THE UNIVERSITY OF MELBOURNE

Eastern Hill Academic Precinct Research Projects 2024

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The University of Melbourne at Eastern Hill – Who are we?

Eastern Hill Academic Precinct comprises of the University of Melbourne Departments:

Medicine, St Vincents Hospital:
https://medicine.unimelb.edu.au/school-structure/medicine/about-us/department-sections/st-vincents-hospital

Surgery, St Vincents Hospital:
https://medicine.unimelb.edu.au/school-structure/surgery/about-us/department-precincts/st-vincents-hospital

Surgery, (Otolaryngology, Royal Victorian Eye and Ear Hospital):
https://medicine.unimelb.edu.au/school-structure/surgery/about-us/department-precincts/otolaryngology

Surgery, (Ophthalmology, Royal Victorian Eye and Ear Hospital):
https://medicine.unimelb.edu.au/school-structure/surgery/about-us/department-precincts/ophthalmology

Medical Bionics:
https://mdhs.unimelb.edu.au/our-organisation/institutes-centres-departments/medical-bionics-department

Our Affiliated Hospital and Institute Partners

Centre for Eye Research Australia:
https://www.cera.org.au/careers-and-study/studying-at-cera/

St Vincents Institute of Medical Research:
https://www.svi.edu.au/study/

https://www.svi.edu.au/study/student-open-day-and-laboratory-visits/

Bionics Institute:
https://www.bionicsinstitute.org/about/study-with-us/

The Aikenhead Centre for Medical Discovery:
https://www.acmd.org.au/

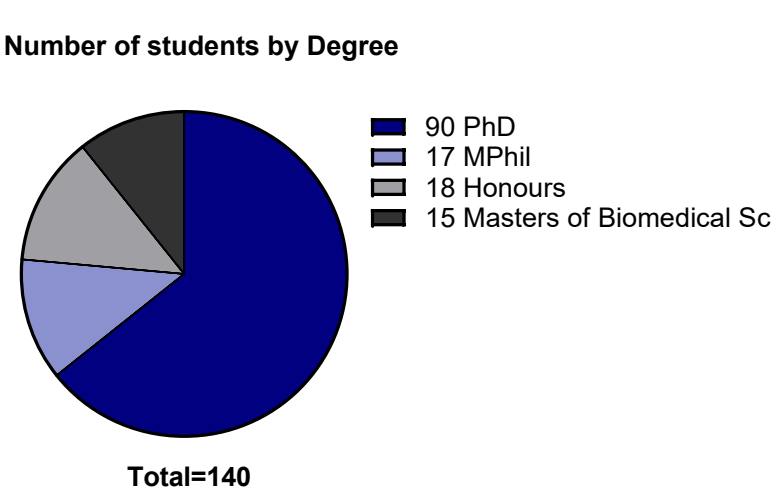
The University of Melbourne at Eastern Hill – Where are we?

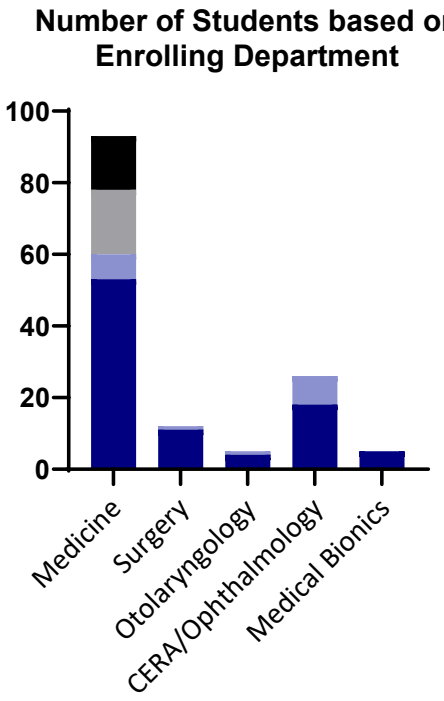
St Vincent's Hospital Melbourne 41 Victoria Parade Fitzroy Victoria 3065	**The Royal Victorian Eye and Ear Hospital** 32 Gisborne Street, East Melbourne Victoria 3002
St Vincents Institute of Medical Research 9 Princes Street Fitzroy Victoria 3065	**Centre for Eye Research Australia** Royal Victorian Eye and Ear Hospital Peter Howson Wing Level 7, 32 Gisborne Street East Melbourne Victoria 3002
Bionics Institute of Australia 384-388 Albert St, East Melbourne Victoria, 3002	

On the land of the Wurundjeri People

https://goo.gl/maps/sQ1qsCvoKRBidwJo7

Eastern Hill Precinct Student Cohort Data – July 2023





Eastern Hill Precinct Student Societies

ORBS (Ophthalmic Research Biomedical Society)

Ophthalmic Research Biomedical Society

Get in touch with us

Email: cera-education@unimelb.edu.au

To join or for more information about ORBS email: orbs.society@gmail.com

OR Follow ORBS on Facebook:

St Vincents Student Society

https://medicine.unimelb.edu.au/school-structure/medicine/study/current-student-resources/networks/student-societies

svss@svi.edu.au

Student led initiatives.

Annual student conference - Biomedlink

Honours and Master of Biomedical Science – How to apply?

Honours

An Honours program provides you with a platform toward clinical pathways, further research or a higher degree including the Doctor of Medicine. For students wishing to undertake an Honours program at St Vincents Institute of Research, applications are open to:

- Internal applicants who have successfully completed or are about to complete the Bachelor of Biomedicine or the Bachelor of Science at the University of Melbourne; and
- External applicants who have successfully completed or are about to complete an equivalent undergraduate degree.

Students can enrol in the Honours program via Bachelor of Biomedicine (degree with Honours) and the Bachelor of Science (degree with Honours).

https://study.unimelb.edu.au/find/courses/honours/bachelor-of-biomedicine-degree-with-honours/

https://study.unimelb.edu.au/find/courses/honours/bachelor-of-science-degree-with-honours/

Masters of Biomedical Science

The Master of Biomedical Science is a coursework Masters degree incorporating a substantial research project.

The Master of Biomedical Science gives you the opportunity to undertake a research project in a field of your choice, as well as a broad range of coursework subjects, including industry-focused subjects. It will equip you with the skills and knowledge to pursue a career in the wide range of commercial and industrial contexts, as well as increasing the industry knowledge and links of the next generation of biomedical researchers.

The Master of Biomedical Science is a pathway to PhD study or entry into industry.

https://study.unimelb.edu.au/find/courses/graduate/master-of-biomedical-science/

Eligibility and Application

More information on eligibility, the application process and scholarships can be found here:

Applications are now open for Semester 1, 2024 start. Application close on October 31st

https://study.unimelb.edu.au/find/courses/honours/bachelor-of-science-degree-with-honours/how-to-apply/

https://study.unimelb.edu.au/find/courses/graduate/master-of-biomedical-science/how-to-apply/

Project Opportunities for Honours and Masters of Biomedical Science

Honours and Masters of Biomedical Science projects listed in this booklet can also be found in the SONIA project database and can be accessed and selected by interested students during the application process.

https://matrix-cms.unimelb.edu.au/__data/assets/pdf_file/0022/162373/How-to-access-Sonia-instructions_Study-Hub.pdf

Graduate Research Degrees

https://research.unimelb.edu.au/study

https://research.unimelb.edu.au/study/options

Doctor of Philosophy (PhD)

A PhD at the University of Melbourne is awarded on the basis of a thesis of approximately 80,000 – 100, 000 words in which a candidate reports on an independent, sustained and academically supervised research project investigating a specialized topic.

The usual duration of PhD study is three years (full time), and all PhDs are assessed via external examination of the research thesis alone.

Master of Philosophy (MPhil)/ Masters by Research

An MPhil is designed to develop advanced skills in carrying out independent and sustained research and is awarded on the basis of a thesis of approximately 30,000 – 40,000 words.

The duration of MPhil study is 1.5 years (full time).

Other Graduate Research Degrees

Please do not hesitate to contact us to discuss your enrolment into other research higher degree programs (e.g. Doctor of Medical Science, Master of Medicine, or Master of Surgery) offered by the University.

Graduate Research Entry Requirements

https://research.unimelb.edu.au/study/how-to-apply

Applicants are normally required to have completed at least a four-year Australian honours degree or equivalent (e.g. an Australian medical degree) and achieved an overall average of greater than 80% in the relevant degree.

Applicants are also normally required to have completed a research project/ component that accounts for at least for 25% of the year's work at 4th year undergraduate or master's level.

Medical graduates from overseas universities will need to have achieved an overall average of greater than 80% in their degree.

International students must also meet the University's English Language entry requirements prior to commencement.

Further information on the University's academic and language entry requirements can be found here:

http://futurestudents.unimelb.edu.au/

Funding and Scholarships

https://gradresearch.unimelb.edu.au/scholarships

Scholarships Available for Local Students

Local* students enrolled in a graduate research degree program at the Eastern Hill Campus precinct are eligible to apply for the following University scholarships:

Research Training Program Scholarships (RTPs)

Established by the Australian Commonwealth Government, this scholarship is available to high achieving domestic students undertaking a Master by research degree or Doctoral by research degree. Benefits of an RTP include a living allowance, a relocation grant for interstate students, a thesis binding allowance and paid sick, maternity and parenting leave.

Selection is based on academic merit. Students must achieve a minimum overall average of 87 to be competitive for an APA.

Faculty Trust-Funded Scholarships

As a result of generous bequests, the University offers a number of prestigious scholarships to students with an outstanding academic record and excellent research potential.

* Local students are Australian citizens and permanent residents, and New Zealand citizens.

