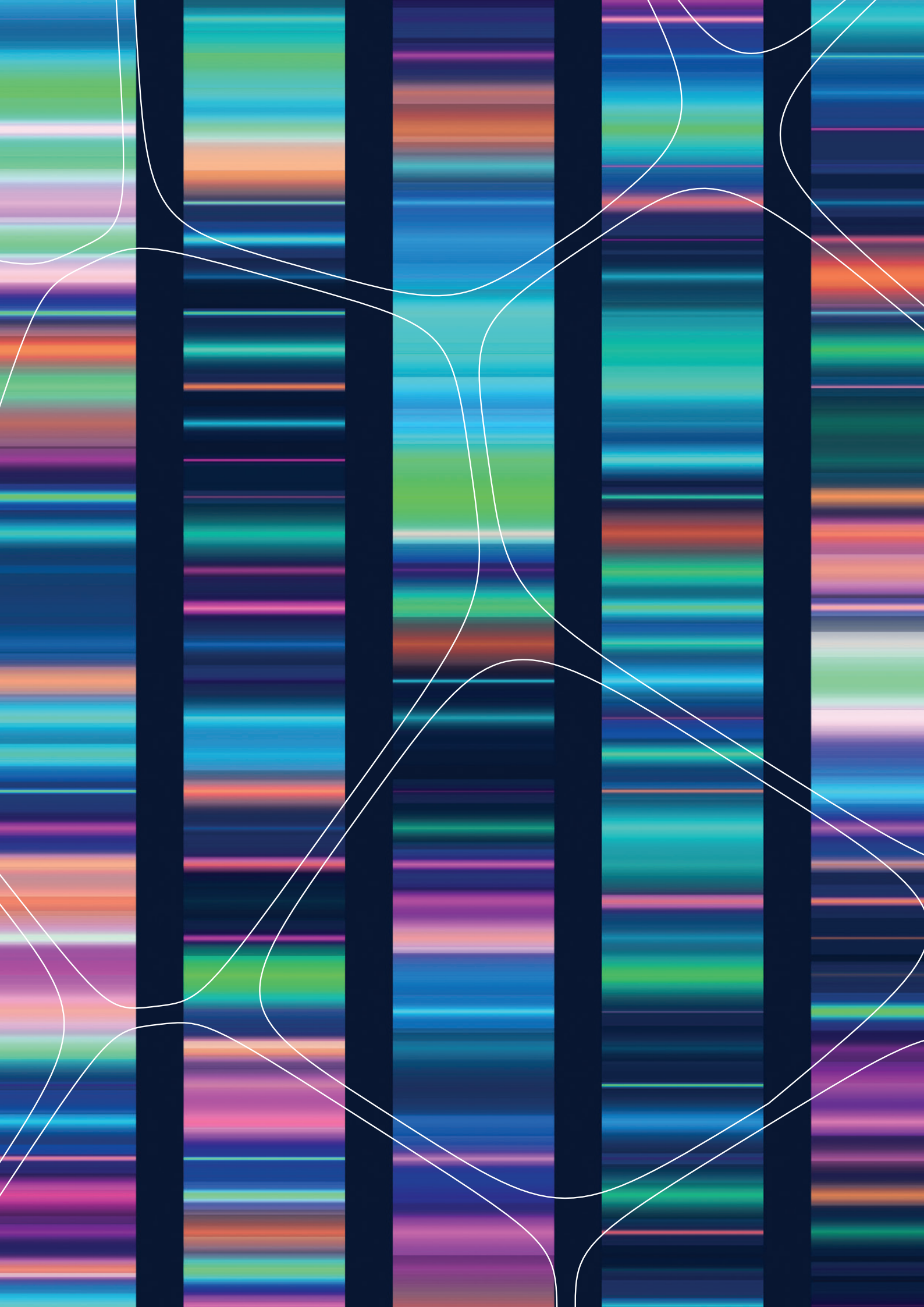
Though all genes exist within every cell in the human body, only a defined gene expression program is executed at any time via reprogramming of the epigenome in response to environmental cues. These dynamic events are elegantly orchestrated by writer and eraser enzymes, generating a 'histone code' within the epigenetic landscape of genes. The therapeutic implications of targeting novel domains of epigenetic enzymes are beginning to be appreciated in immuno-oncology.

The laboratory's focus on immuno-oncology is on metastatic cancers and potential implications for viral therapy and the immune response in the aged population. We are also addressing the potential implications for the utility of epi-therapy in combination with immunotherapy and chemotherapy for a variety of metastatic cancers. The laboratory is in the process of developing sensitive liquid biopsies using our newly identified novel biomarkers for patient responsiveness to immunotherapy in the context of the tumour microenvironment. The team are also in the process of developing clinical based epigenetic platforms for drug screening and biomarker discovery in collaboration with global technology partnerships.



Population Health Program

Our Population Health Program and its team is dedicated to understanding the factors influencing the health and wellbeing outcomes of all Australians and our regional neighbours.

Drawing on the expertise of our clinical scientists, epidemiologists, health economists, and specialist researchers, we examine the causes of disease, their transmission, and identify patterns and changes in the health of the population. This knowledge is used to develop measures to control and prevent diseases, increase early detection and improve treatments to ensure the best possible health outcomes.

The research we do is diverse. It ranges from examining the role of vitamin D supplementation in health outcomes to reducing the incidence of mosquito-borne illnesses and other tropical diseases, and from identifying environmental and genetic risk factors for disease to improving the wellbeing of those caring for cancer patients and evaluating the social and economic consequences of disease.

Our studies are helping develop treatment guidelines to ensure all patients receive the best possible care, prevent hospital admissions, improve well-being and reduce mortality.

The Population Health Program is guided by the ultimate goal of preventing ill-health in communities and improving patient care, quality of life, and survival rates, so that all Australians and our regional neighbours have the opportunity to enjoy good health.

Gynaecological Cancers

Distinguished Scientist: Professor Penelope Webb

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The Gynaecological Cancers Group studies the epidemiology of gynaecological cancers, particularly ovarian and endometrial cancers, from aetiology to diagnosis, patterns of care, quality of life and survival. A particular focus is on the role of environmental (non-genetic) factors in the causation and prognosis of ovarian and endometrial cancer. Much of this work is conducted within two national record-linkage studies (OVARIAN and CURVVE), three national studies (AOCS, ANECS and OPAL) and two international consortia. The group is also leading the PROMISE study – a new hybrid effectiveness-implementation trial evaluating the use of electronic Patient Reported Outcome Measures (PROMs) in routine cancer care..

Use of dietary supplements and outcomes after a diagnosis of ovarian cancer.

Co-Supervisor: Dr Nina Na

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This project is suitable for a Masters (preferably part-time) or Honours student. Some experience in biostatistics and data analysis is essential and a background in epidemiology and/or an interest in cancer is highly desirable.

BACKGROUND

The use of dietary supplements by cancer patients is common but contentious, particularly during chemotherapy. Survivors often take supplements in the hope these will improve their wellbeing, alleviate chemotherapy side effects, boost immune function, and perhaps improve their long-term survival. There is, however, a growing body of evidence suggesting that supplements, particularly antioxidants, might interact with conventional chemotherapeutic treatments and thus be detrimental to health.

In recent analyses of patients with breast cancer enrolled in a randomised clinical trial, there was a suggestion that those who used multivitamin supplements experienced less neurotoxicity during treatment while those who used supplements other than multivitamins had poorer survival.

AIM

To evaluate the relation between use of dietary supplements, particularly antioxidants, during and after treatment for ovarian cancer and (i) wellbeing and (ii) survival.

METHODS

Analysis (linear and logistic regression/survival analysis) using individual-level data from a cohort of 900 women with ovarian cancer women who provided information about dietary supplement use before and 3, 6, 9, 12 and 24 months after diagnosis.

Use of complementary and alternative medicine and outcomes after a diagnosis of ovarian cancer.

Co-Supervisor: Dr Nina Na

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This project is suitable for a Masters (preferably part-time) or Honours student. Some experience in biostatistics and data analysis is essential and a background in epidemiology and/or an interest in cancer is highly desirable.

BACKGROUND

The use of complementary therapies by cancer patients is common but contentious, particularly during chemotherapy. Survivors often use complementary medicine in the hope it will improve their wellbeing, alleviate chemotherapy side effects, boost immune function, and perhaps improve their long-term survival. There is little information about the use of complementary and alternative therapies by women with ovarian cancer, if/how this changes after their cancer diagnosis, what women use during treatment or how this might affect their wellbeing and, ultimately, their survival.

AIMS

To document the prevalence of use of complementary and alternative therapies by women with ovarian cancer, changes in use after diagnosis, and the relation between use and wellbeing and survival.

METHODS

This project could include some/all of the following components:

- A literature review of the current evidence;

- Descriptive analyses of what women use and how this changes from before diagnosis to during treatment, after treatment and after recurrence;
- Analysis of factors associated with use or that predict changes in use;
- Analyses of the relation between use, symptoms and side-effects, and wellbeing; and
- Analyses of the relation between use and survival. Analyses will use individual-level data from women in the OPAL study who provided information about complementary and alternative therapy use before and after diagnosis (3-monthly for the first year then annually to 4 years).

Genomics, Imaging, and AI

Team Head: Associate Professor Puya Gharahkhani

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The Genomics, Imaging, and AI Laboratory has a primary focus on neurodegenerative disorders of the eye and brain, particularly glaucoma, macular degeneration, dementia, and Parkinson's disease. The laboratory employs statistical genetics and deep learning methodologies to advance gene discovery and improve risk prediction for these diseases.

Currently, the laboratory is leading ground breaking projects that integrate diverse modalities through innovative multimodal artificial intelligence (AI) approaches, aimed at enhancing risk prediction for various diseases. The lab also boasts exciting collaborations with industry partners in both clinical and machine learning analytical domains.

Cancer Control

Distinguished Scientist: Professor David Whiteman

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Research undertaken by the Cancer Control Laboratory is conducted with a view to reducing the burden from cancer through identifying risk factors, then translating these research findings into policy and practice. This includes research to identify the environmental and genetic factors that cause cancer, as well as research into early diagnosis, treatment and survival.

The laboratory had two major areas of research focus: melanoma and skin cancer, and upper gastrointestinal neoplasia.

Cancer Aetiology and Prevention

Senior Group Leader: Professor Rachel Neale

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The Cancer Aetiology and Prevention Laboratory focuses primarily on understanding the health benefits of vitamin D supplementation, balancing the risks and benefits of sun exposure and reducing the impact of pancreatic cancer.

Sun Balance: Balancing the harms and benefits of sun exposure.

This project can be scoped to suit Honours, Masters, MPhil, or PhD students.

BACKGROUND

The sun has both harms and benefits. QIMR Berghofer led the development of a new position statement, that includes advice specific to people's risk of skin cancer and where they live. We now need to work out how best to communicate this advice. The Sun Balance project will use co-design methods to design educational materials specific to different settings and populations, then conduct a randomised controlled trial to test their effectiveness and implementation.

METHOD

The project will include qualitative and quantitative methods. We can devise projects that meet the interests of prospective students.

PROJECT POTENTIAL

Sun Balance will ultimately lead to new ways of helping people implement strategies to enable them to gain the benefits of sun exposure while avoiding the harm.

PaC-NOD: Screening for pancreatic cancer in people with new-onset diabetes.

This project can be scoped to suit an Honours, Masters. MPhil, or PhD student.

BACKGROUND

In some people, diabetes in later life is caused by an undiagnosed pancreatic cancer. It is not known, however, whether screening people with new-onset diabetes would reduce pancreatic cancer mortality.

AIM

The PaC-NOD Pilot Study aims to test the feasibility of conducting a large-scale randomised controlled trial of screening people with new-onset diabetes using CT scans.

METHOD

The project will primarily include qualitative methods, with some relatively simple quantitative analyses included.

PROJECT POTENTIAL

This project will determine whether a large-scale screening trial is feasible.

PanLink – using linked data to reduce the impact of pancreatic cancer.

This project is suitable for an MPhil or PhD student.

BACKGROUND

Pancreatic cancer has extremely poor survival. The PanLink dataset is a national linked dataset that aims to understand more about causes, factors influencing survival, and early diagnosis.

AIM

Projects can be designed to fit in with the interests of students. For example, students could examine the association between use of specific medications and risk of pancreatic cancer.

APPROACH

This project uses a lot of complex data management and statistics, and requires students with experience and aptitude using statistical software packages such as SAS and R.

Molecular Cancer Epidemiology

Senior Group Leader:
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The Molecular Cancer Epidemiology Laboratory is focused on translational genomics, aiming to increase the impact of genomics in health practice.

The laboratory primarily studies the epidemiology and genetics of breast, ovarian, and endometrial cancer and conditions of inherited cancer risk. Our research identifying molecular signatures of normal and tumour tissue can point to the genetic and environmental causes of these cancers.

Through studying approaches to diagnostic processes and genomic variant interpretation, our laboratory is improving clinical genomics application for improved patient management for other diseases.

The laboratory covers a range of projects with the themes of clinical genetics, cancer epidemiology and molecular pathology.

Evaluation of variants in known or candidate high-risk cancer genes.

Co-Supervisor:
Dr Aimee Davidson

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This project can be adapted in scope for an Honours or Masters student.

BACKGROUND

Panel gene testing is increasingly applied to identify the underlying genetic cause of cancer in patients with suspected hereditary cancer.

Identification of a pathogenic variant directly influences clinical management for patients and their at-risk relatives, setting the path for preventative and increasingly chemotherapeutic options. Unfortunately, such testing often identifies variants with uncertain impact on function and clinical phenotype. Such variants of uncertain clinical significance create considerable difficulties for counselling and clinical management.

A range of methods can be useful for assessing variants, including bioinformatic analysis, assays of mRNA and protein function, and also investigating association with clinical features such as segregation in families, age at onset /phenotype in case-control studies and tumour pathology.

AIM

To use statistical and laboratory methods to assess the clinical relevance of rare cancer gene sequence variants identified by clinical genetic testing of patients with suspected hereditary cancer, identified in Australia or through the international consortia such as ENIGMA.

APPROACH

This project will assess the effect of variants on gene/protein function using a variety of bioinformatic predictions, molecular biological assays and/or statistical analyses. Techniques may include RNA analyses using LCLs and/or constructs, protein assays in collaboration with other laboratories, pedigree analysis and simple statistical analyses of clinical factors predictive of pathogenic variant status, to develop calibrated measures of association with disease for use in multifactorial likelihood analysis.

OUTCOME

Analysis of specific variants will provide evidence regarding their pathogenicity for translation in the clinical setting. Comparison of assay results with risk will form the foundation for improving bioinformatic prediction tools and incorporating predictions and/or biological assay results in statistical models of risk prediction.

Expanding genetic diagnoses into non-coding regions of the genome.

Co-Supervisor:
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This project is suitable for an Honours, Masters, or MD student.

BACKGROUND

A molecular diagnosis informs many aspects of treatment for a patient with an inherited condition, however current techniques provide a diagnosis in only around 25% of cases. Non-coding regions of the genome remain underrepresented in clinical cases and variants in these regions are therefore a potential source of diagnoses for undiagnosed patients. Non-coding variants remain elusive as there is insufficient evidence to predict their impact and/or disease-causality. In order to improve diagnosis in these regions, we are working to determine which of the current research tools provide sufficient evidence to predict disease-causality in a clinical setting. We are testing methods to determine how to apply bioinformatic tools with best predictive power, to provide evidence based clinical recommendations for clinical diagnostics inclusive of non-coding regions. This work will increase diagnostic yield for patients undergoing genetic testing.

AIM

To improve diagnostic yield for patients with inherited disease by evidencing new methods for applying computational and experimental evidence in variant curation across expanded areas of the genome.

METHOD

We use a range of computational methods and statistics, but can support across levels of skill and experience. Using clinical and public data, we investigate research tools to determine if they can be applied in clinical genomic diagnostics and evaluate their predictive power and impact to determine clinical recommendations. We will access a variety of publicly available data and software, with analysis techniques including those used in health quality assessment and diagnostic evaluation.

PROJECT POTENTIAL

The projects that we offer are very applied and translate well for clinical understanding of genomics and genetic variant curation. We also support building bioinformatic, coding skills, statistics along with research translation and implementation projects aligned with this area. This project has real world translational potential as it will provide results enabling improved clinical diagnostic practice, to improve health care for patients.

Statistical Genetics

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qimrb.edu.au/researchers-and-labs/statistical-genetics

The Statistical Genetics Laboratory studies the role that genetic variation plays in determining risk of disease and its risk factors.