Scholarships Available for International Students

International students enrolled in an RHD program at Eastern Hill are eligible to apply for the following University scholarships:

International Postgraduate Research Scholarships (IPRS)

IPRSs are funded by the Australian Government. Benefits of an IPRS include a waiver of tuition fees, a living allowance (APA-International), a thesis binding allowance and paid sick, maternity and parenting leave.

Selection is based on academic merit. Students must achieve a minimum overall average of 90 to be competitive for an IPRS.

Research Training Program Stipend and Fee Offset Scholarships (RTP)

Fee remission scholarships offered by the University covers full tuition costs but not overseas health cover. MIRSs provide students with a living stipend but do not cover tuition costs. International students are generally awarded both the fee remission and stipend scholarships.

Selection is based on academic merit. Students must achieve a minimum overall average of 85 to be competitive for an RTP.

Further information on the full list of University of Melbourne scholarships can be found here: http://services.unimelb.edu.au/scholarships

Project Opportunities for Graduate Research

To find out more about the Graduate Research (PhD and MPhil) opportunities listed in this booklet, please email the contact person listed on the project directly,

OR go to:

https://research.unimelb.edu.au/study/supervisors

Project Offerings 2024

Department of Medicine, St Vincents Hospital Research Projects

The goal of our research is to improve the treatment of human disease. Driven by clinical questions, our work covers aspects of the basic mechanisms of biology and physiology, clinical and community-based epidemiology, and clinical trials of new therapies and devices. The core research foci have been on diabetes and its complications, kidney disorders, vascular disease, nutritional intervention, inflammation and thrombosis. New areas of activity include epilepsy research, genetics of leukaemia, infectious diseases, inflammatory bowel disease and other gastrointestinal disorders, and health bioinformatics.

https://medicine.unimelb.edu.au/school-structure/medicine/about-us/department-sections/st-vincents-hospital

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Biomedical (Renal and Cardiovascular) Translational Research Group

The Renal and Cardiovascular Translational Research group is focused on developing novel compounds for the treatment of pathological inflammation and fibrosis in diabetic and non-diabetic kidney, heart and eye disease. Our projects adopt a “bench to bedside” approach where we evaluate the efficacy of novel therapies on structural and functional aspects of heart, kidney, liver and eye disease using well characterised animal models that mimic the complications seen in humans.

TREATING FIBROSIS AND INFLAMMATION TO PREVENT END-ORGAN DAMAGE IN DIABETES

Suitable for Honours or Masters

Primary Supervisor: Dr Amanda Edgley
Co-supervisor:Dr Andrew Kompa

Email: aedgley@unimelb.edu.au

Diabetes is associated microvascular complications which lead to diabetic nephropathy, cardiomyopathy and retinopathy. Inflammation and scar tissue formation (fibrosis) contribute to the decline in organ function in both diabetic and non-diabetic disease. At present there is no effective treatment for pathological fibrosis. The Renal and Cardiovascular Translational Research group is focused on developing novel compounds for the treatment of pathological inflammation and fibrosis in diabetic and non-diabetic kidney, heart and eye disease. Our projects adopt a “bench to bedside” approach where we evaluate the efficacy of novel therapies on structural and functional aspects of heart, kidney, liver and eye disease using well characterised animal models that mimic the complications seen in humans. We can then assess the underlying mechanism of action of these compounds using specialised molecular, histopathological and imaging techniques, complemented with cell culture systems. As a team, we have contributed to the discovery of several anti-fibrotic compounds that inhibit the progression of diabetic and non-diabetic kidney disease and these compounds have been advanced into clinical trials in humans. We have a number of projects suitable for Honours or PhD students available to outstanding and enthusiastic students interested with a particular interest in pre-clinical drug development.

EFFECT OF URAEMIC TOXINS ON VASCULAR REACTIVITY

Suitable for Honours or Masters

Primary Supervisor: Dr Andrew Kompa

Email: akompa@unimelb.edu.au

Cardiovascular disease in the setting of chronic kidney disease (CKD) displays unique characteristics, primarily left ventricular (LV) hypertrophy with extensive interstitial fibrosis as well as endothelial dysfunction, arterial stiffness, calcification and inflammation, collectively termed 'uraemic cardiomyopathy'. Uraemic toxins are elevated in the circulation of patients with CKD. Indoxyl sulphate (IS) is one such uraemic toxin that has been extensively examined in cells and animal models of disease. IS has been demonstrated to exert deleterious effects in cardiac, renal, vascular and immune cells, and in tissues from man and animal models. Recently an intracellular receptor for IS was identified, the aryl hydrocarbon receptor (AhR), which, when activated, mediates numerous biological processes including inflammation, vascular remodeling, and atherosclerosis. This project will assess the vascular reactivity of aortic vessels exposed to the uraemic toxin IS and its inhibition using selective AhR antagonists in aortic rings. Following experiments the tissue will be examined using immunohistochemistry and real time PCR. This project will potentially identify a novel agent to treat vascular and inflammatory changes in patients' with CKD.

CHARACTERIZATION OF GPR35 IN MODELS OF CARDIAC AND RENAL DISEASE

Suitable for Honours or Masters

Primary Supervisor: Dr Andrew Kompa
Co-supervisor:Dr Amanda Edgley

For enquiries about current projects please contact: akompa@unimelb.edu.au

G-protein coupled receptor 35 (GPR 35) expression is increased early in the hearts animal models of cardiac disease such as myocardial infarction and models of hypertrophy, and in heart failure patients. Evidence suggests that GPR35 may be an early marker of cardiac pathology and may also be a potential target for the development of novel therapies. This project will assess the expression of GPR 35 in archived tissues from various animal models of cardiac disease, including myocardial infarction, pressure-overload hypertrophy and diabetes using immunohistochemistry and real time PCR.

Clinical Epilepsy Epidemiology Research Group

Group Leader: A/Prof Wendyl D'Souza

Email: wendyl@unimelb.edu.au

Our research group is focused on clinical epilepsy epidemiology, electrophysiology and co-morbidity. Particular research emphasis is currently on neural networks in Idiopathic Generalised Epilepsy and health outcomes of epilepsy using privacy preserving data linkage techniques. In addition, our strong clinical epilepsy emphasis allows unprecedented access to invasive epilepsy monitoring techniques and interpretation of brain wave recordings for seizure localisation, detection and prediction utilising cutting edge techniques.

Our group's main aims are to better understand the prognosis of epilepsy especially outcomes of modifiable public health significance (e.g. psychiatric, injury, cognition, mortality). Our ongoing clinical interest maintains this focus on immediate translation of our research findings.

Prospective students should contact the Research Group Leader in the first instance to discuss potential graduate research opportunities.

Graeme Clarke Institute

The Graeme Clark Institute for Biomedical Engineering promotes and coordinates the extensive bioengineering activities that exist across The University of Melbourne, drawing on emerging scientific and engineering approaches to drive transformative clinical solutions.

The Graeme Clark Institute is located in the Melbourne Biomedical Precinct which has established itself as a major global research and teaching powerhouse, with over 25 collaborators from health services, research and academic partners. The Graeme Clark Institute is at the centre of this precinct, and has unparalleled access to the clinical and research opportunities available across the entire network of partners. The strength of these partners, the relationships and existing collaborations, together with the proximity of the facilities provides unique opportunities to develop transformative health technologies.

By creating a community of engineers, scientists and clinicians in the healthcare system, relevant clinical problems will be identified and strategies for new approaches will be enabled and developed in partnership with industry.

More information about projects affiliated with the institute can be found here:
https://www.cmit.arc.edu.au/projects-university-of-melbourne

EEG/ MEG NETWORK MEASURES AS A BIOMARKER IN PRE-SURGICAL PLANNING FOR EPILEPSY PATIENTS

Suitable for Honours, Masters or PhD

Primary Supervisor: Dr Alan Lai
Co-supervisor:Dr Andre Peterson

For enquiries about current projects please contact: Dr Lai E: alan.lai@unimelb.edu.au or Dr Peterson: E**:** peterson@unimelb.edu.au

In both neuroscience and neurology, there is a plethora of data that has not been quantitatively analysed. One interesting way of analysing this `big data' is to convert it into a functional network that is spatially sampled at different points. This not only reduces the order of the data, but also provides a way of examining the internal structure of the data. Using various network measures, this project aims to find a functional biomarker that indicates cortical hyper-excitability. We can then use this to systematically analyse brain networks for pre-surgical planning for resective surgery in epilepsy patients.

The aim of this project will be to increase the success rate of surgeries, optimise the amount of cortical tissue resected from patients, and be able to successfully evaluate more complex cases that normally would not be eligible for surgery.

This project involves multiple fields such as epileptology, neuroimaging, neuroscience, network science and data analysis. Candidates from neuroscience, computer science, maths/physics/engineering are all suitable.

NEURAL MODELLING OF EPILEPTIC DYNAMICS

Suitable for Honours, Masters or PhD

Primary Supervisor: Dr Andre Peterson
Email: peterson@unimelb.edu.au

This project aims to understand the links between the average single neuron behaviour with the behaviour of a network of neurons. In particular, we would like to understand how the electrical behaviour becomes unstable, for example, when there is a transition to a seizure-like state from a normal or resting state We will use neurophysiology and neuroanatomy on multiple scales in combination with some mathematics to constrain the problem. This would involve some mathematical/ statistical analysis and computational simulations that are strongly grounded in neuroscience.

Students with an interest in brain modelling and some background in either neuroscience/ computerscience/ engineering/ physics/ mathematics, particularly Matlab programming are encouraged to apply. Mathematical/ theoretical skills would be appreciated but are not as important as being interested/ motivated/ curious in a multi-disciplinary project. The project can be tailored to suit the student's background appropriately.