The laboratory develops and applies statistical genetic methods to gene mapping studies across a wide range of traits and diseases.

One major focus is understanding genetic variation in various cancers, including melanoma, ovarian cancer and oesophageal cancer. This work will lead to a better understanding of why particular individuals are affected by cancer or why they respond poorly to cancer treatment.

Another major interest is ophthalmological genetics, with ongoing work to identify the specific genes involved in both eye disease and their underlying quantitative risk factors.

Eye disease genetics.

The project is suited to a PhD student with experience in genetic epidemiology, epidemiology, biostatistics or bioinformatics. Experience in the analysis and manipulation of large datasets and a good knowledge of computing is desirable. Nonstatistical applicants must be able to demonstrate some knowledge of statistics. For applicants with a background solely in statistics, some knowledge of genetics is desirable.

BACKGROUND

Glaucoma is the leading cause of irreversible blindness worldwide. While there is no cure once visual loss occurs, progressive visual loss and blindness can usually be prevented by timely treatment. This means early detection is vital. Unlike many other common complex diseases, the heritability of glaucoma is very high (70%) and traditional epidemiology studies have not identified any means by which risk can be decreased (e.g. via modifiable risk factors). The major role of genetic factors in glaucoma make understanding the molecular mechanisms fundamental to improve screening and develop better therapies. We have developed genetics-based risk prediction tools for glaucoma, and are now exploring how to implement these to prevent blindness.

AIMS

To apply risk prediction tools for glaucoma based on genetic data. To translate these genetic findings into improved screening for the disease. To integrate genetics-based prediction approaches with methods harnessing artificial intelligence. The project may also consider gene-mapping and prediction analysis for other eye diseases such as myopia, age-related macular degeneration and dry eye.

PROJECT POTENTIAL

The QIMR Berghofer Genetics of Glaucoma Study is one of the largest studies of its kind internationally, with large scale genetic data recently collected on thousands of Australians. This will be supplemented with very large-scale genetic data sets (genome wide association studies, exome/genome sequencing, proteomics) which are available in the laboratory. The student will employ a range of statistical genetic approaches to interrogate these data and to determine the genes and pathways underlying glaucoma and use these in prediction models.

Genetics of skin cancer.

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Co-Supervisor:
Associate Professor Matthew Law

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The project is suited to a PhD student with experience in genetic epidemiology, epidemiology, biostatistics or bioinformatics. Experience in the analysis and manipulation of large datasets and a good knowledge of computing is desirable. Experience in cancer genetics is advantageous but not essential. Non-statistical applicants must be able to demonstrate some knowledge of statistics. For applicants with a background solely in statistics, some knowledge of genetics is desirable.

BACKGROUND

Skin cancers, including melanoma and keratinocyte cancers (KCs), are the most common cancers in Australia leading to significant morbidity, mortality and health costs. Each year over 15,300 Australians are diagnosed with melanoma, the deadliest skin cancer with over 1,400 Australians succumbing to advanced or metastatic disease every year. Early diagnosis and appropriate treatment are crucial in improving survival outcomes.

Over the last decade, new drug therapies known as immunotherapy have drastically improved treatment outcomes in patients with metastatic melanoma. Despite this success, there is significant variability in response to treatment amongst patients, with 59% patients experiencing life threatening immune-related adverse events or toxicities, while a third acquire complete remission. The biology underlying why some people do or do not develop immunotherapy-related adverse events, or why others do or do not acquire remission, is poorly understand.

Due to immunosuppression, transplant patients have up to 100-fold risk of developing KC compared to the general population, with the majority (57%) of recipients developing multiple KCs. Unlike in the general population, for transplant patients KC is very aggressive, and highly metastatic. It is also a major cause of death in transplant patients accounting for 15% of cancer deaths, a 51-fold increase compared to mortality in the general population. There is an increasing need to effectively manage these cancers in transplant patients

AIMS

- Explore the genetic predisposition to poor immunotherapy efficacy in patients with metastatic melanoma.
- Assess genetic-based prediction of immunotherapy efficacy in metastatic-melanoma patients.
- Explore putative causal factors for immunotherapy response in patients with metastatic melanoma.
- Explore clinical translation of genetic risk prediction of skin cancers in transplant patients.

PROJECT POTENTIAL

We have large-scale genetic data sets available in the lab for skin cancer risk, treatment, and treatment outcomes. We also have access to other national and international biobanks, as well as deeply phenotyped data sets for transplant patients. The candidate will use a range of statistical genetic approaches to interrogate these data and to determine the genes and pathways underlying melanoma treatment response and use these in prediction models. They will also use these data sets to develop and apply genetic prediction models for skin cancer in transplant patients.

The project may also consider similar gene-mapping and prediction analysis for other complex traits such as other cancers e.g. colorectal carcinoma, and glaucoma in non-European ancestries.

Global Precision Health

Team Head:
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qimrb.edu.au/researchers-and-labs/global-precision-health

The Global Precision Health Lab investigates a broad spectrum of human complex traits, with the overarching aim of strengthening the footprint of precision health research on the global stage. We focus on data-driven strategies and collaborative research to address critical knowledge and capacity gaps in precision health, particularly within diverse and under-represented populations.

Our lab is disease-agnostic: we welcome research proposals across any complex human disease, as long as they align with our core philosophy—that impactful research should have the potential to benefit not only patients, but also one or more of the following stakeholder groups: researchers, policymakers, and early adopters within diverse healthcare systems.

In Australia, our work includes exploring the opportunities and challenges of engaging culturally and linguistically diverse (CALD) communities in biomedical research. We are particularly interested in evaluating and deploying cutting-edge methods for delivering and validating precision health solutions tailored to these populations.

Globally, we contribute to shaping precision medicine ecosystems through strategic partnerships, capacity-building initiatives, and cross-border research collaborations. Our work aims to develop adaptable frameworks and sustainable strategies that support the advancement of inclusive and equitable precision health research worldwide.

Wellness in the tropics – translating ideas into innovations for non-communicable diseases.

This project is suitable for an Honours, Masters, MPhil, MD, or PhD student.

BACKGROUND

Tropical regions have traditionally faced significant health challenges due to infectious diseases. However, with shifting disease patterns, non-communicable diseases (NCDs) such as diabetes are becoming increasingly prevalent, largely driven by lifestyle changes, including rising sugar consumption.

While genomic and multiomic technologies offer transformative opportunities for precision medicine, many tropical communities remain underrepresented in genomic research. Addressing this gap is crucial for ensuring equitable access to cutting-edge healthcare innovations.

AIM

This project aims to review, evaluate, and develop data-driven strategies for integrating genomic science into precision medicine initiatives for tropical communities. Candidates will have the flexibility to focus on a specific disease of interest or explore multiple diseases within this framework, gaining valuable expertise in disease biology, genomic data analysis, and translational research.

METHODS

The project will involve a comprehensive literature review of genomic and precision medicine applications in tropical health, as well as an analysis of existing genetic, omics, and biomarker data to assess their relevance for disease prevention, diagnosis, and treatment.

Candidates will also have the opportunity to develop innovative data solutions to address unmet clinical and research needs. For those interested in policy and implementation science, there will be an option to engage with key stakeholders, including healthcare professionals and policymakers, to identify barriers and opportunities for integrating genomic medicine into existing healthcare systems.

Findings from this research will inform the development of strategic recommendations, tools, or frameworks to enhance genomic research and precision health initiatives in tropical regions.

PROJECT POTENTIAL

This project offers a unique opportunity to contribute to global health equity by advancing precision medicine in underrepresented populations while building research and technical capacity for genomic innovation in communities with a limited research footprint. Through collaborations with leading tropical health researchers facilitated through the Don McManus Tropical Health Research Centre, the candidate will gain hands-on experience in genomic research, multiomics integration, translational science, and stakeholder engagement. Additionally, this work will support the development of data-driven strategies to strengthen healthcare systems in low- and middle-income tropical countries (LMICs), fostering sustainable and impactful genomic research efforts.

Advancing collaborative genomic research with federated learning: Overcoming data sovereignty barriers.

Co-Supervisor:
Associate Professor
Puya Gharahkhani

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This project is suitable for a PhD students with an interest in genomic data science, artificial intelligence, data engineering and/or precision medicine.

BACKGROUND

As genomic research expands globally, data sovereignty, privacy concerns, and regulatory restrictions present significant challenges for cross-border collaboration, particularly among low- and middle-income countries (LMICs). Traditional data-sharing models often conflict with ethics, governance policies, and local regulations, limiting the ability to conduct large-scale multi-ethnic genomic studies. Federated Learning (FL), a decentralised Artificial Intelligence (AI) approach, offers a promising solution by enabling collaborative analysis of distributed datasets without transferring sensitive data. This project will explore FL and similar AI-driven techniques to enhance collaborative synergy in genomic research while safeguarding data sovereignty.

AIMS

- Address data sovereignty challenges in collaborative genomic research across LMICs by developing AI-driven solutions that preserve privacy and comply with local governance frameworks.
- Compare and evaluate the application of FL against other statistical models in disease risk prediction, focusing on complex diseases such diabetes, cardiovascular disease (CVD), or cancer using multi-omics and clinical datasets from diverse populations.
- (Advanced) Develop a framework for a Software-as-a-Service (SaaS) platform that facilitates secure and scalable genomic data analysis for common diseases in Southeast Asia.

METHOD

This project will begin with a comprehensive review of FL applications in biomedical research, followed by testing hypotheses on disease risk prediction models using FL across multiomics and clinical datasets in different languages and healthcare settings.

The study will assess model accuracy, data security, and scalability while addressing computational and infrastructure challenges in LMICs. Based on these findings, the project will explore the design and implementation of a SaaS-based platform that

integrates FL for secure, privacy-preserving genomic analysis in collaborative research environments.

PROJECT POTENTIAL

This project presents an opportunity to pioneer AI-driven solutions for data sovereignty challenges in genomic research, fostering equitable participation of disadvantaged communities in global precision medicine efforts. By leveraging FL, the research aims to unlock the potential of multi-ethnic genomic datasets while ensuring compliance with local policies and ethical guidelines. Additionally, the development of a scalable SaaS platform could lay the groundwork for future commercialisation or public-sector adoption, transforming the way insights from genomic data is analysed and shared across borders.

Global Health and Tropical Medicine

Program Director (Population Health), Senior Group Leader: Professor Darren Gray

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qimrb.edu.au/researchers-and-labs/global-health-and-tropical-medicine

Our research investigates the transmission and control of tropical infectious diseases and diseases of poverty, including some of the most prevalent and important infections that cause much suffering and economic loss worldwide. We aim to develop new public health interventions against these diseases that will lead to their sustainable control and eventual elimination.

Cardiovascular Disease Prevention

Team Head: Associate Professor Ellie Paige

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The Cardiovascular Disease Prevention Laboratory focuses on generating epidemiological evidence to guide policy and practice decisions to improve the prevention of cardiovascular and related chronic diseases. A particular focus is on using big data and modelling to enhance disease risk prediction to guide treatment decisions in primary care and generating evidence to address gaps in implementation of preventive interventions.

Mosquito Genomics

Team Head: Associate Professor Gordana Rasic

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Our laboratory's aim is better control of mosquito-borne diseases through mosquito genomics.

New technologies to control mosquitoes and diseases they transmit are developing rapidly – from the natural pathogen-blocking symbiotic bacteria to the engineered "selfish genes".

In creating and assessing new mosquito control technologies, we take the approach "from the field – to the lab – back to the field". This means that we study natural mosquito populations, do laboratory experiments, and aim to produce practical solutions for field deployment. In doing so, we generate and analyse genomic and other "omics" data from a single mosquito cell to a system of mosquito populations.

We use spatial population genomics and simulation modelling to understand how mosquitoes move, mate and survive in different environments so that we can apply optimal control strategies. We also investigate mosquito genomes to identify and test genes that can be targeted for genetic control, so that we can move away from chemical insecticides.

We collaborate with the leading scientists in Australia, USA, Asia-Pacific and Europe to address the current challenges and predict future obstacles in protecting the communities in Queensland, Australia and around the globe from the mosquito-borne diseases.

Cancer and Chronic Disease Research

Group Leader:
Professor Patricia Valery

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qimrb.edu.au/researchers-and-labs/cancer-and-chronic-disease-research-group

The Cancer and Chronic Disease Research Laboratory lead the Institute's research on the epidemiology of chronic liver disease and liver cancer. To achieve our vision, our research has focused on three broad areas, namely:

- Through data linkage studies, our research targets the disparities in health care use and patient outcomes. We focus on regional areas, First Nations people, and the use of clinical and health service data to identify individuals at highest risk of progression of liver disease and liver cancer.
- Through mixed-methods studies, including qualitative interviews with patients and health professionals, we are examining patients' perspectives and preferences about their care, and their practical, psychosocial and information needs.
- Through interventional studies we are exploring new models of care aimed at improving early identification of patients at risk of liver disease progression and liver cancer, reducing barriers associated with their diagnosis and management, and improving patient outcomes.

Biostatistics

Group Leader:
Professor Gunter Hartel

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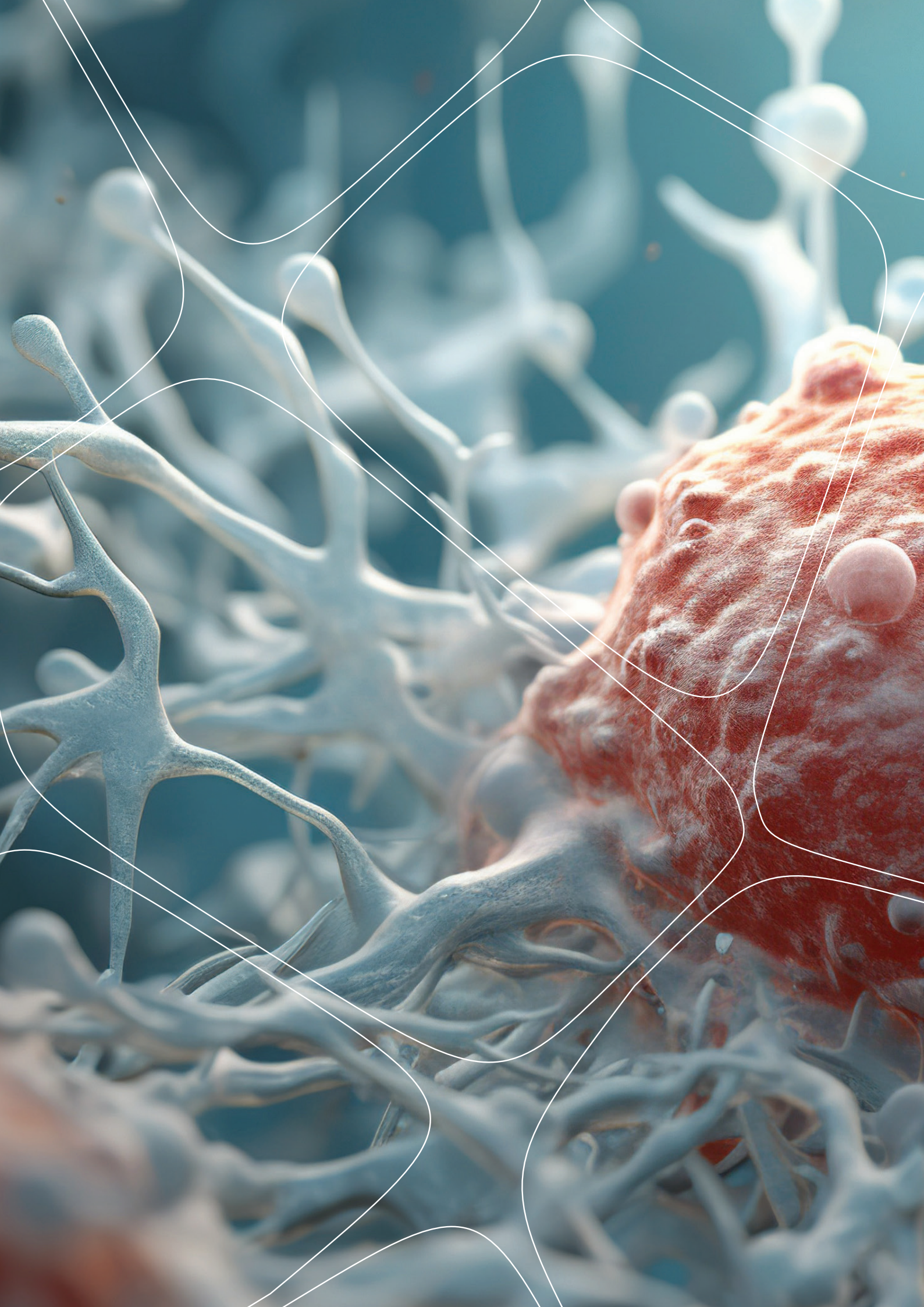
Our Biostatistics Group is dedicated to empowering researchers with expert statistical support and effective collaboration. We provide a comprehensive consultancy service for researchers within QIMR Berghofer, as well as our esteemed partners at Metro North Hospital and Health Service, and Mater Research.

Beyond consultancy, our team actively advances applied statistical methodologies to enhance the impact of biomedical, clinical, and scientific research. By partnering with the Biostatistics Group, clients gain access to specialised expertise in study design, data analysis, and reporting, ensuring robust, high-quality outcomes in their research endeavours.

This includes assistance with:

- formulating research questions;
- study design and analysis plans;
- power and sample size calculations;
- writing research grants and protocols;
- data management plans;
- statistical software packages, including R, STATA, SPSS, SAS, JMP, and GraphPad Prism;
- analysis using statistical methods appropriate for medical and health research;
- presentation and interpretation of data and analyses;
- preparation of and co-authorship on publications;
- addressing reviewers' comments.

We provide statistical training and workshops to improve statistical literacy of clients, researchers, and students.



Infection and Inflammation Program

Our world leading Infection and Inflammation Program develops drugs and vaccines, along with prevention and education strategies to tackle globally important diseases caused by viruses, bacteria, and parasites, as well as systemic chronic inflammation.

We have a distinguished history of studying viruses, gained over many decades, and use this knowledge to develop and deliver new treatments as well as cellular therapies for cancer and diseases of the central nervous system

Our specialist laboratories have an international reputation in malaria volunteer infection studies and test new anti-malaria drugs for deployment in the developing world.

We have a strong record in vector control and work on innovations in mosquito surveillance and measures to interrupt pathogen transmission, and deliver a strong helminth control program resulting in major public health gains.

Our research programs have been adapted to rapidly respond to the COVID-19 pandemic with the Institute establishing a highly secure facility to grow the SARS-CoV-2 virus and test new drugs, vaccines and treatment options.

The Institute has a dedicated Scabies Laboratory which does vital work into the skin infestation that largely affects our indigenous population.

New drugs have been developed by our researchers using tissue organoids that can prevent and/or reverse the effects of chronic inflammation on the heart, lung, brain and skin.

There is also a focus on new treatments for liver disease and gut health, particularly its relationship to childhood diseases.

Immunology and Infection

Program Director (Infection and Inflammation), Group Leader: Professor Christian Engwerda

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The Immunology and Infection Laboratory studies malaria and leishmaniasis, two important parasitic diseases that affect millions of people around the world every year. Our research focuses on CD4+ T cells because of their central role in controlling anti-parasitic immunity. We use our discoveries to improve immune responses following vaccination or drug treatment with the aim of generating long-lasting immunity in communities to reduce the numbers of infections, and ultimately eliminate these diseases. Our findings relate to inflammation, and as such, our work also has important implications for developing treatments for infections, cancer and autoimmune diseases that impact thousands of Australians.

Characterising CD4+ T cell responses during parasitic infections.

This project is suitable for a PhD or Honours student.

BACKGROUND

Inflammation is a complex biological response of the body to injury, infection or other harmful stimuli. It is a protective mechanism that helps to remove the cause of injury and initiate the healing process. Immune regulation refers to the mechanisms that control inflammation to ensure that it functions properly and does not cause damage to the body's own tissues. The immune system has a delicate balance between being responsive to pathogens and harmful invaders, while also avoiding overreaction or autoimmunity. CD4+ T cells play critical roles in coordinating immune responses and differentiating into functional subsets best suited to control pathogen growth, as well as controlling resulting inflammation.

We hypothesise that the composition of anti-parasitic CD4+ T cells subsets that develop during parasitic infection determines the outcome of disease. Furthermore, CD4+ T cell subset composition can be manipulated to improve vaccine and drug efficacy to establish long-term immunity.

AIM

To test this hypothesis, we will address the following aims: 1. Define CD4+ T cell molecular and phenotypic signatures associated with parasite control. 2. Develop strategies to modulate CD4+ T cells to improve their anti-parasitic functions. 3. Test host-directed strategies in pre-clinical disease models and primary human CD4+ T cells.

Genomics and Machine Learning

Group Leader: Associate Professor Quan Nguyen

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qimrb.edu.au/researchers-and-labs/genomics-and-machine-learning-lab

The Genomics and Machine Learning Laboratory (GML) studies cancer and infected tissues in patient samples and mouse models. They generate novel data from spatial and single cell technologies and develop new computational and statistical methods to find clinically important patterns from this complex data.

They pioneered the merging of two big data fields, sequencing and imaging, to advance understanding of pathological processes one cell at a time and across all cells within a diseased tissue.

By mapping cell types, their spatial organisation and cell-cell interactions in tissues, GML focuses on discovering new patterns and cellular regulation mechanisms that are hidden from traditional research approaches.

Examples of outcomes include cell and gene markers for predicting cancer progression risks, stratifying disease subtypes, discovering new drug targets to modulate the immune systems, and adding new capabilities for prioritising drugs most effective to each patient.

AI copilot for spatial transcriptomics-based melanoma diagnosis.

BACKGROUND

The integration of deep learning and spatial transcriptomics is transforming digital pathology, particularly in cancer diagnostics and prognosis. AI-powered pathology assistants, including multimodal large language models (LLMs), have demonstrated the ability to interpret histopathological images and generate clinical insights. However, current models primarily focus on morphological features and do not leverage spatially resolved gene expression data, limiting their diagnostic accuracy.

AIM

This project aims to develop an AI copilot that integrates spatial transcriptomics with histopathological image analysis for melanoma diagnosis. By incorporating molecular information into AI models, this system will provide pathologists with more accurate, explainable, and high-resolution insights into high-risk regions of melanoma tissues.

APPROACH

This project will involve pre-processing and aligning H&E histopathology images with spatial transcriptomics data, developing deep learning models using contrastive learning to integrate multimodal features, and fine-tuning large language models (LLMs) for clinical pathology queries. An interactive AI-powered web interface will be developed for real-time pathology assistance using inhouse melanoma datasets.

PROJECT POTENTIAL

This project offers a unique opportunity to work at the intersection of AI, spatial omics, and digital pathology, contributing to the development of next-generation clinical diagnostic tools. Students will gain hands-on experience with deep learning, contrastive learning, and multimodal AI models. The outcomes of this research could lead to improved melanoma diagnostics, enhanced AI-assisted pathology workflows, and potential clinical translation of AI-powered decision support systems.

Gut Health

Honorary Group Leader:
Professor Graham Radford-Smith

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Inflammatory Bowel Disease (IBD) is a chronic illness and the symptoms, including diarrhoea, rectal bleeding, and abdominal pain, have a significant impact on quality of life. Crohn's disease (CD) and ulcerative colitis (UC) are the major forms of IBD in developed nations such as Australia. It is common for a patient's symptoms to first appear while they are in their 30s, although these diseases can affect children and older adults. Both CD and UC are characterised by a series of relapses and remissions. There is limited understanding of the clinical, environmental and genetic factors that may influence how severe the disease is or how often it recurs.

The origin of IBD is not well understood, but the most favoured theory is that a genetically at-risk individual encounters a single or series of environmental triggers that lead to disease. Discovery of the first susceptibility gene for CD (called NOD2) and its proposed role in the body, support this hypothesis. The Gut Health Lab is currently investigating several other genes for links to IBD. Apart from that, we are also interested in dietary implications on disease progression and drug response.

Enhancing oral mesalazine efficacy in ulcerative colitis through an anti-inflammatory diet: An exploratory double-blinded randomised feeding trial.

Co-Supervisor:
Associate Professor Gareth Walker

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This project is suitable for an HDR or PhD student with a background in dietetics, biochemistry, clinical research, or related fields. The project is already supported by industry funding and has received full HREC approval.

BACKGROUND

Inflammatory Bowel Diseases (IBD), including Crohn's disease and ulcerative colitis (UC), are chronic conditions characterised by gastrointestinal inflammation. While the exact causes remain unclear, both genetic and environmental factors—particularly changes in the gut microbiota—play major roles.

IBD is increasingly prevalent worldwide, and evidence suggests that diet significantly influences disease outcomes. Diets high in ultra-processed foods, fats, and red meat are associated with higher relapse rates in UC, while high-fibre, low-fat diets may help reduce inflammation and improve quality of life.

This study will explore whether an anti-inflammatory diet can enhance the clinical effectiveness of oral mesalazine (5-ASA), the standard first-line treatment for newly diagnosed mild to moderate UC. Using a cutting-edge multi-omics approach, we will examine the interactions between diet, the gut microbiome, inflammation, and drug metabolism.

AIMS

- Test the feasibility and acceptability of a control (sham) diet.
- Assess the impact of diet on treatment response and quality of life.
- Use multi-omics techniques to analyse the effects of diet and mesalazine on the gut ecosystem (oral/faecal microbiome, bile acids, short-chain fatty acids, drug acetylation).

- Measure luminal environment and gut motility using a novel ingestible gas-sensing capsule.
- Investigate changes in gut permeability.
- Develop biomarkers for dietary adherence.
- Biobank biological samples for future research.

METHOD

This is a prospective, randomised, double-blinded, placebo-controlled dietary intervention trial. Participants with newly diagnosed mild to moderate UC will be randomised to receive either: Oral mesalazine + our previously validated Modified Anti-Inflammatory Diet (MAID), or Oral mesalazine + a matched SHAM diet.

PROJECT POTENTIAL

Many UC patients are eager to explore dietary options alongside medication, but robust evidence is lacking. This project aims to close that gap and assess how dietary strategies may enhance the efficacy of existing therapies.

By examining not only clinical outcomes but also mental health, anxiety, gastrointestinal symptoms, and overall quality of life, this study takes a comprehensive, patient-centred approach to managing UC.

RESEARCH ENVIRONMENT

You'll join a highly collaborative, well-supported team with expertise in metabolomics, microbiome science, nutrition, and clinical IBD research, based across QIMR Berghofer, The University of Queensland, Monash University, and UNSW.

We aim to generate evidence that supports integrating dietary therapy with conventional drug treatment, potentially reducing the need for aggressive immunosuppressive therapies and offering a more personalised and sustainable approach to managing UC.

Molecular Parasitology

Honorary Group Leader:
Professor Malcolm Jones

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qimrb.edu.au/researchers-and-labs/molecular-parasitology

The Molecular Parasitology Laboratory was founded by the late Professor Don McManus, and is now headed by Professor Malcolm Jones. The laboratory leads the world in parasitic worm research with the goal of global control of neglected tropical helminthiases. The group translates laboratory findings into effective disease interventions paving the way for improved health outcomes.

Along with a multidisciplinary collaborative team, the laboratory pioneers research on the development/application of schistosomiasis vaccines, in diagnostics, genomics and in tropical/international health, contributing a cohesive and remarkable body of 650 publications. Many are transformational, shaping policy/practice leading to improved treatment/control of worm infections with wide-scale application for informing government agencies, including Australian, globally on intervention options in other parasite-endemic communities.

Development of CRISPR based technology in schistosome bloodflukes.

Supervisor:
Dr Hong You

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This project is suitable for an Honours, Masters, MPhil, MD, or PhD student.

BACKGROUND

Schistosomiasis is a serious global problem and the second most devastating parasitic disease after malaria. Currently, there is no effective vaccine available and treatment is entirely dependent on praziquantel chemotherapy, which raises significant potential threat to public health should drug resistance develop. The paucity of molecular tools to manipulate schistosome gene expression has made an understanding of genetic pathways in these parasites difficult, increasing the challenge of identifying new potential drug and vaccine candidates.

AIMS

- We aim to develop a CRISPR (clustered regularly interspaced short palindromic repeat)- mediated gene editing system in schistosomes for better understanding gene function, providing a powerful approach in the identification of new drug and vaccine targets and the unravelling of potential drug resistance mechanisms.
- We will develop fast, accurate, easy-to-use and low-cost diagnostic tools by using CRISPR/Cas12 and Cas13 based system, for the diagnosis of schistosomiasis, strongyloidiasis, hookworm and other neglected tropical diseases.

PROJECT POTENTIAL

CRISPR-based genome editing in schistosomes has the potential to revolutionise functional genomics by addressing existing technical challenges. It enables

novel drug discovery and provides critical insights into the mechanisms of drug resistance. Additionally, the development of CRISPR-based diagnostic tools for various helminths aligns with the urgent WHO need for ultra-sensitive, portable, point-of-care technologies. These tools can facilitate rapid disease mapping, enhance the monitoring of helminth control programs, and support the assessment of elimination targets.

Innovative point-of-care diagnostic tools for schistosomiasis mansoni.

Supervisor:
Dr Pengfei Cai

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This project is suitable for an Honours and Masters student.

BACKGROUND

Schistosomiasis is a severely debilitating and often fatal chronic parasitic disease. Caused by agents of the genus Schistosoma, it afflicts more than 200 million people worldwide. Sub-Saharan Africa accounts for 93% of the world cases of schistosomiasis. The two main Schistosoma species affecting people in Africa are Schistosoma haematobium and Schistosoma mansoni. By identifying communities with accurate schistosomiasis prevalence, diagnostic tests could help guide the allocation of resources and interventions to where they are needed most. Affordable diagnostic tools for rapid mapping of schistosomiasis in the context of integrated control programmes in Africa thus are urgently needed.

AIMS

- Develop molecular-based POC assays will be via combining rapid DNA extraction, multienzyme isothermal rapid amplification (MIRA) and Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) with a CRISPR-associated protein 12a (Cas12a) system.
- Develop immunological POC tests through antigen screening and incorporating the best antigen into lateral flow immunoassays (LFIAs). Both assays will be assessed with human clinical samples collected from S. mansoni endemic areas in Uganda. To serve as a reference test for both POC assays, qPCR assay will be performed on DNA extracted from the Uganda human faecal samples using commercial kits.

PROJECT POTENTIAL

If successfully developed and deployed, both POC assays will have a significant impact on the monitoring aspect of parasitic control programs, with potential to replace the far less sensitive Kato-Katz procedure currently used to facilitate the control of schistosomiasis mansoni in endemic areas.

Emerging Viral Diseases

Team Head:
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qimrb.edu.au/researchers-and-labs/emerging-viral-diseases

The Emerging Viral Diseases Laboratory focuses on deciphering the molecular mechanisms underlying viral infection and disease, as well as developing effective interventions to combat emerging viral pathogens. Emerging viruses include newly identified viruses, such as SARS-CoV-2, as well as previously known viruses that are experiencing a rapid rise in incidence or geographic range, such as Japanese encephalitis virus (JEV), Chikungunya virus (CHIKV), and Oropouche virus (OROV).

The Emerging Viral Diseases Laboratory has three core research themes:

- Discovering the molecular mechanisms of viral replication and virus-host interactions for the development of antivirals.
- Defining pathogenic versus protective virus-induced inflammation for the development of new anti-inflammatories.
- Development and pre-clinical evaluation of new vaccines.

The Emerging Viral Diseases Laboratory focuses on four emerging viral genera:

- Orthoflaviviruses (Japanese encephalitis, Murray Valley encephalitis, Zika, Dengue, and West Nile viruses);
- Alphaviruses (Chikungunya, Ross River, Mayaro, Getah, and O'nyong'nyong viruses);
- Orthobunyaviruses (Oropouche and Akabane viruses);
- Coronaviruses (SARS-CoV-2).

Mosquito Control

Academic Lead:
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There are no effective vaccines against malaria or most arboviruses. There are no chemotherapeutants for the treatment of arbovirus infection. Mosquito surveillance, management and manipulation remain the mainstays of most mosquito-borne disease control programs. The Mosquito Control Laboratory (MCL) manages state-of-the art pathogen and insect containment facilities with the capacity to undertake studies on all aspects of vector biology and disease transmission. We work on innovations in mosquito surveillance and control that might help interrupt parasite and pathogen transmission.

We are unique in the Southern Hemisphere with regard to our size, capacity and expertise. This makes us a key partner in a national, regional and international network. Our presence significantly enhances Australia's ability to investigate emerging vector-borne disease threats in the region. A major remit of MCL is to exploit our unique facility through building strong collaborative links with parasitology, virology and vector biology laboratories throughout the world.