INVESTIGATING THE ELECTROPHYSIOLOGY OF NEURONAL NETWORK DYNAMICS

Suitable for Honours, Masters or PhD, this project is in collaboration with The Florey Institute

Primary Supervisor: Dr Andre Peterson
Co-supervisors: Prof Steve Petrou. A/Prof Chris Reid

For enquiries about current projects please contact: Dr Peterson E: peterson@unimelb.edu.au, Prof Petrou E**:** steven.petrou@florey.edu.au , A/Prof Chris Reid E: christopher.reid@unimelb.edu.au

One of the current difficulties of treating neurological disease is that it is highly patient-specific, both diagnosis and treatment as everyone's brain is wired differently. The aim of this project is to understand the relationship between brain structure and brain activity. Specifically, the aim is to uncover the relationship between the structure of in vitro and in vivo neuronal networks and their behaviour, specifically their synaptic connectivity and patterns of neuronal firing. Of particular interest is the pathological case of Epileptic networks that produce abnormal electrical activity. Although it is known how various channelopathies can give rise to abnormal neuronal firing, their effect on network dynamics is unclear as it is difficult to take into account the network connectivity. This project uses and develops advanced electrophysiological methods to measure and quantify the relationship between synaptic connectivity and neuronal network activity. Uncovering this relationship has the potential to lead to novel patient-specific treatments of neurological diseases such as Epilepsy that will drive the practice of 21st century Precision Medicine.

Diabetes Technology Research Group (University of Melbourne Dept. of Medicine at St Vincent's Hospital)

Group Leader: Prof David O'Neal

Email: DTRG-t1research@unimelb.edu.au

The Diabetes Technology Research Group lead by Professor David O'Neal for over 16 years has its foundations in patient-centered diabetes technology research. The DTRG work in clinical research primarily in the type 1 diabetes space with tertiary institutions both locally in Victoria, nationally and internationally as well as with patient representative bodies including Diabetes Victoria and JDRF.

The DTRG Mission is to improve the lives of people with diabetes through exceptional research that drives advancement in innovative technologies. Their vision is to be the centre of excellence in Adult Type 1 diabetes technology research in Australia and the leading partner for collaborators, participants, industry and key stakeholders.

CHARACTERIZING THE PREVALENCE OF VITAMIN C DEFICIENCY IN AN AUSTRALIAN CLINICAL COHORT OF ADULTS WITH TYPE 1 DIABETES

Suitable for Honours or Masters

Primary Supervisor: Dr Dale Morrison
Co-supervisor:Professor David O'Neal

For enquiries about current projects please contact: dale.morrison@unimelb.edu.au

Vitamin C has several purported mechanisms that may influence health outcomes, including a role in collagen formation and immune function which is important for wound healing, but importantly it acts as an antioxidant, which is significant as increased oxidative stress is implicated in many health conditions, including cardiovascular disease, myopathy (reduced muscle function), retinopathy, neuropathy and nephropathy. Given the heightened prevalence of Vitamin C deficiency reported in patients with diabetes, along with growing evidence of associations between Vitamin C deficiency and diabetes complications, there is a potentially urgent need to understand the prevalence of inadequate plasma/serum Vitamin C concentrations in patients with diabetes. However, many studies measure dietary intake alone, which does not necessarily provide an accurate picture of Vitamin C status, and high-quality epidemiological studies are lacking, especially in those with type 1 diabetes compared to type 2 diabetes.

This study seeks to collect preliminary data regarding the prevalence of Vitamin C deficiency in a local Australian clinical population of adults with type 1 diabetes

PROTEIN INTERVENTION TO MINIMIZE EXERCISE-INDUCED HYPOGLYCEMIA IN PEOPLE WITH TYPE 1 DIABETES

Suitable for Honours or Masters

Primary Supervisor: Dr Dale Morrison
Co-supervisor:Professor David O'Neal

For enquiries about current projects please contact: dale.morrison@unimelb.edu.au

There is evidence as far back as the 1970s that ingestion of protein can stimulate glucagon secretion, resulting in increased circulating glucose. Since then, several studies have reported that the glucagon response to amino acids is preserved in people with type 1 diabetes, despite an attenuated glucagon response to other stimuli such as exercise or hypoglycemia (low blood glucose). Recent evidence demonstrates that in people with type 1 diabetes, ingestion of whey protein in the evening following exercise can stimulate glucagon and produce a sustained increase in glycemia that may be beneficial for preventing overnight post-exercise hypoglycemia.

Surprisingly, in people with type 1 diabetes, little is known about how glycemic control and glucagon secretion are regulated following pure protein ingestion (in the absence of carbohydrate), nor how this influences glycemic control during exercise. While there is clearly preliminary evidence that protein ingestion in people with type 1 diabetes can effectively

stimulate glucagon secretion, the dose-response, timing and mechanisms involved have not yet been elucidated.

The aim of this study is to characterize the timing and dose-response of whey protein ingestion on glucagon and associated hormone secretion, as well as glucose flux and glycemic responses in adults with type 1 diabetes.

Innate Immunity and Infectious Diseases Laboratory

Group Leader: Prof Kumar Visvanathan

Email: kv@unimelb.edu.au

The Innate Immunity and Infectious Diseases group seeks to understand the role of the innate immune system in a variety of infectious diseases, including viral hepatitis, septic shock and mycobacterial infections; so that we can better dissect the complex interactions between the host and the innate immune system. More recently we have become increasingly involved in collaborations examining the role of the immune system in cancer, specifically in colorectal and Hepatocellular carcinoma where we have developed organoids that can be used to assay the potential success of immunotherapeutic medications in individual patient cancers. Our ultimate goal is to generate a body of research that will clearly define the role of the innate immune system in these diseases so that we can develop new therapeutics and biomarkers.

Prospective students should contact the Research Group Leader in the first instance to discuss potential graduate research opportunities.

DEVELOPMENT OF A DIAGNOSTIC TOOL FOR SEPSIS PATIENTS BASED ON THE FUNCTION OF INNATE IMMUNE CELLS

Suitable for Honours

Primary Supervisor: Prof Kumar Visvanathan
Email: kv@unimelb.edu.au

Sepsis is a life threatening condition due to over responsive inflammatory response to a bacterial infection. Diagnosis is difficult, leading to late presentation and delayed treatment with patients progressing into multi organ failure. There is a need for rapid and effective detection as treatment options are limited and need to be administered quickly to prevent progression of infection. Blood cultures are currently used to identify bacteria responsible, however these are frequently contaminated with bacteria or not identified because of previous antibiotics. Identifying which is the cause of the sepsis, would help direct a more specific treatment. We have developed an immunological test that can broadly distinguish between a Gram+ve and Gram-ve bacteraemia. Thus the aim of the project is to test this assay prospectively. Expanding our research to include cytokine analysis via multiplex assay will investigate disease progression and a pathway of severity sepsis patients will experience based on their immune cell profile. This understanding will aid in the timing of treatment given to severe sepsis patients.

VCCC Palliative Medicine Research Group

Palliative care is a unique medical speciality that focuses on achieving the best possible quality of life for people with serious illness. As an emerging field, palliative care is accruing an evidence base to ensure the best care underpinned by the best research is available to people who have no time to waste.

Our team brings together clinicians, researchers and allied health professionals, under the leadership of the VCCC Chair of Palliative Medicine. We seek to effect positive and systemic change in palliative care practice and accelerate the translation of research-generated knowledge into improved patient care nationally and internationally. Our team is clinically embedded within St Vincent's Hospital Melbourne and other partners of the Victorian Comprehensive Cancer Centre (VCCC).

Our mission is to lead a program of robust, ethical and high-quality research that specifically focuses on improving:

- 'Systems of care' - the ways in which palliative care is provided
- 'Engagement with palliative care' - how we best talk about and come to shared decisions about treatment and care
- 'The evidence for best clinical care' - how we best support the patient and their family

Our team both leads and collaborates on a number of important studies which support our vision to effect positive and systemic change in palliative care practice.

EQUITY IN PALLIATIVE CARE – CARE FOR HOMELESS / STRUCTURALLY VULNERABLE PEOPLE AT THE END OF LIFE

Suitable for Honours or Masters

Primary Supervisor: **Prof Jennifer Philip**
Co-supervisors: **Dr Stacey Panozzo, Dr Anna Collins**

For enquiries about current projects please contact: Prof Philip, E: jphilip@unimelb.edu.au , Dr Panozzo E: Stacey.panozzo@svha.org.au , Dr Collins E: anna.collins@svha.org.au

Populations experiencing homelessness and structural vulnerability face unique barriers when accessing health care and significant inequities in accessing care at the end of life. There are inherent additional complexities and challenges for people experiencing homelessness and life limiting illnesses. There is increasing evidence that early, routine integration of and access to palliative care services can improve quality of life and pain and symptom management for patients and their caregivers.

Access to palliative care has been shown to improve when homeless people, through their interactions with social service, outreach and/or housing services, are intentionally connected to providers with a palliative care orientation and an understanding of social determinants of health. Palliative care services that are aligned with existing organisations actively engaged with and providing services for homeless people can provide quality early, integrated and safe palliative care for those experiencing homelessness and structural vulnerability.

This mixed methods project service mapping and qualitative interviews will: 1) explore the existing mobilised palliative care service models for homeless people locally and internationally; and 2) scope local palliative and end of life needs for homeless people within metropolitan Melbourne through interviews with key service providers.

CONSUMERS IN PALLIATIVE CARE - WHAT IS IN A NAME?

Suitable for Honours or Masters

Primary Supervisor: Dr Anna Collins
Co-supervisors: Dr Stacey Panozzo, Prof Jennifer Philip

For enquiries about current projects please contact: Prof Philip, E: jphilip@unimelb.edu.au , Dr Panozzo E: Stacey.panozzo@svha.org.au , Dr Collins E: anna.collins@svha.org.au

There is widespread acknowledgement that patients and their families should have a key role in shaping and advising on service development, research and educational endeavours within health care. In palliative care there are key challenges to ensuring their voices are available. A current program of work is underway to examine best mechanisms to address these challenges for palliative care.