The MCL has permission to hold a number of exotic mosquito species in addition to native Australian mosquitoes. These include insecticide-resistant and susceptible Aedes aegypti strains, Aedes albopictus and Anopheles stephensi. The MCL is able to perform mosquito vector competence assessments for globally emerging arboviruses, including dengue, Japanese encephalitis, Zika and chikungunya viruses, and for locally transmitted viruses; including Ross River and Barmah Forest viruses. We have field work in progress in Asia, the Pacific, and the Americas.

Mosquito-borne disease transmission in a changing world.

Co-Supervisor:
Dr Brian Johnson

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BACKGROUND

In recent decades, arthropod-borne viruses (arboviruses) have emerged or re-emerged as human and animal pathogens with important implications for public health. These include dengue, Zika and chikungunya viruses, which circulate between humans and the urban mosquitoes, Aedes aegypti and Aedes albopictus, as well as zoonoses with complex transmission pathways that involving multiple vectors and vertebrate hosts. These include Japanese encephalitis virus (JEV), Murray Valley encephalitis virus (MVEV) and Ross River virus (RRV).

We are particularly interested in incriminating transmission pathways, and the factors that drive human spill-over for JEV, MVEV and RRV. The former is vaccine preventable, but in Australia we do not know where and when to target vaccination campaigns because the disease is highly unpredictable in its spatial and temporal prevalence. MVEV is endemic to Australia and Papua New Guinea, but in this case there are no vaccines or therapeutants for a disease whose appearance is also impossible to predict across regions or years. Both MVEV and JEV are deadly and untreatable in a small proportion of human cases. RRV is Australia's commonest mosquito-borne disease (ca 5000 cases per annum) causing debilitating arthritogenic symptoms. It has caused explosive epidemics in the Pacific countries and territories, involving > 100,000 human cases. Recent sero-surveys suggest that it may now be endemic across the Pacific and that transmission is becoming more common in urban Australia.

Globally, anthropogenic and ecological changes, particularly those related to climate and extreme weather events, may increase vector and host prevalence, expose new reservoirs to infection or induce arboviruses to adapt to new maintenance cycles. These factors may favour the emergence and spread of human zoonotic infectious diseases. Detailed studies on JEV, MVEV, RRV, and their vectors and its hosts are required to 1) track the diversity and evolution of viruses across habitats, 2) understand their key transmission dynamics, and 3) determine the risks of human spill-over.

OBJECTIVES

- Demonstrate how new surveillance technologies (mosquito trapping, and molecular xeno-monitoring) can incriminate vectors and vertebrate reservoirs of disease.
- Identify key pathways of arbovirus transmission and human spill-over in urban and rural environments in Australia.
- Apply these new insights to prioritise future research and to target interventions (i.e. health communication, insecticidal control, and vaccines).

SUB-OBJECTIVES

- Gain a fine-scale understanding of how specific virus variants emerge, spread and dominate particular habitats.
- Support the longitudinal collection and identification of mosquitoes (including blood-fed individuals) and vertebrates around areas associated with virus transmission.
- Employ a range of diagnostic tools (serology of mosquito blood meals, metabarcoding and virus sequencing of trap collections) to identify transmission pathways.
- Application of modelling techniques (SIR or matrix models) to explore the impacts of different vectors and hosts on transmission.

PROJECT POTENTIAL

- This work will draw on recent developments in arbovirus surveillance, molecular xeno-diagnostics, and risk mapping to define key transmission pathways (virus variants, habitat, vectors and reservoirs) for mosquito-borne zoonoses.
- The resulting "toolbox" of methods, and their interpretation, will have relevance for risk prediction and control campaigns.
- The project is pertinent, not only for Australia, but for the emergence of zoonotic arboviruses in the Pacific.

Scabies

Senior Group Leader:
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Scabies is one of the most common infectious skin disorders worldwide, particularly among children and in tropical regions. In Aboriginal and Torres Strait Islander communities of remote northern Australia, scabies prevalence is high and there are extreme rates of scabies-associated streptococcal and staphylococcal infections.

Scabies mites are host-specific, 'obligatory' parasites without environmental reservoirs. Chemotherapy is the only way to combat scabies and its transmission in humans. There is no vaccine and the broad-spectrum anti-parasitic drugs available fail to control the disease.

Emerging mite resistance against leading drugs is of growing concern. Another problem is diagnosis. There are numerous skin conditions with similar symptoms but no reliable, simple methods to detect scabies. This makes efficient therapy, management and surveillance at individual, household and community levels very difficult.

Novel drugs and diagnostic tools to treat scabies are urgently needed. A central challenge is to comprehend mite biology and scabies pathogenesis, which are poorly understood, resulting in a lack of knowledge of specific drug targets in the parasite.

The Scabies Laboratory is focused on understanding the molecular interactions of scabies mite molecules with host defence systems in the skin. The group, which has been working on scabies since the early 2000s, aims to develop new options for reducing scabies incidence and improving disease outcomes.

Disease mechanisms, novel therapeutics and molecular diagnostics for scabies.

Co-Supervisor:
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This project is suitable for an Honours, Masters, or PhD student, who will learn a wide range of molecular biology techniques, protein technology, including protein expression and purification techniques, microscopy, animal work and more.

Scabies and associated co-infections cause substantial illness and a major health burden in Indigenous communities of Northern Australia. In particular scabies-caused childhood pyoderma (bacterial skin infection) can cause severe complications in later life. Scabies-associated Streptococcus infections for example, significantly contribute to an immune complication of streptococcal infection that can leads to heart and kidney disease (rheumatic heart disease and post-streptococcal glomerulonephritis).

Diagnosis of scabies relies mostly on epidemiological and clinical algorithms rather than pathogen detection. Incorrect diagnosis can result in rapid community transmission and pathology exacerbation. New scabicides are urgently needed, as current drugs often fail because they do not kill parasite eggs and/or have short half-lives. Drug resistance is emerging.

Several research projects are underway in our laboratory:

- Recognising the health risk of scabies-associated pathogens, we have commenced dissecting the link between scabies and bacterial infections at a molecular level and we lead the international scabies microbiome program to define the impact of scabies on the healthy skin flora and examine the synergy between mites and bacteria.
- Drug resistance is an emerging problem in controlling the mites (causing scabies) and the bacteria (causing secondary infections). Our current research program combines cutting-edge basic research and unique pre-clinical studies, to compare the efficacy of several new candidate drugs that kill all stages of the scabies parasite including eggs to develop new candidate drugs.
- Early and accurate diagnosis of scabies is critically important, as it can help prevent transmission and/or stop scabies outbreaks, it can improve the effectiveness of treatment and clinical management and avoid long-term disease complications in patients. Inappropriate treatment of undiagnosed scabies can cause further serious disease and contribute to emerging parasite resistance. For these reasons, we are developing the first Scabies Rapid Antigen Test (RAT) System for Point-of-Care.
- Understanding the molecular mechanisms underpinning this disease is crucial to the development of diagnostics, treatments and cures. Therefore, we are also studying key aspects of mite biology and scabies pathogenesis. These more basic research projects are for example aimed at understanding the skin immune modulation by the parasitic mites or the severe itching, which is the main debilitating symptom of scabies infection. We have generated comprehensive integrated multi-omics databases from which we hope to identify and analyse molecular mechanisms unique to scabies. We have a powerful in vivo model and supporting technologies for pre-clinical work. We collaborate nationally and internationally with researchers and clinicians with a wide range of expertise.

Our program was developed in consultation with consumers and in response to concern over persistent high rates of scabies in remote A&TSI communities across Australia.

Translational and Human Immunology

Group Leader:
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The Translational and Human Immunology Laboratory focuses on understanding the mechanisms that regulate human immune responses in health and disease. We have a keen interest in understanding how persistent viral infections contribute to a range of diseases, including autoimmune diseases and cancer. We aim to develop a deep understanding of differences in our immune systems that contribute to the susceptibility to different viral-associated diseases. Knowledge gained from these studies forms the basis for developing novel immune interventional and diagnostic strategies that can implemented in clinical settings.

Tumour Immunology

Distinguished Scientist:
Professor Rajiv Khanna

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The major goal of the Tumour Immunology Laboratory is to obtain a deeper understanding of the mechanisms by which an immune response to tumours may be generated, augmented and applied to the inhibition of tumour growth. The members of this laboratory share the expectation that such insight will be applicable to the treatment and/or prevention of cancer.

Cellular immunotherapy – engineering "custom built" cells to treat cancer.

Co-Supervisor:
Dr Paulo Martins

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This project is suitable for a Masters or PhD work and is flexible for clinical students.

BACKGROUND

Current standard approaches for the treatment of human cancers typically employ broad acting radiotherapeutic and chemotherapeutic approaches. There has been growing interest in approaches using immunotherapy with adoptive cell transfer (ACT): using the patient's immune cells to treat their cancer.

A specific type of ACT uses chimeric antigen receptors (CARs). These are genetically engineered molecules, which are custom built to specifically target protein antigens expressed on malignant cells. There are multiple FDA-approved CAR T cell-based therapies. CAR19 treatment, of children with relapsed or refractory acute lymphoblastic leukaemia (ALL), and of adults with advanced lymphomas, has demonstrated remarkable success and complete remission in some patients. Although approved therapies are limited to blood cancers, a growing number of CAR T cell therapies are being developed and tested in clinical studies in multiple solid tumours. There are promising clinical data targeting tumour-associated antigens in melanoma, lung, liver, breast, and brain cancers.

There are major differences between CAR therapies, mostly at the tumour-antigen recognition site, but CARs share similar components known as signalling domains that can affect the cells' overall function, such as their ability to produce more cells after infusion into the patient (expansion), and to survive longer in circulation (persistence). The ability to manipulate these domains to custom build CAR T cells to specifically target certain tumours, and avoid toxicity, is critical for the success of CAR T cell therapy.

AIM

The CAR T cell program at the Tumour Immunology Laboratory aims to design and test novel CAR T cell therapies for virus-associated cancers. We have designed a CAR T cells which targets a glioblastoma (GBM)-specific antigen, EphA3, that is has been tested for the treatment of GBM, an aggressive form of brain cancer (Martins et al., 2024).

In our clinical trial of ACT to treat GBM (Smith et al., 2020) we identified a distinct T cells expression signature associated with favourable long-term survival of GBM patients, The project will use this knowledge and expand the potential of the EphA3-specific CAR T cells. We will customise these products and ultimately build a CAR better suited for the treatment of GBM.

Hepatic Fibrosis

Deputy Director and
Chief Scientist, Group Leader:
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The Hepatic Fibrosis Laboratory investigates the cellular and molecular mechanisms of scar tissue formation in the liver. This leads to fibrosis and cirrhosis in adult liver diseases such as haemochromatosis and in children in diseases such as cystic fibrosis and biliary atresia. If left untreated chronic liver disease can lead to liver cancer.

MicroRNAs as anti-fibrotic agents to treat liver scarring, fibrosis and cirrhosis in chronic liver disease.

This project can be adapted to suit an Honours, PhD, or clinical student.

Virtually all biological processes in eukaryotic cells are regulated by microRNAs that control protein-coding gene expression. Our laboratory has identified a number of different microRNAs that regulate the expression of collagen in liver disease and that can be manipulated to control liver scarring or fibrosis. This project is designed to generate novel, chemically

modified microRNAs that can be used as anti-fibrotic therapeutics to treat hepatic fibrosis and thus control the development of cirrhosis and liver cancer in patients with chronic liver disease.

Anti-inflammatory small molecule inhibitor development to control liver inflammation associated with hepatic fibrosis in chronic liver disease.

This project can be adapted to suit an Honours, PhD, or clinical student.

Inflammation is integral in driving early liver scarring (fibrogenesis). The association between hepatic inflammation and circulating ferritin levels in chronic liver disease is well known. However, rather than simply acting as a marker of inflammation, our research has demonstrated that the H-subunit of Ferritin (FTH), released upon hepatocellular injury, actually mediates inflammation. This project will utilise state-of-the-art molecular modelling techniques to identify FTH binding sequences on cell surface receptors we have identified on liver fibroblasts that signal to the nucleus to produce pro-inflammatory cytokines. Therapeutic small molecule inhibitors will then be developed to treat chronic liver disease-inducing hepatic inflammation.

MOTiF: Mechanisms of toxicity in multi-organ fibrosis.

External supervisor:
Associate Professor Helen Healy

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External supervisor: Dr Andrew Kassianos

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This project can be adapted to suit an Honours or PhD student.

BACKGROUND

Exposure to toxic insults (carcinogens, poison, drug overdose) is an everyday event. At the cellular level, it triggers acute injury pathways of cell death and inflammation across multiple solid organs (liver, kidney). Rapid recovery is common and is seen in most people. However, the recovery pathway in a significant proportion of people is maladaptive, characterised in the liver and kidney by scarring (fibrogenesis). This project tests the proposition that maladaptive repair in two solid organs is indistinguishable at the cellular and molecular level. The findings will provide important evidence of efficacy for anti-fibrotic agents beyond a single organ system.

APPROACH

To identify the common pro-fibrotic molecular signals in the cellular pathways that trigger toxin-induced scarring in liver and kidneys.

PROJECT POTENTIAL

The study will use an unbiased multi-omics 'biomarker discovery' platform to identify the key signalling mechanisms (exosomes, genes, small RNA, proteins, metabolites) that trigger toxin-induced scarring in liver and kidneys. Data will be generated in established clinical/experimental models, including:

- Human kidney tissue (biopsies from patients with toxin-induced acute kidney injury);
- In vitro models of liver (primary murine hepatic stellate cells) and kidney (primary human kidney tubular cells) fibrosis, and
- A murine model of multi-organ liver-kidney fibrosis (thioacetamide-induced toxicity);
- The discovery of novel biomarkers will guide next-phase check-point therapeutic targeting in these toxin-induced fibrosis models.

TECHNOLOGIES

- Spatial multi-omics (RNA-seq, miRNA scope, proteomics, metabolomics);
- Extracellular vesicle and multi-omic profiling;
- Multi-parameter immuno-fluorescent microscopy;
- In vitro and in vivo check-point targeting.

OUTCOME

The study will generate a functionally validated set of biomarkers activated in toxin-induced liver and kidney fibrosis, guiding future clinical therapeutic translation to patients at presentation that will prevent long-term outcomes of multi-organ scarring.

Molecular Nutrition

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The Molecular Nutrition Laboratory studies the processes responsible for nutrient homeostasis and how they relate to health and disease. We focus predominantly on disorders of iron homeostasis and we are passionate about improving the health of people with iron-related conditions, such as iron deficiency and the iron loading disorder hereditary haemochromatosis, both of which affect a surprisingly high number of Australians. In fact, iron-related disorders represent

some of the most common conditions affecting humans worldwide. In the Molecular Nutrition Laboratory, we are working hard to understand the molecular basis of these disorders and to use this knowledge to develop better treatments for affected individuals.

Iron homeostasis during pregnancy and the effect of iron supplements.

This project is suitable for a PhD student.

BACKGROUND

Adequate dietary iron intake is vitally important during pregnancy as the consequences of iron deficiency at this time can be severe. Complications can include pre-term delivery, intrauterine growth restriction and irreversible neurological damage in the developing infant. With a recent study suggesting that a staggering 60-70% of pregnant women in Australia are iron deficient, it is not surprising that oral iron supplements are widely consumed.

What is surprising, however, is that the effect of such supplements has not been well studied, and while the benefits of supplementation on maternal iron stores and haemoglobin levels are well accepted, any benefit to pregnancy outcomes and fetal development is less evident, with many studies showing little or no improvement in a range of parameters, including prematurity and birth weight. In addition, the supplementation of iron replete pregnant women has been shown to be detrimental to both maternal and infant health, increasing the risk of both preterm delivery and small for gestational age births.

AIM

To investigate how iron homeostasis is regulated during pregnancy and to determine the effect of various forms of iron supplementation, with particular emphasis on the placenta and fetus.

PROJECT POTENTIAL

With iron deficiency affecting so many pregnant women, it is critical that we determine the cause of these effects so that optimal supplementation regimens can be implemented to reduce the prevalence of iron deficiency and maximise the health and safety of both mother and infant.

Iron homeostasis in developing red blood cells.

This project is suitable for a PhD student.

BACKGROUND

Most of the iron in the body is contained within red blood cells in the form of haemoglobin, which is important for the transport of oxygen around the body. During development, red blood cells must have a highly efficient iron uptake pathway to obtain sufficient iron for haemoglobin synthesis. While many proteins involved in this pathway have been identified, recent data from our laboratory has shown that our understanding of this process is incomplete, particularly in utero. Many red blood cell disorders also detrimentally affect systemic iron homeostasis, although, again, the molecular pathways are not completely understood.

AIMS

There can be a range of aims associated with this project, broadly split into the following:

- Determining the molecules involved in red blood cell iron uptake in adulthood and during development.
- Investigating how red blood cell development affects whole body iron homeostasis.

PROJECT POTENTIAL

Many red blood cell disorders are associated with pathological changes in iron homeostasis. A greater understanding of how developing red blood cells handle iron, and the associated effects on systemic iron levels, could lead to the development of more effective treatments for these conditions.

The regulation of body iron homeostasis.

This project is suitable for a PhD student.

BACKGROUND

Human conditions with disrupted iron homeostasis are very common and most involve the inappropriate production of the peptide hormone hepcidin, which regulates body iron metabolism. Hepcidin is produced by the liver and secreted into the bloodstream where it acts as a negative regulator of intestinal iron absorption and storage iron release. Prominent examples of conditions associated with altered hepcidin production are the anaemia of inflammation and the iron loading conditions hereditary haemochromatosis and β-thalassaemia.

AIMS

To investigate the pathways regulating hepcidin production and to develop ways to manipulate these pathways to treat disorders of iron homeostasis.

PROJECT POTENTIAL

Inherited iron loading disorders, such as hereditary haemochromatosis and β-thalassaemia, represent some of the most prevalent genetic disorders known and the anaemia of inflammation is the most frequent anaemia in hospitalised and chronically ill patients. The development of new treatments for these conditions would have a major impact on the quality of life for those afflicted with these disorders.

Mucosal Immunology

Team Head: Associate Professor Severine Navarro

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The Mucosal Immunology Laboratory seeks to develop innovative treatments for inflammation and chronic illnesses, like allergies, asthma and inflammatory bowel diseases, with a particular focus on children. We work in collaboration with other academics, clinicians, paediatricians, dietitians, chemists, and computational biologists to translate our efforts to the clinic and bring our findings to the public. We are interested in the mechanisms of immune dysregulation, the role of the microbiome and its interaction with the different immune compartments to understand disease onset.

Investigation of a hookworm-derived tolerogenic protein to induce immune tolerance.

This project is suitable for a Masters, Honours, or PhD student.

BACKGROUND

Allergy is a major global health issue, especially in children, with no cure available. Allergy arises from defects in immune tolerance, our body's way of discerning microbiological friend from foe. We recently discovered a novel protein, AIP-2, which can restore immune tolerance and thus prevent the onset of allergy.

AIM

Our goal is to understand how AIP-2 achieve this, which would not only advance the field of immune tolerance but help to translate AIP-2 to the clinic.

METHODS

In this project, students will help decipher the molecular mechanisms of AIP-2, using techniques in the following areas: cell culture, flow cytometry, molecular cell biology, metabolic biochemistry and/or systems biology (single cell / single nuclei RNAseq, Spatial transcriptomics) and modelling.

PROJECT POTENTIAL

Experience with drug development and translation; work with human tissues, computational biology and modelling.

Solving "obesogenic memory" in human adipose tissues and organoids.

This project is suitable for a Masters, Honours, or PhD student.

BACKGROUND

Obesity is a risk factor for many chronic diseases, including heart disease, diabetes, and various cancers. Current strategies to reduce obesity, including dieting, bariatric surgery or Ozempic, have been hampered by the body's natural tendency to regain weight. A recent discovery showed weight regain is caused by an 'obesogenic memory' imprinted onto adipose (fat) tissue. Specifically, this involved epigenetic modifications in both adipocytes and immune cells within the adipose tissue.

AIM

Our goal is to address the knowledge gaps required to translate this breakthrough into new therapies.

METHODS

To achieve this, students will use techniques in the following areas: cell culture, organoid engineering, molecular cell biology, metabolic biochemistry, rodent work [optional] and/or systems biology (single cell / single nuclei RNAseq, Spatial transcriptomics) and modelling.

PROJECT POTENTIAL

Experience with drug development and translation; work with human tissues, computational biology and modelling.

Respiratory Immunology

Senior Group Leader: Professor Simon Phipps

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The Respiratory Immunology Laboratory focuses on identifying pathogenic pathways that underpin the onset, progression, and exacerbations of asthma and chronic obstructive pulmonary disease. To achieve this, high-fidelity pre-clinical models of disease are developed that recapitulate key gene-environment interactions and allow for elucidation of cellular and molecular mechanisms. Where possible, scientific findings are translated with ex vivo model systems using primary human cells and by analysing clinical material.

Insights into the influence of a maternal high-fat diet on infant susceptibility to severe lower respiratory tract infections.

This project can be adapted in scope and is suitable for an Honours, MPhil, or PhD student.

Viral bronchiolitis is an infection of the small airways (bronchioles) characterised by the infiltration of neutrophils, oedema, and shedding of the epithelial cells that line the airway. A recent population study found that the offspring of mothers who ate a poor diet in the third trimester were predisposed to severe viral bronchiolitis. We have modelled this association in mice, and established that the maternal diet affects the nascent microbiome in the offspring and associated immune development. This project will explore the cellular and molecular mechanisms by which the microbiome affects immune development and susceptibility to infection in the lungs.

Understanding the mechanisms by which the assembling neonatal microbiome promotes neonatal immune development.

This project can be adapted in scope and is suitable for an Honours, MPhil, or PhD student.

The microbiome is known to affect immune development. For example, germ-free mice have fewer Peyer's patches in the gut wall, suggesting that the gut microbiome regulates the formation of this lymphoid tissue. Other studies have shown that germ-free mice have fewer natural killer T cells. Both the microbiome and the immune system develop post-nataly (predominantly if not exclusively), and there is considerable bi-directional crosstalk. In this project, we will study this relationship, with a focus on the seeding of innate lymphoid cells in mucosal tissues such as the gut and the lungs.

Clinical Malaria

Group Leader:
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The focus of the Clinical Malaria Laboratory is the evaluation of the safety and efficacy of candidate antimalarials, using the induced blood stage malaria (IBSM) model in healthy human volunteers. Developed by the previous group leader Professor James McCarthy, the model has been used to evaluate 10 investigational medicinal products. Models have been established for an artemisinin-sensitive and an artemisinin-resistant P. falciparum strain, and other Plasmodium species including P. vivax and P. malariae. The model has also enabled the conduct of studies to evaluate transmission-blocking interventions, and has enabled the conduct of exploratory studies to evaluate immunological and pathophysiological response to infection.

Immunopathology

Team Head:
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The Immunopathology Laboratory is focused on understanding the cellular and molecular mechanisms that drive immune-mediated pathologies. Our recent focus is on adaptive immune polarisation following allogeneic stem cell transplantation and its influence on graft versus host disease (GVHD).

Designing better T cells for use in stem cell transplantation.

This project can be adapted in scope and is suitable for an Honours, Masters, MPhil, or PhD student.

BACKGROUND & HYPOTHESIS

Donor stem cell/bone marrow transplantation (allo-SCT/BMT) is an important curative therapy in the treatment of blood cancers, however its application is limited by serious complications such as graft-versus-host disease (GVHD) that have a significant impact on patient mortality and quality of life. Early inflammatory responses during preparative transplant conditioning initiate a cascade of adaptive immune responses that manifest as acute and/or chronic tissue damage in >50% of transplant recipients.

GVHD treatment options are relatively limited and focused on immunosuppression and steroidal therapy, which are problematic due to opportunistic infection and refractory disease, therefore new therapies are urgently needed. Donor-derived T cells are known to be the key drivers of GVHD pathology but are also critical to maintain ongoing anti-tumour immunity, also known as Graft-versus-leukaemia (GVL) effects, which prevent cancer relapse in these patients. Identifying novel ways to target GVHD whilst maintaining GVL is key to improving patient outcomes. We propose that in vivo screening of potential therapeutic targets via manipulation of donor T cells pre-transplant will accelerate therapeutic development in this area.

AIM

In this study, we will utilise recent advances in CRISPR-mediated gene therapy to modulate T cell function in naïve primary T cells for allo-SCT.

APPROACH

This will involve optimisation, testing and validation of CRISPR gene editing of novel targets in naïve mouse T cells in vitro prior to transplant into allogeneic mice.

PROJECT POTENTIAL

Students will develop new skills in techniques relevant to immunology research such as immune cell isolation, gene modification and exposure to in vivo models of inflammatory disease. This research has the potential to develop novel treatment approaches for blood cancer patients.

Molecular Virology and Viral Therapeutics

Group Leader:
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We investigate dengue and SARS-CoV-2 virus replication. Our dengue and SARS virus research includes development of novel inhibitors called defective interfering particles.

We have uncovered and developed defective interfering RNAs (DI RNA) from dengue virus and SARS-CoV-2.

DI RNAs are created by RNA viruses due to replication errors, resulting in incomplete viral genome copies lacking crucial replication genes. DI RNAs block parent virus replication in several ways:

- They compete for limited host cell resources, such as enzymes and nucleotides.
- They obstruct replication by serving as a template for RNA synthesis, generating more DI RNAs instead of viral genomic RNA.
- DI RNAs hinder viral particle assembly and release, and their innate immune responses.

We've created virus-like particles called DIPs and nanoparticles to deliver DI RNA, inhibiting virus growth in cells and animal models of human viral diseases. Our goal is to develop potent antiviral agents based on DI RNA to reduce virus spread and disease.

Cardiac Bioengineering

Senior Group Leader:
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The Cardiac Bioengineering Laboratory aims to develop state-of-the art bioengineering approaches for human myocardium. The team uses our screening platforms in house, in collaboration with research partners, and together in industry partnerships for a variety of different discovery science and therapeutics development applications. These include understanding the mechanisms of cardiac maturation, interactions between different cell populations in the heart, the role of metabolism in maturation and regeneration and development of new therapeutics for patients to prevent heart failure.

Cardiac Drug Discovery

Team Head:
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The Cardiac Drug Discovery Laboratory aims to develop new drugs to treat cardiac fibrosis and heart failure by understanding the signalling networks that regulate heart function. Our lab uses classical pharmacology and cell signalling approaches with an innovative combination of cutting-edge 'omics and advanced microscopy in human heart tissue and stem cell-derived human cardiac organoids.

Our team's work is driven by a major unmet need, as one in three deaths in Australia are due to cardiovascular disease. In particular, heart failure has become a major clinical burden and this is only expected to worsen in our aging population. We have a particular focus on cardiac fibrosis, observed in >90% of heart failure patients, which is characterised by excessive production of extracellular matrix proteins that can prevent the heart from contracting effectively. However, the mechanisms that regulate these processes are unclear and there are currently no effective treatments for cardiac fibrosis.

Decoding extracellular matrix protein heterogeneity in cardiac fibrosis using 3D cardiac organoids.

This project can be adapted in scope and is suitable for an Honours, Masters, MPhil, or PhD student.

BACKGROUND

Cardiac fibrosis is a common feature observed in heart failure patients. Fibrosis is often defined as the excessive production of extracellular matrix (ECM) proteins, which negatively impact the ability of the heart to contract and relax. As fibrosis is so common in heart failure patients, it is a promising target for therapies. However, development of antifibrotic treatments is a huge challenge as we do not fully understand the signalling pathways that drive fibrosis.

One of the main goals of the Cardiac Drug Discovery Laboratory is to improve our understanding of what exactly fibrosis is and how it develops. Using human cardiac organoids – a live contracting 3D model incorporating many important heart cell types, including cardiomyocytes and fibroblasts – we have established a model for cardiac fibrosis. By treating these organoids with profibrotic mediators, we can study how this impacts gene and protein expression, signalling and importantly, cardiac function. This work has led us to discover that different profibrotic stimuli lead to different functional and ECM changes, highlighting that fibrosis is highly heterogeneous.

AIM

This project aims to further tease apart how cardiac dysfunction and ECM changes are interconnected.

METHOD

This project involves laboratory experiments using profibrotic stimuli on human cardiac organoids (hCOs), together with functional analysis, immunohistochemistry, microscopy (light, fluorescence and confocal) and mass spectrometry-based proteomics.

PROJECT POTENTIAL

This project will improve our understanding of the fundamental mechanisms that are involved in the development of cardiac fibrosis, which may have major implications for antifibrotic treatment strategies.

Establishing how contraction modulates fibrotic remodelling and ECM homeostasis.

Co-Supervisor:
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This project can be adapted in scope and is suitable for an Honours, Masters, MPhil, or PhD student.

BACKGROUND

The pathophysiology of heart failure is highly complex and different risk factors including inflammation, high blood pressure, myocardial infarction and diabetes contribute to disease development and progression. Despite different aetiologies, fibrosis is a common feature in >90% of heart failure patients, marked by excessive production of extracellular matrix (ECM) proteins. Presumably, the ECM remodelling negatively impacts the ability of the heart to contract and relax. In our lab, we make use of human cardiac organoids (hCOs), a live contracting 3D model incorporating many important heart cells, including cardiomyocytes and fibroblasts. We can stimulate these organoids with profibrotic mediators to investigate how they influence gene and protein expression, signalling and cardiac function. For this project, we are interested in how cardiac contraction interacts with pro-fibrotic signalling. Preliminary results have shown that different pro-fibrotic stimuli induce functional changes within 1 hour of treatment, well before ECM remodelling occurs. It is unknown how these processes are linked. As an extension of this idea, we are interested in whether functional unloading (reducing contractility) can reverse ECM remodelling in the hCOs. Mechanical unloading in heart failure patients using a left ventricular assist device has been found to allow for some level of tissue remodelling. However, little is known about the mechanisms driving this response.

AIMS

This project has two aims:

- Assess if cardiac dysfunction induced by profibrotic mediators contributes to the fibrotic ECM phenotype.
- Model the functional unloading response in the hCOs using contraction inhibitors to assess ECM remodelling.

METHOD

This project will use human cardiac organoids to model the fibrotic ECM response following treatment with profibrotic stimuli. Contraction inhibitors will be used to interfere with hCO function after which functional and

immunofluorescent protein detection analysis (using light and fluorescence microscopy) will be used to gain insights into the ECM remodelling.

PROJECT POTENTIAL

There are many unknowns about the development of cardiac fibrosis and how ECM remodelling is regulated. This project will help us better understand the fundamental regulators of cardiac fibrosis. This knowledge could aid the identification of therapeutic targets and future development of antifibrotic therapies.

Exploring metalloprotease and extracellular matrix dynamics in cardiac fibrosis.

Co-Supervisor:
Dr Harley Robinson

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This project can be adapted in scope to suit a winter and summer undergraduate course, or Honours, or PhD students.

BACKGROUND

Cardiac fibrosis is often defined as the excessive production of extracellular matrix (ECM) proteins, which negatively impact the ability of the heart to contract and relax. Alongside production, the ECM undergoes extensive remodelling facilitated by metalloproteases and other ECM modifying enzymes, leading to changes to matrix crosslinking, structure and ultimately quality. Using human cardiac organoids – a live contracting 3D model incorporating many important heart cell types – we have established a model for cardiac fibrosis to monitor these changes. We have also discovered that different pro-fibrotic drivers will elicit divergent changes in ECM components and contractile outcomes. These findings suggest that ECM quality may be governing irregular contraction rather than matrix protein quantity.

AIM

This project aims to investigate the nuances of ECM production and degradation during cardiac fibrosis-related tissue remodelling.

METHOD

The first part of this project involves bioinformatics analysis on the extensive RNA sequencing datasets already generated in the lab and through publicly available sources. We will use these data to define enzyme expression changes during the development of cardiac fibrosis. Depending on the duration of the project, these regulatory targets will be experimentally modulated using human cardiac organoids followed by functional analysis, mass spectrometry-based proteomics and advanced microscopy techniques to monitor ECM remodelling. As an extension of this work, we may have the opportunity to cross-validate these organoid studies with fibrotic human and/or mouse heart proteomics.

PROJECT POTENTIAL

This project will improve our understanding of the fundamental mechanisms that are regulating ECM during the development of cardiac fibrosis, which may pave the way for future anti-fibrotic treatment strategies.

Lung Inflammation and Infection

Honorary Group Leader:
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A major focus of the Lung Inflammation and Infection Laboratory is to investigate the interaction between bacterial pathogens and the host innate immune response within the lung. Chronic respiratory diseases characterised by chronic infection are highly prevalent in Australia and globally.

We are especially interested in the role of iron and other biologically active metal ions in promoting bacterial infection in the lungs of patients with the genetic disease cystic fibrosis (CF) and other suppurative lung diseases. To do this, our group is studying bacterial and host immune system interactions in vivo using a number of biochemical, molecular and cell imaging methods and also modelling these interactions using mouse models.