As part of this work, the use of the word 'consumer' has been raised as a point of contention with differing views of how we should refer to those people contributing to these bodies of work. This mixed methods project using qualitative interviews and a follow up survey will explore the views of people and families regarding their preferred nomenclature. The outcomes of this project will guide work in the program and elsewhere in Australia in this important and evolving area of healthcare.

*A SYSTEMATIC REVIEW OF END OF LIFE QUALITY OF CARE INDICATORS

Suitable for PhD, Masters by Research, Master of Biomedical Science

Primary Supervisor: Prof Jennifer Philip
Co-supervisor:Dr Anna Collins

For enquiries about current projects please contact: Prof Philip, E: jphilip@unimelb.edu.au , Dr Collins E: anna.collins@svha.org.au

Increasingly services around the world are seeking to benchmark the quality of the care that is provided to patients receiving palliative care. A series of indices have been developed to seek to enable assessment between and within services of the quality of palliative care delivered. However, different indices are used in different settings and such indices cross domains including health service use indicators, and patient and family reported outcomes. A systematic understanding of the indices available and their strengths and limitations is required in order to take this important field of work forward.

*A SYSTEMATIC REVIEW OF THE MANAGEMENT OF SLEEP IN PALLIATIVE CARE CANCER PATIENTS

Suitable for Masters by Research, Master of Biomedical Science

Primary Supervisor: Prof Jennifer Philip
Co-supervisor:Dr Anna Collins

For enquiries about current projects please contact: Prof Philip, E: jphilip@unimelb.edu.au , Dr Collins E: anna.collins@svha.org.au

Sleep disturbance is very common in a cancer illness, resulting from symptoms from the cancer itself, symptoms related to cancer treatment and the psychological effects of having a cancer diagnosis. This problem frequently escalates in patients with advanced disease. The management of sleep in this setting is currently the subject of a developing program of clinical trials using pharmacological agents. This systematic review would provide the foundational tenets for this program of work.

***AN EXPLORATION OF THE EXPERIENCE OF CARE AT THE END OF LIFE FOR PATIENTS WITH A HISTORY OF ILLICIT DRUG USE: A QUALITATIVE MEDICAL RECORD REVIEW**

Suitable for PhD, Masters by Research, Master of Biomedical Science

Primary Supervisor: Prof Jennifer Philip
Co-supervisor:Dr Anna Collins

For enquiries about current projects please contact: Prof Philip, E: jphilip@unimelb.edu.au , Dr Collins E: anna.collins@svha.org.au

People with a current or past history of illicit drug use who are receiving palliative and end of life care have unique and significant care needs, including managing symptoms, particularly pain, finding an appropriate setting for healthcare delivery, managing concurrent physical and psychological comorbidity, which can be concealed by ongoing drug use, and navigating complex psycho-social circumstances. We have a program of work examining the end of life care of this patient cohort, with mixed methods data collection from patients and health care professionals. We are seeking to add a qualitative medical record review to provide an additional dimension to facilitate understanding and improve care.

Diabetic Retinopathy and Health Informatics Collaboratory

Group Leader:Dr Laima Brazionis

Email: laimab@unimelb.edu.au

The Diabetic Retinopathy and Health Informatics Collaboratory is a group of academic, clinical and technical staff brought together to address the multidisciplinary challenges associated with chronic disease diagnosis and management. The group comprises medical and information scientists from the fields of endocrinology, epidemiology, eye care, nutrition, data modelling and software development with research nodes at The University of Melbourne, University of Sydney and La Trobe University.

There is growing evidence of multiple associations between chronic diseases and behavioural, biomedical and dietary risk factors across academic disciplines. Increased quantities and granularity of data and improved communication technologies represent a paradigm shift in patient information management and knowledge sharing. As holistic approaches and technology become more integral to health service delivery, it is critical that we apply the same rigour and evidence-based assessment to these new interventions that we do to traditional practices

We conduct clinician-initiated research to produce evidence-based research development, implementation processes and tools to assist the health sector in the areas of:

- Diabetic Retinopathy Assessment
- eHealth Interoperability
- Nutritional Epidemiology (inc. dietary interventions)
- Health literacy, education & lifestyle assessment

With a focus on regional/remote communities and Indigenous Health.

St Vincent's Hospital Departments Research Projects

St Vincent's Hospital is a major teaching, research and tertiary referral centre providing acute or chronic medical and surgical services, as well as clinical training.

Some of our active research departments/ unit include:

Endocrinology and Diabetes

Director: **Prof Richard Macisaac**

The Endocrinology and Diabetes unit comprises a multidisciplinary team of physicians, diabetes educators, dietitians, and podiatrists.

Prospective students should contact the Graduate Research Programs Coordinator at easternhill-gr@unimelb.edu.au in the first instance to discuss potential graduate research opportunities OR look for Graduate Research Opportunities here: https://findanexpert.unimelb.edu.au/GROT

Gastroenterology

Director: **Prof Alexander Thompson**

The Department of Gastroenterology strives to provide quality care for our patients through a focus on patient satisfaction, ongoing research, and the education and development of department faculty, research fellows and junior doctors. The Department of Gastroenterology at St Vincent's Hospital provides a comprehensive range of consultative and diagnostic procedures in gastroenterology. It has a particular interest in chronic viral hepatitis and other liver diseases, inflammatory bowel disease, therapeutic endoscopy and oesophageal disorders.

Prospective students should contact the Graduate Research Programs Coordinator at easternhill-gr@unimelb.edu.au in the first instance to discuss potential graduate research opportunities OR look for Graduate Research Opportunities here: https://findanexpert.unimelb.edu.au/GROT

Haematology

Director: **Prof Constantine Tam**

Research in the Department of Haematology focuses on general haematological disorders including lymphomas, chronic leukaemia, multiple myeloma, anaemia, and thrombotic and general bleeding disorders.

Prospective students should contact the Graduate Research Programs Coordinator at easternhill-gr@unimelb.edu.au in the first instance to discuss potential graduate research opportunities OR look for Graduate Research Opportunities here: https://findanexpert.unimelb.edu.au/GROT

Immunology Research Centre

Director: **Prof Peter Cowan**

Email: peter.cowan@svha.org.au

Prospective students should contact the Graduate Research Programs Coordinator at easternhill-gr@unimelb.edu.au in the first instance to discuss potential graduate research opportunities OR look for Graduate Research Opportunities here: https://findanexpert.unimelb.edu.au/GROT

Neurology

Director: Prof Mark Cook

Research in the Department of Neurology focuses on the following conditions: epilepsy, movement disorders, dizziness and migraines.

Prospective students should contact the Graduate Research Programs Coordinator at easternhill-gr@unimelb.edu.au in the first instance to discuss potential graduate research opportunities OR look for Graduate Research Opportunities here: https://findanexpert.unimelb.edu.au/GROT

NEUROLOGICAL COMPLICATIONS OF CAR T CELL THERAPY

Suitable for Honours

Primary Supervisor: A/Prof Katrina Reardon
Co-supervisor:Prof Hang Quach

Email: katrina.reardon@neurologynetwork.com.au; reardonk@unimelb.edu.au

Review of Car T cell therapy and neurological complications.

Oncology

Director: A/Prof Sue-Anne McLachlan

The Department of Oncology works collaboratively with Palliative Care, Psychosocial Cancer Care and other allied health professionals. The Department also have an active clinical trial portfolio and collaborate with Australian and international trial groups.

Prospective students should contact the Graduate Research Programs Coordinator at easternhill-gr@unimelb.edu.au in the first instance to discuss potential graduate research opportunities OR look for Graduate Research Opportunities here: https://findanexpert.unimelb.edu.au/GROT

Department of Surgery, St Vincents Hospital Research Projects

The Department of Surgery at St Vincent's Hospital constantly strives to provide the highest level of complex and innovative surgical care, comprehensive surgical training for tomorrow's leaders as well as ground-breaking basic science and clinical research. We undertake a wide range of research spanning from basic to clinical research.

Our approach to new discoveries is to apply a multidisciplinary research framework engaging orthopaedic surgeons, clinicians, biomedical engineers and basic biologists to address problems such as:

- Development and progression of cancer as typified by primary and secondary cancers of bone, breast, prostate and lung;
- Disease progression and drug interventions in musculoskeletal tissues;
- Repair of bone and joint defects using tissue engineering and regenerative technology;
- Clinical assessment of outcomes following joint replacement surgery and the prognostic indicators and determinants of outcome;
- Evaluation of risk and progression of musculoskeletal conditions affecting lower and upper body joints, using innovative motion sensors and custom developed software.

https://medicine.unimelb.edu.au/school-structure/surgery/about-us/department-precincts/st-vincents-hospital

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Advanced Limb Reconstruction Research Programme

Musculoskeletal disease, the second highest cause of disability globally, underpins research within the Department of Surgery at St. Vincent's. The Advanced Limb Reconstruction Research Programme (Director - Prof. Peter Choong) addresses a spectrum of conditions including degeneration, tumour, trauma and infection, and is divided into clinical (Arthritis Surgery, Musculoskeletal Oncology), tissue engineering (Cartilage, Muscle, Nerve Regeneration), bioengineering (3D printing, Advanced biofabrication, Medical devices), and robotics (Neural Prosthetic Interface, Limb Bionics, Robotic Surgery) streams.

INVESTIGATING THE EVIDENCE BASE FOR SURGICAL PROCEDURES

Suitable for Honours

Primary Supervisor: Prof Peter Choong

Email: pchoong@unimelb.edu.au

Surgery is an important form of treatment of many medical conditions. While many procedures are successful some are associated with significant complications, and others are held with equipoise by clinicians. It is important that surgical treatments are based on appropriate evidence particularly because of the risk of real harm, rising costs and the availability of potential alternatives. This project looks at the evidence behind common surgical procedures, and the impact that these have on the health system as well the community. During this project the student will learn about how to

conduct a narrative and systematic review, as well as formulating ethics applications. This will lead to the design of a simple health services study to assess the efficacy and cost of surgical care.

BioFab3D@ACMD

BioFab3D@ACMD, located at St Vincent's Hospital, Melbourne, is Australia's first hospital-based biofabrication, robotics and biomedical engineering research centre. Here, researchers, clinicians, engineers and industry partners are working to build biological structures such as cartilage, muscle, bone, nerves and organs: almost anything that requires repair through disease and physical trauma.

The Cartilage Regeneration Program

Cartilage defects and diseases remain major clinical issues in orthopedics. The most common cartilage disease is osteoarthritis (OA), a degenerative joint disease that results from an imbalance in cartilage matrix remodeling marked by gradual loss of cartilage on the joint surface.

The cartilage regeneration project aims at preventing the onset of osteoarthritis by regenerating cartilage using unique 3D bioprinting technologies. Our group has developed a revolutionary device, called the Biopen, which allows surgeons to literally "draw" an implant composed of hydrogel material and stem cells, directly into a defect in the patient's knee. Preliminary results of both in vitro and in vivo studies for the Biopen-generated bioscaffolds are very promising.

The Biopen is often cited as one of the most exciting biomedical research programs in Australia. The project has already garnered significant national and international media attention, (e.g. Daily Mail, UK; Gizmodo US,; Forbes Magazine US, The Project on Channel 10, Australia), has been listed (twice) on the Timeline of Key Australian Medical Technology Inventions, has been nominated for the Eureka Prize, and is on track for commercialization via an Australian engineering firm.

Figure 1: The Biopen is a handheld device for surgical bioprinting.

BIOFABRICATION OF AN IN VITRO 3D OSTEOSARCOMA MODEL

Suitable for Honours, Masters or PhD

Group Leader: A/Prof Claudia di Bella
Primary Supervisors: Dr Serena Duchi
Co-supervisor: Dr Carmine Onofrillo, A/Prof Claudia Di Bella

For enquiries about current projects please contact: Dr Duchi E: serena.duchi@unimelb.edu.au, Dr Onofrillo, E: carmine.onofrillo@unimelb.edu.au

Osteosarcoma (OS) is a rare and highly aggressive bone cancer, with poor prognosis. Unfortunately, current *in vitro* preclinical models such as monolayer cell culture, fail to recapitulate the Tumour MicroEnvironment (TME) and thus accurate neoplastic behaviour, ultimately hindering therapeutic discovery. The employment of Three-Dimensional OS cell culture Models (3D-OSM) has the potential to better recreate the spatial, mechanical, and biological complexity of the TME, key elements crucial for understanding tumour prognosis and treatment effectiveness.

The goal of this project is to generate a 3D in vitro model of osteosarcoma using primary tumor cells and 3D biofabrication technologies. This project will train the candidate in tumour cells culturing, molecular and immunostaining analysis, 3D bioprinting, material science, fluorescence microscopy, microCT imaging.

This project is suited for an Honors/Master/PhD research project. The experimental work for this project will be conducted at the 3DBioFab@ACMD, St.Vincent's Hospital, Melbourne.

IN SITU TISSUE ENGINEERING FOR CARTILAGE REPAIR

Suitable for Honours or Masters

Group Leader: A/Prof Claudia di Bella
Primary Supervisors: Dr Carmine Onofrillo
Co-supervisor: Dr Serena Duchi, A/Prof Claudia Di Bella

For enquiries about current projects please contact: Dr Duchi E: serena.duchi@unimelb.edu.au, Dr Onofrillo, E: carmine.onofrillo@unimelb.edu.au

The goal of our research is to prevent the onset of Osteoarthritis by regenerating cartilage using biofabrication of Human Mesenchymal Stem Cells in hydrogel bioscaffolds. Understanding the biophysical induction of the cartilage generation process with novel techniques is a necessary step to translate our approach into the clinical practice.

*CASE: CARTILAGE ANALYTIC SCREENING ENVIRONMENT

Suitable for PhD or Masters

Group Leader: Dr Claudia di Bella
Primary Supervisors: Dr Carmine Onofrillo, Dr Serena Duchi
Co-supervisor: Prof Peter Choong

For enquiries about current projects please contact: Dr Onofrillo, E: carmine.onofrillo@unimelb.edu.au Dr Duchi E: serena.duchi@unimelb.edu.au,

The goal of our research is to prevent the onset of Osteoarthritis by regenerating cartilage using a unique 3D printing technology, that requires multiple iteration steps to select the optimal combination of a biocompatible material and stem cells, to efficiently regenerate cartilage.

The aim of this project is to generate a novel bio-physical tool to simultaneously monitor the biodegradation of a hydrogel material and the production of Collagen II matrix from stem cells. The tool will be used to discover novel materials for cartilage repair strategies.

This project will train the candidate in stem cells culturing, chondrogenic differentiation, DNA amplification and transfection, CRISPR/CAS9 technology, molecular and immunostaining analysis and fluorescence microscopy, 3D bioprinting, material science.

This project will provide an opportunity for a Master/PhD student to take part in a discovery project embedded in a multidisciplinary team based at the 3DBioFab@ACMD, St Vincent's Hospital, Melbourne.

Centre for Research Excellence in Total Joint Replacement – OPUS

Is surgery appropriate for me? Is it worth it? What other options do I have?

Total joint replacement is a revolutionary treatment for people with severe osteoarthritis (OA), but operative costs, increasing demand and post-operation dissatisfaction is unsustainable within Australia. Our health system needs to appropriately balance the needs of patients with those of the health care economy.

OPUS is a Centre for Research Excellence that uses evidence-based research to revolutionise osteoarthritis care for better patient outcomes. We want to help people with OA ask the right questions and open a dialogue with health professionals to understand the best care that is right for them.

OPUS is working towards its mission by focusing on five streams that have been designed to improve and streamline the OA journey. This is a more personalised approach to produce better patient outcomes rather than a 'one size fits all' management program for all people with OA.

The aims of the five OPUS streams are:

1. Developing a tool to identify the most appropriate OA patients for TJR.
2. Identifying patient and surgeon perceptions of risk and decision-making.
3. Developing non-surgical alternatives for OA patients.
4. Redesigning a recovery program for TJR.
5. Identifying cost efficiencies and eliminating waste in the patient OA journey.

For more information about OPUS: http://www.opus-tjr.org.au/

Department of Surgery - Otolaryngology Research Projects

Otolaryngology which is co-located at The Royal Victorian Eye and Ear Hospital is a world leader in the treatment of hearing loss and ear (otological) surgery. The Department remains at the fore-front of research into cochlear implantation, and the preservation of hearing and balance function while operating on the inner ear. The direct interface that we have between lab-based or clinical research, and direct otolaryngology patient care leads to highly productive translational research outcomes.

Laboratory research seeks to understand the biological response of the inner ear to surgery and other types of stress, and applies drug delivery, gene therapy and regenerative strategies to the protection of restoration of hearing and vestibular function. We have a strong track record in developing new therapies in the laboratories and bringing them to clinical trials.

The Department is a leader in the application of Virtual Reality to surgical simulation, working closely with engineers and psychologists at the University, together with commercial partners to create sophisticated 3D rendered simulations that provide force feedback, and real-time training.

Otolaryngology has an interest in ear infection (otitis media) amongst Indigenous Australians, as this leads to early childhood hearing loss and contributes to disadvantage amongst these children. Our focus is upon large scale clinical trials.

https://medicine.unimelb.edu.au/school-structure/surgery/about-us/department-precincts/otolaryngology

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Hearing Regeneration and Protection

UNDERSTANDING COCHLEAR IMPLANT OUTCOMES WITH ADVANCED ELECTRICAL MEASUREMENTS.

Suitable for Honours or Masters

Primary Supervisor: Dr Christofer Bester
Co-supervisors: Dr Aaron Collins, Prof Stephen O'Leary

For enquiries about current projects please contact: Dr Bester E: christofer.bester@unimelb.edu.au, Dr Aaron Collins E: aaron.collins@unimelb.edu.au , Prof O'Leary E: sjoleary@unimelb.edu.au

Cochlear implants are able to return the perception of hearing to the profoundly deaf, however they are not always successful. A substantial proportion of patients receiving an implant do no better than they were previously, but they have gone through an invasive surgery with the associated risks. Improving these outcomes requires us to understand exactly what affects outcomes, from sensory cells to neurons, as well as the human body's foreign body reaction. In this project, you will take advantage of our novel electrophysiological biomarkers in the late post-operative period to understand how these biomarkers affect speech reception outcomes.

This project will provide an opportunity for an Honours or Masters of Biomedical Science student to take part in a project based at the Department of Otolaryngology at The Royal Victorian Eye and Ear Hospital.