Using this knowledge, we aim to develop more targeted treatments that are widely applicable to many severe chronic airway diseases, including asthma, chronic obstructive pulmonary disease and idiopathic pulmonary fibrosis.

Investigating the effect of iron overload in a murine model of cystic fibrosis.

This is suitable for an Honours student.

BACKGROUND

Cystic fibrosis (CF) is a genetic disorder caused by mutations in the cystic fibrosis transmembrane regulator (CFTR) gene, which impairs chloride transport across cells and leads to the excessive secretion of sweat and mucus, particularly affecting the lungs. As a result, CF lungs are highly susceptible to chronic bacterial infections, which contribute to disease exacerbations. Elevated iron levels have been observed in the airways of CF patients, and this iron overload is associated with increased bacterial infections Iron is a biologically active metal required for normal physiological processes, but it can also produce damaging reactive oxygen species that may contribute to disease pathogenesis. We have a mouse model of CF (CftrG551D/G551D) that has been treated with iron dextran to mimic human disease. CF animals have also been crossed with Hemochromatosis mice, a genetic model of iron overload caused by mutations in the HFE gene, to determine how the presence of these mutations also contribute to disease phenotype.

AIMS

- Quantify iron and mediators of iron homeostasis in lung, liver and spleen tissue;
- Investigate immune responses to changes in iron levels;
- Investigate the microbiome and effect of iron and HFE mutations on the microbiome.

APPROACH

To achieve this aim, we have already collected tissues, serum, and Broncho alveolar lavage fluid (BALF) from G551D CFTR mutant mice and wild-type (WT) controls. These samples will undergo a range of analyses, including protein and gene expression studies, histology, immunohistochemistry, iron assays, and ICP-MS. Additionally, serum and BALF will be analysed for cytokine levels to assess inflammation and immune responses.

PROJECT POTENTIAL

This project has significant potential to advance our understanding of iron dysregulation in CF. By investigating the mechanisms of iron overload in the G551D CFTR mouse model, the findings could reveal novel therapeutic targets to reduce oxidative damage and improve lung function in CF patients. Ultimately, the project has the potential to influence both CF treatment strategies and the broader understanding of iron-related pathologies in other diseases.

How have CFTR modulator therapies improved cystic fibrosis disease outcomes?

This project is suitable for an Honours student.

BACKGROUND

Cystic fibrosis (CF) is a debilitating, life-threatening disease characterised by airway inflammation, oxidative stress, persistent airway exacerbations and abnormal lung microbiome. CF is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, and predominantly affects the lungs, gastrointestinal tract, liver and pancreas. Several drugs have been developed in the last few years to treat CF with varying degrees of success, but we still need in-depth studies of how these therapies perform over time in a wide range of patients.

AIMS

- Assess longitudinal clinical outcomes, such as lung function, while using modulators;
- Investigate markers of immune regulation, inflammation and iron status over time;
- Investigate how CFTR therapies have changed the microbiome over time.

APPROACH

We have collected thousands of patient samples (including whole blood, plasma, sputum, saliva and PBMCs) in a Biobank to examine disease progression and how treatment has improved patient outcomes. These samples will be analysed using techniques such as protein and gene expression studies, iron assays and sequencing to address the above aims.

PROJECT POTENTIAL

This research is vital in order to contribute to the understanding of how these CFTR modulator drugs work in CF patients, how they can be changed to improve patient outcomes and potentially help to identify new therapeutic targets in the future. All this data will contribute to several papers that we hope to publish in the near future.

Applied Tropical and Molecular Parasitology

Supervisor:
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The Applied Tropical and Molecular Parasitology Laboratory focuses on developing new diagnostics for, primarily, helminth infections and utilising molecular tools to investigate epidemiology of disease. We have a particular focus on zoonotic parasites such as *Schistosoma* sp., *Strongyloides* sp., and hookworm, applying a One Health lens to research projects with an aim for prevention of parasite infection. We collaborate closely with the Global Health and Tropical Medicine Laboratory to develop multifaceted control programs to achieve this goal.

Brain and Mental Health Program

The research is critical with about half of all Australians experiencing mental ill-health at some stage in their lives. It focuses on a range of mental health areas including anxiety, depression, ADHD, autistic spectrum disorder, bipolar disorder, eating disorders, and schizophrenia.

Our neuroscientists, geneticists, epidemiologists, and clinical researchers are devoted to developing treatments, finding the causes, and working out how to prevent these conditions. This includes investigations into innovative neuro-stimulation and psychopharmacological interventions for people with serious mental disorders. Our understanding in the areas of psychiatric genetics, neuroimaging and neuroscience will inform new strategies for prevention, early intervention, and the treatment of complex syndromes.

Neurological conditions such as Parkinson's disease, multiple sclerosis (MS), motor neuron disease, epilepsy, and dementia, including Alzheimer's disease, are a growing health issue in Australia, often with limited treatment options. Our researchers are providing a broad interdisciplinary expertise in advancing understanding of this area from infancy to the elderly.

Psychiatric Genetics

Distinguished Scientist:
Professor Sarah Medland

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The Psychiatric Genetics Laboratory focuses on investigating the genetic and environmental factors that influence mental health conditions and the impact of non-psychiatric conditions on mental health across the lifespan. The group also have a strong focus on the genetics of brain structure and on women's health.

The role of genomics in understanding psychiatric and neurological disease.

This project is suitable for a PhD student only. Applicants with backgrounds in psychology, psychiatry, statistics or public health are preferred.

Over the past decade, large-scale collaborative projects have significantly increased our knowledge and understanding of the genetic risk factors for mental health and neurological conditions across the lifespan.

Translation of genetic findings is usually conceptualised as a process involving the characterisation of implicated loci, identification of treatment targets, drug development and clinical trials. However, the accurate communication of the promises and limitations of new research findings is an essential part of research translation as is examining the utility of analytic techniques such as polygenic risk scores.

This project will focus on examining the ways genomic data could be used in clinical practice and the accuracy and specificity of these techniques. The project will require a strong background in statistics and research methodology.

Please note this is a dry lab analysis focused project.

Health and wellbeing in people with bipolar disorder.

This project is suitable for PhD students only.

Bipolar disorder is a lifelong and severe psychiatric illness characterised by recurrences of episodes of depression and hypomania or mania. Lithium is the first option in the pharmacotherapy of bipolar disorder. However, only one third of patients have a good response to this treatment, i.e., they often recover and remain well as long as they continue taking lithium. The rest have a partial or deficient response.

QIMR Berghofer is part of an international effort to identify individual differences in lithium response. We are collecting data across Australia on mental health, wellbeing and treatment response on bipolar disorder. We offer a project to analyse lithium response in bipolar patients, comorbidity with other disorders and quality of life.

Please note this is a dry lab analysis focused project.

Genetic and environmental influences on brain structure and function.

Supervisor:
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The project is suitable for an Honours student.

BACKGROUND

Genetic and environmental factors influence the structure and function of the human brain. Disentangling and quantifying these sources of variation (genetic and environmental) may be crucial to understanding the brain's genetic architecture and how it relates to typical and atypical brain function.

AIM

To provide a normative reference of healthy brain structure for future studies of neurological and psychiatric disorders by establishing a robust map of genetic and environmental influences on the brain.

METHOD

This project uses brain structure and function measures collected in genetically informative datasets. Statistical approaches such as twin modelling and polygenic risk scores will be applied to neuroimaging measures to elucidate genetic and environmental influences on brain structure and function.

PROJECT POTENTIAL

To identify the factors contributing to differences in brain structure and function between individuals and highlight brain regions especially vulnerable to genetic and environmental influences.

Identifying risk factors for problematic internet use and video gaming in Australian adults.

Supervisor:
Associate Professor Penelope Lind

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This project is suitable for an Honours student only. This project is most suitable for students with a strong background in psychology/psychiatry and statistical analysis.

The proliferation of computers, gaming consoles and widespread use of the internet in the last 15 years has resulted in the emergence of behavioural addictions to digital technology, namely the internet and video games. Pathological internet use and video-gaming have been associated with mental health issues (such as anxiety and depression), increased rates of obesity, introversion, a high degree of loneliness, disrupted family relationships and academic problems.

I have previously recruited a cohort of university-aged Australian adults who completed an online questionnaire in order to (1) identify risk factors associated with these behaviours, (2) investigate the emotional and educational or occupational impacts of these behaviours, and (3) examine the co-occurrence of these behaviours with other personality characteristics and psychopathologies such as substance use and mental health disorders. We have also recently collected similar data in a cohort of Australian adults living with anxiety.

I offer a project to analyse the collected online questionnaire data, and to provide the Honours student access to the online questionnaire in order for them to potentially recruit a third cohort.

Brain Modelling

Group Leader:
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The Brain Modelling Group models and analyses brain structure and dynamics in health and disease. This work currently follows two major themes: developing new diagnostic methods for neonatal brain health and modelling large-scale brain activity across the lifespan.

In neonates, the group uses techniques from physics and machine learning to extract more information than ever before from intensive care monitoring of babies born prematurely. The goal is to enable early detection of injuries and early prognosis of developmental outcomes, so that clinicians can optimise care with personalised markers of brain health, potentially opening the window for new treatments.

On the modelling side, the group is harnessing the rapid developments in neuroimaging technology and connectomics to develop new mathematical models of brain activity, in particular at the spatial scales most relevant to human health. The goal is to fill in some of the large gaps in our knowledge of how neuroimaging brain signals emerge from brain structure, on how this relationship varies as we grow and age, and how things can go wrong leading to neurological and psychiatric disorders.

Modelling brain dynamics across the lifespan.

This project is suitable for an Honours or PhD student with a background in physics, maths, or a related discipline, and an interest in computational neuroscience, with some experience in programming (e.g., in MATLAB).

A major challenge for neuroscience is to understand how the brain's densely interconnected network of neurons—the "connectome"—gives rise to the rich repertoire of brain activity. The overarching aim of this project is to reveal how complex patterns of neural activity emerge from the connectome across the lifespan. This will entail using a novel combination of cutting-edge large-scale modelling of brain dynamics and state-of-the-art neuroimaging data (both structural and functional). There will be numerous applications depending on interests, examples include:

- How ageing brain structure changes our brain activity.
- How non-invasive brain stimulation perturbs brain network activity.
- How disorders such as epilepsy, schizophrenia, or ADHD may emerge from biologically-plausible changes to model parameters.
- Modelling sleep dynamics.
- Developing novel analysis methods for complex spatiotemporal dynamics.
- Model the early development and maturation of brain networks (collaboration with experimental neuroscientists at UQ).

Physiological signal analysis from infancy to adolescence.

This project is suitable for an Honours, Masters, or PhD student.

The advent of precision medicine demands better tools for measuring human structure and function. A particularly important period of development where this lack of diagnostic and prognostic tools is felt in earnest, is the period from infancy to adolescence. We measure the function of the brain, heart and lungs during sleep to reveal important information on human health in this cohort. By taking advantage of advances in data analysis and computation, we develop tools that can track developmental trajectories more accurately, leading to improved patient stratification.

In this project, we will implement head models that mature with a patient to convert electroencephalogram signals into source space for improved assessment of brain connectivity, and network/graph analysis to discover the interplay between brain, heart and lung function. The resultant tools will be evaluated as developmental biomarkers as well as diagnostic tools to detect disease and monitor the response to interventions.

Modelling neural circuit control of effort under stress.

This project is suitable for an Honours, Masters, or PhD student.

BACKGROUND

The decision to put in effort to attain rewards is essential for success in life, and critical for survival. Yet, we understand very little about the brain processes that promote persistence and enable individuals to 'keep going' instead of 'give up' when increasing amounts of effort are required. This project is a collaboration with experimental neuroscientists at The University of Queensland and the University of Newcastle.

AIM

We aim to investigate how the decision to persist in exerting effort to obtain a reward is encoded in the brain and affected by stress. In particular, we will develop a computational model of the neural circuits involved in decision-making under stress, aiming to identify mechanisms that explain the experimental results of our collaborators.

PROJECT POTENTIAL

This work will generate new knowledge on the neural mechanisms of stress and decision-making—core processes that underpin adaptive behaviours essential for survival. You will become well-versed in both computational neuroscience and the data emerging from animal experiments.

Translational Neurogenomics

Senior Group Leader:
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The Translational Neurogenomics Laboratory is headed by Professor Eske Derks. The group currently consists of 10 members (two postdocs, four PhD students, a visiting scientist, a research assistant, and an undergraduate student). The Translational Neurogenomics Laboratory has identified genetic risk factors for a range of neuropsychiatric conditions, including substance use disorders, schizophrenia, depression, and obsessive compulsive disorder. Researchers in this group use genetic data to address questions, such as: Which genetic variants in the DNA increase the risk of developing a neuropsychiatric disease? What is the genetic overlap across different psychiatric disorders? What are the downstream molecular consequences underlying statistical genetic associations? Which existing drugs may be repurposed for prevention and treatment of neuropsychiatric diseases?

The interplay between environmental and genetic risk factors in the aetiology of substance use disorders.

Co-Supervisor:
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This project is suitable for an Honours or PhD student. We are seeking a highly motivated student with a strong interest in statistics and quantitative studies.

BACKGROUND

Mental health disorders (e.g., depression, anxiety, and substance use) are the leading cause of global disease burden in the young adult population. Twin and family studies show that both genetic and environmental factors play a large role in the aetiology of these disorders. The Translational Neurogenomics group aims

to identify genetic risk factors for a range of mental health and substance use disorders, and investigate the interplay between genetic and environmental risk factors.

UK Biobank is a major national and international health resource with the aim of improving the prevention, diagnosis and treatment of a wide range of serious and life-threatening illnesses. UK Biobank recruited 500,000 people aged between 40-69 years in 2006-2010 from across the country to take part in this project. They have undergone measures, provided blood, urine and saliva samples for future analysis, and detailed information about themselves and agreed to have their health followed. Over many years, this will build into a powerful resource to help scientists discover why some people develop particular diseases and others do not. Extensive information on mental health has been collected from a subset of 150,000 individuals.

POTENTIAL PROJECTS

- Substance use and substance use disorders (SUDs) are explained by a combination of genetic and environmental factors. Exposure to traumatic experiences, particularly in childhood, has been linked with both substance abuse and dependence. Is this link stronger in people with a genetic predisposition to SUDs? This project will investigate the interaction between genetic liability to substance use and traumatic experiences in the UK Biobank.
- A network approach to psychopathology is an alternative way of conceptualising mental illness. A disorder is conceptualised as a system of interacting relationships between symptoms, rather than the set of symptoms resulting from a single latent factor (the disorder). This project will conduct a network analysis of substance use disorders (SUDs) using symptom-level data from the UK Biobank. Networks will be estimated for groups with a high vs. low genetic predisposition for substance use in order to determine whether genetic risk is associated with differences in psychopathological network structure.

WHAT DO WE OFFER

- A position in a dynamic research environment and the opportunity to conduct high-quality studies.
- Access to large-scaled datasets through (inter) national collaborations.
- Being a part of a successful research team.

Investigating the genetic relationships of Alzheimer's disease and sleep apnea.

This project is suitable for an Honours student.

BACKGROUND

Alzheimer's disease is the most prevalent forms of dementia in elderly people characterised by cognitive impairment and loss of memory, affecting the quality of life. Unfortunately, there is no cure for Alzheimer's disease yet, therefore, identifying risk factors and the molecular factors that underlie increased susceptibility to Alzheimer's disease, will help early diagnose risk individuals to offer preventive care.

Burgeoning evidence, particularly from animal and human studies, is pointing towards an intricate comorbid association between sleep disorder, particularly obstructive sleep apnea (OSA)-most prevalent forms of disorder in mid to elderly people. In this project, we aim to establish whether OSA has any causal association with risk of Alzheimer's disease leveraging genome-wide association studies (GWAS). Next, the project will also seek to discover molecular factors i.e., gene regulation that underlie this relation between Alzheimer's disease and OSA via integrating GWAS with molecular quantitative trait loci (QTLs) datasets. This will be an ideal project for a motivated and enthusiastic Honours student to study role of OSA (if any) on the risk of Alzheimer's disease and molecular factors that underlie this association.

APPROACH

We will offer hands-on training to students on various methods, particularly, analysis of GWAS and molecular QTLs datasets, required for successful completion of this project. Students will be highly skilled and efficient on handling large-scale genomics datasets and analysis of such datasets using bioinformatics and statistical genetics methods.