***IMPEDANCE TRIGGERED THERAPEUTIC INTERVENTION AFTER COCHLEAR IMPLANTATION**

Suitable for PhD

Primary Supervisor: Dr Christofer Bester
Co-supervisors: Prof Stephen O'Leary, Aaron Collins

For enquiries about current projects please contact: Dr Bester E: christofer.bester@unimelb.edu.au, Prof O'Leary E: sjoleary@unimelb.edu.au ,Dr Aaron Collins E: aaron.collins@unimelb.edu.au

A goal of modern cochlear implantation is to protect any natural, residual hearing the patient may have. Despite advances in electrode design and "soft surgery" techniques, up to 70% of implant recipients lose this hearing. We are pioneering the use of intra-operative monitoring of hearing function during cochlear implantation to actively preserve this function in theatre. However, even after an atraumatic surgery, many patients lose their residual hearing function in the following weeks. The loss of this hearing is often accompanied by a sudden, drastic increase in the electrical impedance of the implant. The purpose of this project is to test whether the monitoring of electrical impedances can be used to trigger a therapeutic intervention to prevent subsequent hearing loss. The project aims for the translation of research conducted in the department into improving clinical outcomes, during which you will be working closely with cochlear implant recipients as well as our industry partner (Cochlear Ltd).

Indigenous Ear Health

SURGERY FOR TREATING OTITIS MEDIA IN AUSTRALIAN INDIGENOUS CHILDREN

Primary Supervisor: Prof Stephen O'Leary
Email: sjoleary@unimelb.edu.au

Otitis Media is exceedingly prevalent in Australian Indigenous children, and causes a hearing loss that lasts throughout childhood and often into adult life. The hearing loss hinders learning and educational opportunities, and may have life-long impacts. The long term outcomes of the results of various treatments has been debated but never documented.

This surgical sub-study is a multi-centred, randomized trial to compare the outcomes of two surgical interventions on chronic Otitis Media in Indigenous children living in remote communities of Australia. This project seeks to inform evidence-based guidelines for the best surgical intervention for Indigenous children with OME living in rural and remote communities.

The outcome measures will be a reduction in the prevalence of OME/AOM, hearing impairment, aural discharge/perforation, and also the effect of treatment on nasal colonisation with pathogenic bacteria. Reducing the high burden of otitis media and hearing loss will improve the long-term educational and social prospects of young Australians growing up in remote communities.

Department of Medical Bionics/ Bionics Institute Research Projects

The Bionics Institute is a world leading centre of medical bionics. Our mission is to research, innovate and deliver technologies that improve human health.

For more than thirty years, we have been building on our experience and technological expertise in cochlear implants to pioneer new technologies that address otherwise untreatable, poorly treated or drug-resistant medical conditions.

The Institute creates, designs, evaluates, and improves bionic devices that interface with the human body to restore impaired sensory or other nervous system and bodily functions. Our bionic technologies seek to address the symptoms and impacts of living with hearing loss, vision loss, epilepsy, Parkinson's disease, and inflammatory bowel disease. We also develop novel clinical tools to objectively assess treatment effectiveness and improve clinical management of these conditions. This work is underpinned by fundamental research aimed at understanding the nervous system's response to electrical stimulation.

Our goal is to translate our research and innovation, using engineering and science, to address unmet clinical problems by delivering innovative implantable technologies to patients. To achieve this goal, we work closely with clinicians from Melbourne's major hospitals to ensure that all of our research programs are driven by a clearly identified health need.

https://mdhs.unimelb.edu.au/our-organisation/institutes-centres-departments/medical-bionics-department

https://www.bionicsinstitute.org/

Honours and Masters projects are offered through either the Department of Otolaryngology or Medicine.

PhD projects are offered through the Department of Medical Bionics.

Please note the Bionics Institute is not restricted to the specific projects detailed below and generally welcomes project ideas from students provided they are compatible with our overall research themes. Please contact for all project enquiries: student.enquiries@bionicsinstitute.org

HEARING BUT NOT LISTENING: USING BEHAVIOURAL TRAINING IN PRE-CLINICAL STUDIES TO TEST THE ABILITY TO LISTEN TO COMPLEX SOUNDS

Suitable for Honours or PhD

Primary Supervisor: A/Prof James Fallon

Email: JFALLON@bionicsinstitute.org
Please cc enquiry to the student coordinator: student.enquiries@bionicsinstitute.org

Behavioural training of animals allows the testing of perception of complex sounds. When applied to animals with cochlear implants or treated with hearing therapeutics, this provides important information on the performance of the intervention. This can provide more clinically relevant information than is obtained with traditional functional measurements or from histology. This added information is important, as many treatments or stimulation techniques look promising in

pre-clinical models but fail in the clinic. Using behavioural training, we aim to reduce the gap between pre-clinical and clinical studies.

This project will develop new techniques for behavioural training of animals and test responses to complex stimuli. Results will be compared against traditional electrophysiological recordings and histology.

General methods to be used in the project:

behavioural training, signal processing, electrical engineering, electrophysiology.

Suitable background of students:

This PhD project would suit a student with a background in science (e.g. biomedical) or engineering (biomedical, electrical).

UNDERSTANDING HOW THE BRAIN PROCESSES COMBINED ELECTRICAL AND ACOUSTIC STIMULATION

Suitable for Honours or PhD

Primary Supervisor: A/Prof James Fallon

Email: JFALLON@bionicsinstitute.org
Please cc enquiry to the student coordinator: student.enquiries@bionicsinstitute.org

The expansion of criteria for cochlear implantation to include patients with substantial residual hearing has focused interest on the benefits of combined electro-acoustic stimulation (EAS). Although such stimulation via a hybrid cochlear implant (CI) and hearing aid in the same ear has been shown to improve speech understanding, particularly in noise, and to increase the aesthetic quality of sound, almost nothing is known about the physiological mechanisms underlying these benefits. A number of animal studies have been performed, but they have used normal hearing animals and used simple acoustic and electrical stimulation that are not representative of complex electrical and acoustic information that represent speech and have limited clinical relevance.

This project will address this deficiency by investigating EAS in an appropriate animal model with clinically relevant acoustic and electrical stimuli.

General methods to be used in the project:

Electrophysiology, behavioural training, electrical stimulation

Suitable background of students:

This PhD project would suit a student with a background in science (e.g. biomedical) or engineering (biomedical, electrical).

CLOSED-LOOP BIOELECTRICAL NEUROMODULATION CONTROL OVER BLADDER FUNCTION

Suitable for Honours or Masters

Primary Supervisor: Dr Sophie Payne
Co-supervisor:A/Prof James Fallon

Email: spayne@bionicsinstitute.org, jfallon@bionicsinstitute.org

Please cc enquiry to the student coordinator: student.enquiries@bionicsinstitute.org

The urinary bladder stores urine produced by the kidneys and voids it from the body at behaviourally appropriate times (micturition). However, following prostectomy or colorectal resections, the nerves that control the process of urination are often damaged, leading to urinary incontinence or retention. Although not life threatening, this condition is socially debilitating and often leads to depression, anxiety and increased rates of suicide. Controlling urination with a bionic device implanted onto nerves that innervate the bladder is a novel technique for the treatment of bladder incontinence/retention. An electrode array can be used to activate or inhibit neural signals in order to trigger or prevent urination. However, for this technology to be useful, precise timing of the application of electrical neuromodulation is essential. Therefore, developing a recording feedback system that detects neural signals in order to allow accurate and timely delivery of the stimulation (i.e. closed loop) is highly advantageous. Ultimately, this technology will detect when a bladder is nearly full, and will send electrical signals to the bladder nerve to stimulate urination at an appropriate time. This project will use the rodent urogenital system to develop neural recording technology to be able to distinguish between different neural fibre types so that this technology can be utilized to develop closed-loop control over bladder function.

Suitable background of students:

This project would suit honors or master students that have experience in the following disciplines: neuroscience; bioengineering; physiology; biomedical science.

FIGHTING DISEASE WITH ELECTRICITY: VAGUS NERVE STIMULATION AS A TREATMENT OF ARTHRITIS

Suitable for Honours

Primary Supervisor: Dr Sophie Payne

Email: spayne@bionicsinstitute.org
Please cc enquiry to the student coordinator: student.enquiries@bionicsinstitute.org

Using electricity to alter the activity of peripheral nerves, dubbed ‘electroceutical therapy’, has the potential to treat a wide range of diseases that are poorly controlled by pharmaceutical drugs. Instead of circulating throughout the body and causing side effects as drugs do, electroceutical therapy sends therapeutic messages more precisely to the organs. As peripheral nerves affect many of the organs in our bodies, electroceutical intervention has been used to treat a number of diseases including inflammatory bowel disease, urinary and faecal incontinence, heart failure, obesity and gastroparesis. Previously at the Bionics Institute we have developed, tested, and validated a novel electroceutical device that stimulates the vagus nerve, to activate an internal anti-inflammatory pathway, for the treatment of inflammatory bowel disease. In this project, we will apply existing

technology to investigate the efficacy of vagus nerve stimulation as a treatment of experimental arthritis in rats.

DEVELOPING A DRUG THERAPY FOR HEARING LOSS

Suitable for Honours or PhD

Supervisor: A/Prof Andrew Wise

Please enquire to the student coordinator: student.enquiries@bionicsinstitute.org

Overexposure to noise, ageing or certain antibiotics can cause deafness due to hair cell loss in the inner ear. There currently is no pharmacological treatment for hearing loss apart from devices such as cochlear implants or hearing aids that provide only partial hearing function. This project aims to screen for drug candidates that promote hair cell regeneration using in vitro organoid assays, molecular biology techniques and animal deafness models.

TESTING NANOENGINEERED DRUG DELIVERY SYSTEMS TO TREAT HEARING LOSS

Suitable for Honours or PhD

Primary Supervisor: A/Prof Andrew Wise

Please enquire to the student coordinator: student.enquiries@bionicsinstitute.org

It has long been established that hair cells in the inner ear are susceptible to damage. Recent evidence has revealed that the synapses between hair cells and neurons are the first to degenerate in the ageing or noise-exposed inner ear. Loss of the synaptic connections between hair cells and auditory neurons can impair our ability to understand speech in noisy environments and may be associated with the generation of tinnitus and/or hyperacusis.