OUTCOME

The anticipated outcomes of this project are to assess whether sleep disorders contribute to induce or accelerate the risk of Alzheimer's disease and identify molecular factor that could serve as potential biomarkers for this association. The findings from this study are expected to provide new insights into the genetic relationships between sleep disorders and Alzheimer's disease. The student will gain valuable computational and analytical skills by applying bioinformatics and statistical genetics methods.

REQUIRED SKILLS OR EXPERIENCE

Possess a basic understanding of genetics, molecular biology and bioinformatics. Have a keen interest in neurogenetics and familiarity with R programming language will be advantageous but not necessary.

Understanding the shared and unique genetic risk factors between neuropsychiatric disorders and their comorbidities.

This project is suitable for an Honours student.

BACKGROUND

Neuropsychiatric disorders have been demonstrated to have strong heritable components, allowing research to focus on, and differentiate between, the genetic and environmental risk factors which contribute to these disorders. The diagnosis of one europsychiatric disorder is associated with an increased risk that someone will also have other diagnoses, including both physical diseases and other neuropsychiatric disorders. Examining the shared and unique genetic risk factors underlying the relationship between these comorbidities can break down variations in genetic influences, elucidate shared aetiology, and improve treatment options and outcomes. In this project, students can build their research question around neuropsychiatric disorders they have an interest in and choose which comorbidities to explore.

APPROACH

Students will develop their ability to identify gaps in the literature and formulate an appropriate research question to fill this gap with assistance from supervisors, and be trained to use a diverse set of methodologies in bioinformatics in addition to coding languages.

- Genome-Wide Association Studies;
- Genomic Structural Equation Modelling;
- Linkage Disequilibrium Score Regression;
- RStudio and Bash.

OUTCOME

Students will identify shared and/or unique genetic risk factors of their chosen comorbidities. Students will gain proficiency in versatile skill sets, including bioinformatics approaches, statistical analysis, problem-solving, and communication. The project offers strong potential for the publication of the research in a journal, while working with a diverse team passionate about supporting new researchers.

REQUIRED SKILLS OR EXPERIENCE

We seek motivated Honours students interested in genetics, statistics, and bioinformatics. Some background in psychology or genetics may be helpful, but is not required for success.

Neurogenetics and Dementia

Team Head:
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Dementia is the second leading cause of death for all Australians. Alzheimer's disease is the most common form of dementia, predicted to affect 152M globally by 2050.

Common late onset Alzheimer's disease is caused by age-related failure of clearance of toxic proteins (β-amyloid and tau) from the brain leading to an immune response. Successful treatment or prevention relies on the ability to identify those at high risk or the earliest disease stages.

We run one of the largest cohort studies in the world focused on those at high risk and in the earliest disease stages of Alzheimer's disease, for the identification of affordable, accessible and scalable biomarkers for dementia diagnosis and screening, to be prepared for the best use of newly developed drugs and lifestyle interventions as they become available.

In addition, we carry out large scale genetic studies, including the use of genetic risk prediction and the identification of causal disease processes in Alzheimer's disease and dementia.

Methylation-based biomarkers for Alzheimer's disease.

This project is suitable for an Honours, Masters, MPhil, MD, or PhD student. For those with experience in coding and statistics, and an interest in dementia, DNA methylation analysis, genetic epidemiology, and bioinformatics.

BACKGROUND

DNA methylation (DNAm) patterns derived from blood samples correlate strongly with chronological age, thereby referred to as the 'epigenetic clock'. Epigenetic clocks are also associated with differences in physical and cognitive fitness. Epigenetic changes in Alzheimer's disease (AD) affected brain regions have been shown to associate with AD pathogenesis, and significant differences in DNAm patterns are identified in the blood between AD cases and controls. Therefore, there is great potential for epigenetic patterns to be diagnostic markers for prodromal AD.

AIM

Test whether the 'epigenetic clock' associated with ageing also associates with genetic risk of AD and prodromal dementia phenotypes. Data from this project will also contribute to a large international consortia carrying out world leading collaborative analysis on the genetics of DNA Methylation.

PROJECT POTENTIAL

This study will identify DNA methylation patterns from the entire genome, in the blood which associate with dementia related phenotypes, and future decline in a population at high risk of AD. These could be used as an accessible AD biomarker, allowing the use of early treatment, and enabling monitoring of disease progression.

Accessible biomarkers for early stage Alzheimer's disease.

This project is suitable for an Honours, Masters, MPhil, or PhD student. For those with experience in statistics and an interest in dementia, genetic epidemiology, psychology, bioinformatics and machine learning.

BACKGROUND

Dementia affects an estimated 353,800 Australians, with up to 80% diagnosed with Alzheimer's disease (AD). Newly developed anti-amyloid drugs are set to revolutionise the treatment of AD. These are likely to have the most significant impact at the earliest stages of disease. Therefore, there is an urgent need for early-stage biomarkers that are affordable, accessible, and scalable.

AIM

To investigate genetic risk prediction and biomarkers for early-stage Alzheimer's disease, including the combination of traditional and digital biomarkers, which opens up opportunities for simple, accurate, and effective screening to identify early-stage AD.

METHOD

The student will build on our current work in PISA (the Prospective Study of Aging, Genes, Brain, and Behaviour) in this data analysis project (dry lab). They will test the integration of genetic risk prediction, blood-based protein biomarkers, and digital biomarkers, such as online cognitive testing, speech analysis and hand movement patterns. Predictive algorithms will be developed using statistical and machine-learning approaches.

PROJECT POTENTIAL

Accessible screening for early-stage Alzheimer's disease will identify individuals suitable for more in-depth diagnostic tests, treatment, interventions and participation in clinical trials.

The identification of early-stage Alzheimer's disease biomarkers in individuals with Down syndrome (Trisomy 21).

This project is suitable for a Masters or Honours student. This project involves conducting a literature review and does not include lab work or data analysis. Suitable for those with a background in neuroscience, psychology or medicine, with an interest in dementia. Experience in the use of PubMed, Scopus or similar databases, and strong writing skills.

BACKGROUND

Individuals with Down syndrome (Trisomy 21) are at a greatly increased risk of developing Alzheimer's disease due to the overexpression of the amyloid precursor protein (APP) gene on chromosome 21. Most individuals develop neuropathology by age 40. Understanding the conversion to dementia in individuals with Down syndrome is confounded by factors such as varying degrees of baseline intellectual disability, associated medical comorbidities and potential differences in early disease processes. The refinement of early-stage biomarkers specific to individuals with Down syndrome is essential for equitable availability of Alzheimer's biomarkers, facilitating access to early-stage treatment.

AIM

To carry out a systematic review of the literature investigating biomarkers for detecting early-stage Alzheimer's disease in individuals with Down syndrome, including the utility of MRI, cognitive tests, blood and CSF-based protein biomarkers, digital biomarkers and genetic modifiers (outside of APP).

METHOD

The student will be part of a team conducting a literature review in accordance with a standard systematic review protocol. Work will include planning the review, sourcing and reviewing the literature, and reporting the results.

PROJECT POTENTIAL

The future publication of the review findings will provide a comprehensive overview of the research area and identify gaps for future research studies.

Cellular and Molecular Neurodegeneration

Senior Group Leader:
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The Cellular and Molecular Neurodegeneration Laboratory investigates the cause and potential treatments for brain diseases including dementia (Alzheimer's disease), motor neuron disease (amyotrophic lateral sclerosis) and Parkinson's disease. These disorders (collectively known as neurodegenerative diseases) are a growing health issue in Australia and worldwide, with few treatment options available. In order to gain a better understanding of these diseases and develop new therapeutic approaches, the research team is currently developing new human brain cell culture methods for microglia, brain endothelial cells, organoids (mini-brains), and olfactory (nasal) cells.

The lab is utilising these new 2D and 3D human brain cell models to derstand brain disease pathways, and the impact of environmental factors such as air pollution, SARS-CoV-2, and bushfire smoke on brain health. We have also established platforms for drug screening to identify potential new therapeutics for treatment of brain diseases.

Development of metal-based therapeutics for neurodegenerative diseases.

This is a PhD project but may also be considered for an Honours project.

Biological trace elements, also known as trace minera, or biometals include copper, zinc, iron, selenium and manganese. These and other biometals have essential roles in many areas of brain function including energy metabolism, transcription factor activity, antioxidant regulation and synaptic signalling. During ageing and brain disease, regulation of biometals is dramatically altered with changes to cellular and subcellular handling and localisation. This leads to impairment of brain cell function, in both neurons and surrounding cell types (astroglia and microglia) and contributes to neuronal cell death in disorders such as Alzheimer's, Parkinson's and motor neuron diseases, as well as in lysosomal storage disorders such as Batten disease (childhood brain disorder). Our research has uncovered some of the processes involved in the loss of biometal regulation and found this to be an early event in many disorders. We are also developing compounds that can help restore biometal stasis in the brain.

This project involves the investigation of new metal-based compounds as potential therapeutic or diagnostic agents for Alzheimer's disease and other brain disorders. These compounds have unique properties including modulation of brain cell signalling, control of anti-oxidant function, and regulation of neuro-immune responses. The project examines the action of the compounds on a range of cell types including animal and human neurons, astrocytes and/or microglia, and we aim to understand the molecular pathways that contribute to therapeutic action. Longer-term projects will involve the examination of the compounds as therapeutics in specific animal models of brain disease to determine if they are suitable for further therapeutic or diagnostic development towards the clinic.

The wet lab project will utilise a range of tools and techniques including brain cell culture, analysis of immune response (cytokine analysis), phagocytosis assays, anti-oxidant assays, X-ray analysis of biometal distribution and metalloproteomic studies on metal-protein interactions.

Generating patient-derived microglia to investigate neuroinflammation in MND.

This is a PhD project but may also be considered for an Honours project.

This project will build important new tools for understanding the role of the immune system in amyotrophic lateral sclerosis (ALS), a form of motor neuron disease (MND). Inflammatory responses by the resident brain and spinal cord immune cells (microglia) have an important role in ALS/MND and are key targets for therapy. Until now, research on microglia has been largely restricted to cells of animal origin. We now have new techniques to generate microglia directly from ALS/MND patients to help understand the disease and test patient-specific drugs to modulate the immune response in the brain and spinal cord. This project will provide a new approach to investigating and treating inflammation in MND.

Generating Alzheimer's disease microglia for testing patient responses to disease immune-modulating compounds.

This is a PhD project but may also be considered for an Honours project.

Alzheimer's disease is anticipated to affect 100 million patients with an annual cost of US$1 trillion by 2050. Promising amyloid-clearing therapies have failed to

translate to clinical outcomes, and new approaches targeting the underlying molecular pathways of Alzheimer's disease are urgently required. There has been a 're-awakening' to the critical role of microglia in Alzheimer's disease pathology. However, our ability to translate abnormal microglial biology into clinically relevant advances has been greatly impaired by inadequate cell models. Microglia-like cells can now be routinely generated from human peripheral blood monocytes. The approach is cost-effective and rapid, and these induced microglia reveal a remarkably close relationship to mature human microglia in terms of cell surface marker expression, functional assays, and gene expression.

In this project, we will generate microglia-like cells from blood samples collected from Alzheimer's patients, and people who are considered at high risk for Alzheimer's disease. We will compare the cultured microglia to identify patient-specific immune abnormalities using a range of assays currently established in our lab. We will then screen individual patient microglia for the efficacy of immune-modulating compounds to identify effective patient-specific neurotherapeutics in 'real-time'. This project will produce highly significant advances in patient-specific drug targeting for neuroinflammation in Alzheimer's disease, leading to the development of real-time, individual therapeutic approaches with major clinical benefits, including identifying patient-specific drugs, selecting suitable patients for clinical trials, and monitoring drug efficacy during trials.

Olfactory stem cells for investigating the causes and progression of dementia.

This is a PhD project but may also be considered for an Honours project.

BACKGROUND

With no clinical success yet achieved from amyloid-targeting strategies, there is an urgent need to gain new insights and develop effective treatments for people who have dementia. New stem cell-based approaches have generated much excitement in dementia research with the potential to study patient-derived neurons and supporting cells. However, the commonly used 'pluripotent' stem cells are artificially generated and do not possess all needed cell types, which makes them unsuitable as tools to understand the disease process in the majority of late-onset (sporadic) cases of dementia.

Olfactory (nasal) tissue contains a unique population of naturally occurring stem cells that renew the nasal receptor neurons and supporting cells in the nose throughout life. These exceptional stem cells can be collected through a routine procedure with local anaesthetic and readily grown in a culture dish in a laboratory to produce neurons and other key brain cell types that accurately reflect the same types of brain cells that occur in the patient of origin. These cells provide a unique tool to study patient-specific disease processes and develop therapeutics for personalised dementia medicine.

OBJECTIVE

Our plan is to collect nasal tissue from people with dementia and from people who are at high risk for dementia (together with matching control samples). The olfactory stem cells will be grown in our lab and studied using a range of molecular approaches to provide unique insights into the early disease changes in a person's brain cells. We are also attempting to grow brain 'organoids' from stem cells. These are 'mini-brains' that represent the 3-dimensional structure of a small part of a human brain and allow a much more accurate understanding of how brain cells work (or fail to work) in dementia. This will enable us to understand how brain cells are affected by dementia differently for each patient (i.e., derived neurons will retain patient-specific epigenetic markers) and will allow the screening of potential therapeutic drugs on an individual basis.

Drug repurposing to treat childhood dementia.

This project is suitable for an Honours, Masters, MPhil, MD or PhD student.

BACKGROUND

Childhood dementia is caused by a group of genetic disorders which have effects on infants and children that include dementia (loss of normal brain function). There are no cures, and treatments limited effects. We are collaborating with Proffessor Eske Derks and Dr Zac Gerring at QIMR Berghofer to screen currently used drugs to determine if any have therapeutic effects on childhood dementia.

AIM/S

Drugs and drug targets are identified using computational approaches, and the leading drugs will be tested for effectiveness in pluripotent stem cell derived brain cell models of childhood dementia.

METHOD

Growth of human stem cell-derived brain cell cultures.

PROJECT POTENTIAL

Potential to identify new drugs to treat childhood dementia.

The potential impact of bushfire smoke on brain health.

This project is suitable for an Honours, Masters, MPhil, MD, or PhD student.

BACKGROUND

In this project, we are using our monocyte and pluripotent stem cell-derived brain cell models to understand how bushfire smoke affects the human brain, particularly its ability to include neuroinflammation. We are also working with Associate Professor Michelle Lupton, and Dr Jodi Thomas at QIMR Berghofer to determine if exposure to bushfire smoke affects the likelihood of being diagnosed with neurodegenerative diseases such as dementia.

AIMS

- Determine the impact of bushfire smoke on human brain cells.
- Determine if exposure to bushfire smoke increases risk of dementia or other brain diseases.

PROJECT POTENTIAL

Potential to understand the impact of bushfire smoke exposure on human brain health.

Cognitive Fitness

Program Director (Brain and Mental Health), Group Leader: Professor Murat Yucel

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The Cognitive Fitness Group uses cognitive neuroscience to create digital tools that measure, monitor and help optimise brain health.

Professor Murat Yücel's work primarily focuses on developing innovative approaches to digital medicine. This includes:

- A gamified measurement tool for assessing cognitive and brain function for use in clinical research, aiming to comprehend the cognitive mechanisms of clinical dysfunction and guide mechanism-targeting interventions to enhance them;
- An ultra-brief tool for measuring cognitive fitness in clinical conditions, which can be used to build resilience against mental ill-health and improve performance in high-stakes situations, such as those faced by first responders, military professionals, and competitive athletes.

The novel digital medicine also includes an interactive virtual reality platform that delivers exposure/response prevention interventions for disorders like obsessive-compulsive disorder (OCD) and gambling disorder.

Professor Murat Yücel is also involved in clinical trials in Lifestyle Medicine, focusing on the neural and cognitive effects of physical exercise and mindfulness meditation. Additionally, he participates in clinical trials of Psychedelic Medicine, examining the cognitive and mental health effects of psilocybin and MDMA.

Child and Youth Mental Health

Honorary Senior Scientist and Group Leader: Professor James Scott

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qimrb.edu.au/researchers-and-labs/child-and-youth-mental-health

The Child and Youth Mental Health Research Group conducts research with a particular focus across three areas.

The first are studies examining the causes and consequences of mental illness in young people. This enables identification of factors that influence mental health and illness in children and adolescents. Modifying these risk factors can prevent the onset of mental illness and improve the wellbeing of children and adolescents.

Much of Professor Scott's research is devoted to understanding interpersonal violence experienced by children. This includes child maltreatment, exposure to domestic and family violence and bullying victimisation in school. Prevention of these adverse childhood experiences can lead to substantial improvements in mental health across the lifespan.