This project will focus on developing a treatment strategy to repair the synaptic connections in the damaged inner ear. We have recently made significant progress in the development of a nanoparticle-based drug delivery system. Here, we are interested in further interrogating the elution profile and bioactivity of the nanoparticle released drugs. The project will involve developing an in vitro model that mimics the loss of cochlear synapses to test the efficacy of nanoparticle-delivered drugs in promoting synaptic regeneration. In addition, this model will be used to investigate the molecular mechanisms underlying synaptopath.

General methods to be used in the project:

The study will involve micro-dissection, cell culture, and standard molecular biology and immunostaining techniques.

Suitable background of students:

This PhD project will suit a student with a background in cell or molecular biology, biomedical, genetics or neuroscience.

DRUG DELIVERY TO TREAT HEARING LOSS

Suitable for Honours or PhD

Primary Supervisor: A/Prof Andrew Wise

Email: AWISE@bionicsinstitute.org
Please cc enquiry to the student coordinator: student.enquiries@bionicsinstitute.org

Recent discoveries have shown that the synaptic connections between sensory hair cells and neurons in the inner ear are susceptible to damage from ageing and noise exposure. This type of damage leads to hearing impairment with particular problems of understanding speech in noisy environments, tinnitus and/or hyperacusis. There are currently no approved drug treatments that can prevent or repair hearing loss once it has occurred. This project will focus on developing a treatment for hearing loss. We have recently made significant progress in the development of a nanoparticle-based drug delivery system that overcomes some of the barriers for drug delivery to the inner ear. The project will involve in vivo deafness models to characterise the drug delivery system, and to test its safety and efficacy in repairing hearing loss. The project involves a multidisciplinary team of researchers with skills in biomedical and chemical engineering, molecular biology, systems physiology, and clinical research.

General methods to be used in the project:

The project will use a diverse range of experimental techniques including drug pharmacokinetics, behavioral, electrophysiological and histological techniques.

Suitable background of students:

This PhD project will suit a student with a background in physiology, cell or molecular biology, biomedical science, or neuroscience.

UNDERSTANDING CHANGES IN AUDITORY PROCESSING FROM NOISE INDUCED HEARING LOSS

Suitable for Honours or PhD

Primary Supervisor: A/Prof Andrew Wise

Email: AWISE@bionicsinstitute.org
Please cc enquiry to the student coordinator: student.enquiries@bionicsinstitute.org

This project will investigate auditory impairment (hearing loss and/or tinnitus) brought about by exposure to noise and the potential of drug therapy to treat pathologically changes in the auditory pathway.

OPTOGENETICS FOR PRECISE NEURAL STIMULATION

Suitable for Honours or PhD

Primary Supervisor: A/Prof Rachael Richardson

Email: RRICHARDSON@bionicsinstitute.org
Please cc enquiry to the student coordinator: student.enquiries@bionicsinstitute.org

The aim of this project is to develop the next generation of neural stimulation devices that use optical stimulation or combined optical/electrical stimulation in order to improve the precision of neural activation. The project will use cutting edge optogenetic techniques to express a light sensitive ion channel in neurons so that they can be activated with low-powered blue micro-LEDs. Electrophysiological recordings will be used to examine whether optical stimulation strategies can improve the spatial precision of neural activation. A significant advantage of improved precision of stimulation of the auditory nerve, for example, would be the ability to stimulate independent channels that would greatly enrich the auditory percept from a cochlear implant, such as the ability to perceive music.

General methods to be used in the project:

Electrophysiology, viral gene therapy, surgical device implantation, optical/electrical stimulation, optical modelling, cell culture, histology, immunohistochemistry, behavioural testing.

Suitable background of students:

This PhD project will suit a student with background in any of the following disciplines: neuroscience, physiology, biomedical engineering, or similar degrees. Electrophysiology and cell culture skills are desirable.

*USING BRAIN IMAGING TO EXPLORE LANGUAGE DEVELOPMENT IN INFANTS

Suitable for PhD

Primary Supervisor: Prof Colette McKay

Email: CMcKAY@bionicsinstitute.org
Please cc enquiry to the student coordinator: student.enquiries@bionicsinstitute.org

Functional near-infrared spectroscopy (fNIRS) is a child-friendly brain imaging technique that uses light to detect brain activity. It uses a cap containing light emitters and detectors that the person being imaged wears while doing tasks of interest. In this project, working directly with young normal hearing and hearing impaired infants and children, the student will first obtain normative fNIRS data about the development of important language areas in the brain in normal hearing children. They will then explore the effect of deafness and early intervention on this brain development in individual hearing impaired children.

General methods to be used in the project:

fNIRS imaging, language assessments, signal processing

Suitable background of students:

This PhD project has capacity for several students. It would suit graduates with qualifications in audiology or speech pathology with motivation to become familiar with fNIRS technical techniques and analyses methods. Experience working with young deaf children and their families is desirable.

Graduates with backgrounds in neuroscience, engineering or related disciplines are also welcome to apply. These applicants should have strong data analysis or signal processing skills including use of MatLab and have the interpersonal skills to work with young children and their families.

*BRAIN CONNECTIVITY IN COCHLEAR IMPLANT USERS

Suitable for PhD

Primary Supervisor: Prof Colette McKay

Email: CMcKAY@bionicsinstitute.org
Please cc enquiry to the student coordinator: student.enquiries@bionicsinstitute.org

This project will develop and apply new fNIRS imaging signal processing methods to investigate connectivity in cortical language networks in both cochlear implant candidates (for prognosis) and new cochlear implant users (for diagnosis). The PhD extends the current work in developing new individualised diagnosis and clinical management to address the poor outcomes of up to a third of new adult cochlear implant recipients. It is hypothesised that the plastic changes of interest that affect outcomes are related to connectivity between different multisensory language areas. This PhD will develop signal processing techniques that can be also applied to other fNIRS applications in the Bionics Institute.

General methods to be used in the project:

fNIRS imaging, signal processing, data collection with cochlear implant users, speech understanding assessments

Suitable background of students:

This PhD project would suit an Engineer graduate or data scientist with high-level signal processing skills and who is interested in applying their skills to address important clinical needs.

*IMPROVING OBJECTIVITY AND ACCURACY OF NEUROIMAGING ANALYSIS FOR DEEP BRAIN STIMULATION

Suitable for PhD

Primary Supervisor: Dr Thushara Perera

Email: TPerera@bionicsinstitute.org
Please cc enquiry to the student coordinator: student.enquiries@bionicsinstitute.org

DBS entails the surgical implantation of miniature electrode arrays deep within the brain. These electrodes are connected to a pacemaker-like neurostimulator implanted under the skin in the chest. Similar to the way a pacemaker jolts the heart to keep rhythm, the neurostimulator provides pulses of electricity to the brain to suppress abnormal activity. This therapy has been used for over two decades and has resulted in remarkable outcomes for patients. One of the most important aspects of DBS surgery is the accurate placement of the electrodes. The neurosurgeon must carefully guide

the electrode array (1.3mm diameter) to a target deep within the brain which is about 5mm in length – the size of a pea. Being just a millimetre off-target reduces treatment efficacy and leads to unwanted side-effects (such as slurred speech). Consequently, poorly positioned electrodes are often removed and (if possible) re-positioned during a second surgery. Neurosurgery is not without risk, and a second revision surgery is avoided at all costs.

This project will develop signal processing algorithms that aim to address current difficulties of DBS surgery to improve the safety and outcomes.

General methods to be used in the project:

Algorithm development, Data science (Python or equivalent), Digital signal processing (particularly image processing: co-registration and normalisation techniques), Mathematics (Matrices, Transformations, Vector operations), Statistics and machine learning, Data visualisation (2D/3D), Clinical trial execution and management

Suitable background of students:

This PhD project would suit electronics or biomedical engineer with a background in programming, data science, and mathematics. Previous experience with image processing and neuroimaging analysis will be highly regarded. Strong communication skills (verbal and written) must be demonstrated and a willingness to work in a flexible environment with a multidisciplinary team is crucial.

St Vincent's Institute of Medical Research Projects

Affiliated with the University of Melbourne and St Vincent's Hospital, St Vincent's Institute is an independent medical research institute conducting medical research into the cause, prevention and treatment of diseases that are common and have serious effects on health. Diseases studied at SVI include Type 1 and 2 Diabetes, obesity and heart disease, arthritis and osteoporosis, cancer, infectious diseases, and Alzheimer's and other neurological disorders. Students are enrolled either through Medicine or Surgery.

https://www.svi.edu.au/

Bone Cell Biology and Disease Laboratory

We study the cells inside the skeleton that control bone strength so we can design better ways of treating bone diseases like osteoporosis.

There are many diseases that affect the skeleton: these range from common conditions like osteoporosis through to rare bone diseases like osteogenesis imperfecta. Even though we have therapies that can treat the symptoms of bone diseases, there are no cures that can give a patient a healthy skeleton.

There is hope in our research, though. While it may seem that our bones just sit there, the skeleton is constantly being renewed to adapt to changes in diet and activity levels. Some bone cells (osteoclasts) dissolve small pockets of old bone, while new replacement bone is formed by other cells (osteoblasts). These two cell types are controlled by a third cell type (osteocytes), that form a signalling network inside the bony tissue itself.

By studying how our different bone cells behave, we will learn ways to control them. Bone cell research opens opportunities for conditions like osteoporosis and osteogenesis imperfecta to be treated more effectively, as well as to find ways to protect the skeleton in diseases such as arthritis, cancer and chronic inflammatory conditions.

https://www.svi.edu.au/laboratories/bone-cell-biology-disease/

HOW DO OSTEOBLASTS DIFFERENTIATE?