The second is psychoneuroimmunology. Our research in this area has demonstrated the interplay between the nervous system and the immune system where we have shown some people have psychosis arising from inflammation in the central nervous system.

The third research area focuses on clinical trials and health service research. These studies evaluate the effectiveness of innovative treatments for young people at risk of or living with, mental illness and the outcomes following the implementation of clinical services and lifestyle support for young people living with mental illness.

Computational Neurogenomics

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qimrb.edu.au/researchers-and-labs/computational-neurogenomics

At the Computational Neurogenomics Laboratory, we work at the intersection of human genetics, data science, digital biomarkers, and brain health. Our research focuses on understanding the genetic and molecular foundations of complex brain-related traits and diseases, particularly Parkinson's disease (PD). We are building world-leading resources by integrating genomics, neuroimaging, wearable-derived digital biomarkers, and electronic health data to accelerate discoveries in disease prediction, progression, and personalised care.

We lead major national and international initiatives such as the Australian Parkinson's Genetics Study (APGS), now the largest PD genetics cohort in Australia, and collaborate globally through programs like the Global Parkinson's Genetics Program (GP2), the Psychiatric Genomics Consortium (PGC), and the Enhancing NeuroImaging Genetics through Meta-Analysis (ENIGMA) Consortium. Our work combines big data analysis, statistical genomics, and translational science to uncover the biological drivers of clinical heterogeneity and to develop real-world tools to monitor and predict disease progression.

We welcome enquiries from motivated students interested in exploring Honours, Masters, or PhD projects, as well as MD students seeking internship opportunities. Our group offers a multidisciplinary and supportive environment, with opportunities to contribute to impactful, high-profile research at the interface of genetics, brain health, and digital medicine. If you're passionate about advancing personalised healthcare through data-driven discovery, we would love to hear from you.

Genetic Epidemiology

Distinguished Scientist:
Professor Nick Martin

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The Genetic Epidemiology Laboratory seeks to identify the particular genes involved in complex disease aetiology. It performs longitudinal studies with twins on a wide range of complex traits of medical and behavioural interest. Particular research over recent years has moved to genome wide association studies (GWAS) to locate genes influencing complex traits including anxiety, alcoholism, and dizygotic twinning. Most recently, the laboratory initiated projects to recruit large patient samples for GWAS of anorexia, depression and other psychiatric disorders.

Exploring the genetic basis of depression.

Co-Supervisor:
Dr Brittany Mitchell

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This is a suitable for an Honours or PhD project. Seeking a motivated student with experience in psychology, genetics, epidemiology or statistics for dry lab analysis focused project.

BACKGROUND

Depression is a major public health challenge, affecting one in five Australians over their lifetime. Alarmingly, about a third of those diagnosed do not respond to conventional treatments, highlighting an urgent need for a deeper understanding of the biological factors driving both depression and treatment outcomes. While genetics is known to play a role in depression risk, less is understood about how it influences specific features of the disorder—such as age of onset, recurrence, and sex differences—or why some individuals respond well to treatment while others do not. This project aims to unravel these complexities by investigating the genetic basis of depression characteristics and treatment response, shedding light on the biological mechanisms that shape individual experiences of the disorder.

AIMS

This project will:

- Identify genetic factors that contribute to depression risk and key clinical features, such as age of onset and recurrence.

- Explore the relationship between depression and related traits.
- Determine whether treatment response traits—such as medication efficacy, tolerability, and side effects—are influenced by genetic variation.

METHODS

Leveraging large-scale national and international genetic datasets (N=20,000 and N=500,000), this project will apply cutting-edge statistical genetics approaches—including genome-wide association studies (GWAS) and polygenic risk scoring (PRS)—to uncover the genetic architecture of depression-related traits. The student will explore how depression risk factors differ between males and females and investigate genetic links between depression and other health conditions.

PROJECT POTENTIAL

This project has the potential to significantly advance our understanding of the genetic underpinnings of depression, with a particular focus on identifying genetic factors that influence clinical features like age of onset, recurrence, and treatment response. By integrating large-scale genetic datasets with advanced statistical techniques, this research could pave the way for more personalised and effective approaches to depression treatment, particularly for individuals who do not respond to conventional therapies.

Investigating sex differences in mental health disorders using genetic data.

Co-Supervisor: Dr Jodi Thomas

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Co-Supervisor: Dr Brittany Mitchell

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This is a PhD or Honours project. Seeking a motivated student with experience in psychology, genetics, epidemiology or statistics for dry lab analysis focused project.

BACKGROUND

Mental health disorders, such as depression and anxiety, exhibit notable sex differences in prevalence, age of onset, and symptomatology. Women are more likely to be diagnosed with depression and anxiety, whereas men have higher rates of certain externalising disorders. While social and environmental factors contribute to these differences, genetic and biological mechanisms also play a crucial role. Advances in psychiatric genetics have enabled researchers to explore sex-specific genetic influences on mental health, yet many studies continue to overlook these differences.

AIMS

This project aims to investigate whether genetic risk factors for depression and anxiety differ between males and females. Specifically, it will:

- Identify sex-specific genetic variants associated with these disorders.
- Assess whether sex-specific polygenic risk scores (PRS) have differing associations between sexes.
- Examine potential gene-by-sex interactions that contribute to mental health outcomes.

METHODS

The project will use large-scale genome-wide association study (GWAS) data from studies such as the Psychiatric Genomics Consortium (PGC) and the Australian Genetics of Depression Study (AGDS). This project provides an opportunity to develop skills in genetic data analysis, statistical programming, and genetic epidemiology. The findings may improve our understanding of the biological mechanisms underlying sex differences in mental health disorders and contribute to more personalised treatment approaches.

PROJECT POTENTIAL

This project has the potential to provide valuable insights into the genetic basis of sex differences in mental health traits, such as depression and anxiety, by identifying sex-specific genetic risk factors and exploring how they influence the onset, severity, and treatment response of these disorders. The findings could pave the way for more tailored, sex-specific interventions and improve our understanding of the biological mechanisms driving mental health disparities between men and women.

Unravelling the genetic architecture of acne.

Co-Supervisor: Dr Brittany Mitchell

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This is a PhD or Honours project.

BACKGROUND

Acne is a common skin condition that affects individuals worldwide, with significant variation in severity and response to treatment. While environmental factors such as diet, hygiene, and skincare play a role, genetics also contributes substantially to acne risk. Previous genome-wide association studies (GWAS) have identified genetic variants associated with acne,

highlighting the involvement of immune function, sebum production, and hormonal pathways. However, further research is needed to understand how genetic risk factors contribute to acne development and severity.

AIMS

This project aims to explore the genetic basis of acne by:

- Identifying genetic variants associated with acne risk and severity.
- Investigating whether genetic risk for acne overlaps with other conditions such as depression or metabolic traits.
- Evaluating the predictive power of polygenic risk scores (PRS) for acne.

METHODS

The project will utilise data from large genetic studies, including the largest GWAS of acne to date. PRS will be calculated and compared across different acne severity groups. Genetic correlation analyses will assess shared genetic risk factors between acne and other conditions. Statistical analyses will be conducted using software such as PLINK and R.

Project Potential: This project offers the opportunity to gain experience in genetic epidemiology, bioinformatics, and statistical genetics, with potential implications for understanding acne pathophysiology and informing personalised treatment strategies.

Exploring the genetic causes of migraine and its links to other traits.

Co-Supervisor: Dr Brittany Mitchell

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This is a PhD or Honours project.

BACKGROUND

Migraine is a highly prevalent neurological disorder characterised by recurrent headaches, often accompanied by nausea, sensitivity to light and sound, and other disabling symptoms. While environmental triggers such as stress and diet contribute to migraine attacks, genetic factors play a significant role in susceptibility. Genome-wide association studies (GWAS) have identified numerous genetic variants associated with migraine, implicating pathways related to neuronal signalling, vascular function, and pain processing. Additionally, migraine has been genetically linked to other conditions, including depression, anxiety, and cardiovascular disease, suggesting shared biological mechanisms.

AIMS

This project aims to investigate the genetic basis of migraine and its relationships with other traits by:

1. Identifying genetic variants associated with migraine risk.
2. Examining genetic correlations between migraine and other traits and disease.
3. Evaluating whether polygenic risk scores (PRS) for migraine can predict risk for related conditions.

METHODS

The project will utilise GWAS summary statistics from large migraine studies and other relevant datasets. Genetic correlations between migraine and related traits will be assessed using linkage disequilibrium score regression (LDSC). PRS will be calculated and tested for associations with other traits in independent cohorts. Statistical analyses will be performed using R and bioinformatics tools such as PLINK.

PROJECT POTENTIAL

This project provides an opportunity to develop expertise in genetic epidemiology, statistical genetics, and data analysis while contributing to a better understanding of the biological links between migraine and other complex disorders.

Psychedelic Medicine and Supportive Care

Team Head: Associate Professor Vanessa Beesley

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qimrb.edu.au/researchers-and-labs/psychedelic-medicine-and-supportive-care

The Psychedelic Medicine and Supportive Care Laboratory is dedicated to advancing psychedelic medicine and developing supportive care interventions for cancer and mental health.

Our research aims to maximise quality of life by:

- Using population and person-centred approaches to assess supportive care needs.
- Identifying the most promising interventions and models of care.
- Embracing innovation and using cost-effectiveness and implementation trial designs.
- Championing equity and inclusivity for culturally safe, responsive and accessible care.

- Fostering interdisciplinary partnerships with clinicians, consumers and healthcare providers to facilitate translation.

Our current projects target cancer-related supportive care, adjustment disorders, prolonged grief and post-traumatic stress disorder (PTSD) in disaster-affected communities.

Investigating the impact of structured counselling for carers of people with pancreatic cancer on patient and carer outcomes.

This project is suitable for an Honours student starting as early as Q1 2025 or could expand for a PhD student.

BACKGROUND

Pancreatic cancer is rare and deadly. Patients and their families have little time to adjust to this devastating diagnosis. Family carers of patients are confronted with the need to assist in the management of complex physical symptoms and provide emotional, financial, and spiritual support, typically with minimal support or guidance.

AIM

The Pancreatic cancer Relatives Counselling and Education Support Service or PRoCESS trial aims to determine whether talking to a trained nurse-counsellor via video or phone is helpful for carers and whether it may also affect patient outcomes.

PROJECT POTENTIAL

The student may assess the effect of the counselling intervention compared with the control on various outcomes including patients' emergency department presentations, time spent in hospital, time to specialist palliative care referral and overall survival. Additionally, thematic analysis of qualitative (video) data from intervention participants' final counselling sessions and their unsolicited feedback may be used to provide insight into consumers' perceptions of the support service. The student will be responsible for writing up the findings for scientific publication.

Investigating MDMA-assisted therapy for treatment-resistant PTSD related to natural disasters.

This project is suitable for a PhD student starting in Q1 2026.

BACKGROUND

The escalating frequency and severity of extreme weather events due to climate change have led to increasingly complex mental health challenges. In February 2023, the Therapeutic Goods Administration (TGA) reclassified MDMA for therapeutic use in treating PTSD. MDMA, as a medicinal agent, primarily influences trauma processing by mitigating avoidance and fear-based responses in the amygdala while fostering social connection.

AIM

This project aims to examine the impact of group-based MDMA-assisted therapy on individuals affected by treatment-resistant PTSD resulting from the 2022 Lismore and northern NSW floods.

PROJECT POTENTIAL

The trial is assessing the effect of the intervention on various outcomes including PTSD, posttraumatic growth, depression/anxiety, social connectedness, self-compassion, climate change anxiety and health-related quality of life. The student will delve into relevant literature concerning the high-intensity intervention and may explore innovative analyses of the psychological processes likely to yield the most significant impact in a post-disaster context. The student will produce 4-5 scientific publications from this body of work.

Clinical Brain Networks

Group Leader:
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With the goal of progressing knowledge on brain disorders and evidence-based psychiatric therapies, the Clinical Brain Networks Laboratory focuses on understanding how the structural and functional wiring of the brain underpin health and pathology.

The laboratory uses a variety of neuroimaging, brain stimulation, and computational techniques and operates one of the first transcranial focussed ultrasound stimulation facilities in Australia.

We work closely with a not-for-profit brain stimulation clinic, the Queensland Neurostimulation Centre to rapidly translate our scientific insights into effective new treatments for refractory mental disorders.

Our research is supported by philanthropic and government bodies including the National Health and Medical Research Council (NHMRC).

Cerebellum and Neurodegeneration Research

Group Leader:
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qimrb.edu.au/researchers-and-labs/cerebellum-and-neurodegeneration-research-group

The Cerebellum and Neurodegeneration Research Group (CNRG) uses neuroimaging, fluid biomarkers, and digital assessment tools to understand brain and behavioural changes in people with cerebellar diseases, other forms of neurodegeneration, and aging.

We use a range of magnetic resonance imaging (MRI) and positron emission tomography (PET) approaches to investigate and track brain changes in people with neurodegenerative diseases.

Human neuroimaging and blood biomarkers for inherited neurodegenerative diseases.

This project is suitable for a PhD student.

BACKGROUND

Can new human brain imaging techniques allow us to better understand, track, and treat neurodegenerative diseases?

Can blood-based proteomics/metabolomics help us to better define and predict heterogeneity in the onset and progression of neurodegeneration?

Can machine learning be applied to complex, multi-domain clinical and biological data to identify disease subtypes?

These are some of the burning questions that are at the forefront of research in our lab. Hereditary cerebellar ataxias (HCAs) are inherited neurodegenerative diseases that are associated with motor, cognitive, and neuropsychiatric impairments. These diseases result in profound disability and mortality. There are currently no cures, but the field is on the precipice of gene therapies, stem cell interventions, and targeted pharmaceuticals. Next-generation magnetic resonance imaging (MRI) and proteomics/metabolomics approaches offer powerful new methods to characterise the onset and progression of disease, to define disease subtypes, and to optimise clinical trial design by improving patient selection (stratification) and outcome monitoring (sensitive endpoints).

AIMS

Multiple projects are available to undertake one or more of the following in cohorts of individuals with hereditary cerebellar ataxias:

- Application of novel quantitative MRI approaches to assess changes in myelination, iron metabolism, inflammation, and tissue microstructure.
- Determine the proteomic and metabolomic profile of disease expression and progression.
- Machine learning approaches to define disease clusters (subgroups) and predictive models of disease progression using clinical, imaging, and biological data.

PROJECT POTENTIAL

These projects will improve biological understanding, treatment targeting, and outcome monitoring for debilitating, fatal, and currently intractable neurodegenerative diseases.

Neuroimaging big data in rare neurodegenerative diseases: An international collaboration.

This project is suitable for an Honours, Masters, MD, or PhD student.

BACKGROUND

Hereditary Cerebellar Ataxias (HCAs) are rare neurodegenerative diseases that are associated with profound and extensive motor control impairments, predominantly affecting the cerebellum and brainstem. Neuroimaging provides a powerful tool to investigate the functional and structural alterations occurring in HCAs, and ultimately advance our understanding of these diseases. However, current studies of these diseases usually rely on small samples and are therefore limited in there scientific and clinical significance.

Our laboratory has teamed up with clinicians and researchers from around the world to overcome these barriers by establishing international consortia (such as the ENIGMA-Ataxia working group) and multisite research studies (including TRACK-FA and the RFC1 Natural History Study). Combined with new tools for multi-site image harmonisation (COMBAT, SynthSeg), these initiatives provide unprecedented power to define the profile, evolution, and heterogeneity of rare neurological diseases.

AIMS

This study will undertake the large-scale analyses of structural and connectivity changes in HCAs using data from international consortia of clinical research sites. This work will include functional and structural MRI methods including resting state fMRI and diffusion tensor imaging (DTI) to examine cerebellar anatomical, microstructural, and connectomic changes in these diseases.

PROJECT POTENTIAL

This project will define the profile of anatomical, functional, and connectivity changes that occur in the brain and spinal cord of individuals with hereditary cerebellar ataxias, improving efforts to define sensitive markers of disease progression (biomarkers) and characterise inter-individual variability in disease expression.

Acknowledgement

QIMR Berghofer acknowledges the Traditional and Cultural custodians of the lands, waters, and seas across Queensland, pay our respects to Elders past and present, and recognise the role of current and emerging leaders in shaping a better health system. We recognise the First Nations peoples in Queensland are both Aboriginal peoples and Torres Strait Islander peoples and support the cultural knowledge, determination, and commitment of First Nations communities in caring for health and wellbeing for millennia.

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