Suitable for Honours

Primary Supervisor: Dr Natalie Wee
Co-supervisor:Prof Natalie Sims

For enquiries about current projects please contact: Dr Wee E: nwee@svi.edu.au , Prof Sims E: nsims@svi.edu.au

New targeted therapies are needed to improve bone strength. This project will study the cells that are located on cortical bone surfaces, using lineage tracing (genetically-introduced fluorescent labels), to identify and track cell populations. We will test how these cells respond to a known treatment that stimulates bone growth. By studying the cells and molecular mechanisms involved, we hope to identify novel targets and pathways that may be used in the future to improve bone

strength. Techniques: mouse models, cryohistology, cell culture, RNA extraction and/or flow cytometry.

HOW ARE LYSOSOMAL PROCESSES INVOLVED IN BONE MINERALISATION?

Suitable for Honours

Primary Supervisor: Prof Natalie Sims
Co-supervisor:Dr Natalie Wee

For enquiries about current projects please contact: Prof Sims E: nsims@svi.edu.au , Dr Wee E: nwee@svi.edu.au

The mechanisms that control the quantity of mineral crystals that are incorporated into the skeleton are poorly understood, even though this is a major contributor to bone strength. Our recent discoveries indicate that intracellular vesicles, including lysosomes, are involved in mineral secretion by osteoblasts (bone forming cells) and osteocytes (cells embedded in the bone). This project will use cell culture techniques, cell-based assays, and analysis of mouse bone structure to determine the function of lysosomes in osteocytes and osteoblasts.

DNA Damage and Cancer Therapy Laboratory

Relapsed ovarian cancer kills 3 women every day in Australia. Women with the most common type of ovarian cancer, high-grade serous, initially respond to chemotherapy. This is usually followed by cancer relapse and the development of drug resistance. Our studies will provide an understanding of the biology of resistant ovarian cancer, identify novel therapeutic targets in ovarian cancer and test new therapies including the novel drug CX-5461.

CX-5461 has shown promising activity in early phase clinical trials in blood and solid cancers and our pre-clinical studies demonstrate significant efficacy for CX-5461 in ovarian cancer models. Our studies are focused on identifying optimal CX-5461 combination therapies and biomarker of response to this novel therapy. With this work we hope to identify effective treatment options for the 300,000 women around the world diagnosed with ovarian cancer each year.

If you are interested in applying for a PhD or Honours in the DNA Damage and Cancer Therapy Lab at St Vincent's Institute, please contact Dr Elaine Sanij (email: esanij@svi.edu.au) for further details.

https://www.svi.edu.au/laboratories/dna-damage-cancer-therapy/

ACTIVATION OF NUCLEOLAR-SPECIFIC DNA DAMAGE RESPONSE AS A THERAPEUTIC STRATEGY FOR OVARIAN CANCER

Suitable for Honours

Primary Supervisor: A/Prof Elaine Sanij
Co-supervisor:Dr Jian Kang

Email: esanij@svi.edu.au

Ovarian cancer is the major cause of death from gynecological cancers. The most common and aggressive subtype, high-grade serous ovarian cancer (HGSOC), accounts for 70-80% of all ovarian cancer deaths. HGSOC patients are treated by surgery and/or chemotherapy, yet within 5 years most women experience cancer relapse making the development of new treatment options an essential priority.

We developed a "first in class" drug, CX-5461 that inhibits RNA polymerase I transcription of ribosomal RNA genes and induces high levels of stress and growth arrest in cancer cells. CX-5461 is demonstrating promising activity in early phase clinical trials in haematologic and solid cancers. We have shown that CX-5461 activates the DNA damage response at the ribosomal RNA genes within the nucleoli leading to global DNA replication stress in HGSOC cells. Importantly, our studies demonstrate substantial efficacy for CX-5461 in chemotherapy-resistant models of HGSOC.

50% of HGSOC is characterized by frequent alterations of genes involved in the homologous recombination (HR) DNA repair pathway. Aberrations in DNA repair provide a weakness that can be exploited therapeutically with genotoxic chemotherapy and inhibitors of DNA repair such as PARP inhibitors (PARPi), now approved in the clinic. Our data demonstartes that CX-5461 in combination with PARPi has significant therapeutic benefit in HGSOC pre-clinical models. This project aims to investigate the molecular mechanisms underlying the improved efficacy of CX-5461 in combination with DNA repair and DNA damage response inhibitors against ovarian cancer. Specifically, we aim to characterise the molecular and cellular response to CX-5461 in combination with PARPi and cisplatin (chemotherapy) in primary and cancer ovarian cell lines.

Cancer and RNA Biology Laboratory

We are interested in how RNA editing by ADAR proteins changes the RNA landscape and contributes to normal physiology and cancer. We are studying the physiological roles of ADAR1 and the consequences of its editing of cellular RNAs. We are particularly interested in how A-to-I editing intersects with the cellular innate immune system – the cell's defence against foreign RNA, such as virus – and how these pathways intersect. This is relevant to understanding how mutations in ADAR1 cause human disease, such as the rare childhood disease Aicardi-Goutières Syndrome.

We are also interested in understanding how rare human disease syndromes, particularly those related to cancer predisposition. In this area we are focused on Rothmund-Thomson Syndrome and how the gene identified in this disease, RECQL4, functions. We generate models to identify and develop new understanding of how the key genes identified in these syndromes function and to use to identify and test potential new therapeutic options for these diseases.

https://www.svi.edu.au/laboratories/cancer-rna-biology/

DEFINING THE ROLES OF RNA MODIFICATIONS IN MODULATING IMMUNE PATHWAYS.

Suitable for Honours or Masters by Research

Primary Supervisor: **A/Prof Carl Walkley**
Co-supervisors: **Dr Jacki Heraud-Farlow**

For enquiries about current projects please contact: Prof Walkley E: cwalkley@svi.edu.au , Dr Heraud-Farlow, E: jhfarlow@svi.edu.au .

Our work is focussed on understanding the roles and functions of A-to-I RNA editing by the ADAR family of proteins. ADAR proteins can bind to RNA and change adenosine bases to inosine – essentially changing the sequence of the RNA from that encoded in the DNA. There is a rapidly expanding understanding of the roles of ADARs, particularly ADAR1. Our work has made key biological findings that are impacting the understanding of ADAR1's functions in diverse settings, including cancer, immunotherapy, behaviour and immunology.

A key function of ADAR1 is to prevent the cells own RNA being immunogenic (essentially the cells own RNA being perceived as a virus). Editing by ADAR1 is essential that cells can tell the difference between RNAs that are made by the cell and so not a threat compared to nucleic acids derived from pathogens such as viruses that invade the cell. We know that when this process goes wrong it can have deadly consequences in humans, exemplified by Aicardi-Goutieres Syndrome (AGS) and autoimmunity.

We have determined that a specific RNA modification termed Adenosine-to-Inosine (A-to-I) editing is a key regulator of the cells ability to discriminate "self" from "non-self" RNA. A-to-I editing is mediated by ADAR enzymes, with ADAR1 activity critical for this immune sensing pathway. We will use genome-wide screens and functional genomics to define the depth and breadth of the cellular network that can regulate the immunogenicity of the cells own RNA. We will use genetics, transcriptomics and saturation mutagenesis to understand how these proteins interact and modulate immunogenicity of self RNA. This will be key to understanding how the innate immune system detects RNA and how we can promote or suppress this response.

We use mouse models, cell culture, molecular and biochemical techniques to understand how ADAR1 – its editing activity or its specific isoforms – contribute to how cells deal with their own dsRNA. Projects include:

- Characterize new proteins that regulate immunogenicity of cellular dsRNA.
- Comparing the effects and roles of the two isoforms of ADAR1, p110 and p150, using genetic models and RNA-sequencing.
- Understanding how A-to-I RNA editing affects complex behaviours.

Techniques – RNA biology, genetics, cell culture, molecular biology, biochemistry, CRISPR/Cas9, genome-wide screening, bioinformatics.Disease focus: Rare disease; auto-inflammatory disease; fundamental knowledge

***NOVEL GENETIC INTERACTIONS WITH THE DOUBLE-STRANDED RNA-INDUCED AUTOIMMUNITY PATHWAYS**

Suitable for Masters by Research

Primary Supervisor: **A/Prof Carl Walkley**
Co-supervisors: **Dr Alistair Chalk, Dr Jacki Heraud-Farlow**

For enquiries about current projects please contact: Prof Walkley E: cwalkley@svi.edu.au , Dr Heraud-Farlow, E: jhfarlow@svi.edu.au , Dr Chalk E**:** achalk@svi.edu.au

This project aims to dissect genetic interactions with a form of RNA modification termed, Adenosine-to-Inosine (A-to-I) editing. A-to-I editing results in a change to the encoded RNA sequence and its misregulation can have diverse consequences such as the development of the severe autoimmune disease, Aicardi-Goutieres syndrome, where the editing enzyme ADAR1 is mutated. Changes in RNA editing have also been implicated in cancer progression, and several neurological conditions such as autism, schizophrenia and epilepsy. The primary function of ADAR1 is do edit self double-stranded RNA (dsRNA) and mask it from our own immune system. We use mouse models, cell culture and molecular and biochemical techniques to model loss of editing by ADAR1 to better understand how cells deal with their own dsRNA. This project would characterize new players in this pathway identified in a genome-wide CRISPR/Cas9 screen.

Techniques: RNA biology, mouse genetics, cell culture assays, molecular biology/biochem, CRISPR/Cas9, bioinformatics

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Genome Stability Laboratory

We investigate the process of DNA repair, with applications in treatment of genetic disorders, cancer diagnosis and cancer therapy.

DNA is the ideal biological molecule for encoding genomes due to its inherent stability. DNA damage repair (DDR) processes further promote genome stability during replication or upon exposure to endogenous or environmental DNA damaging agents. As such, DDR is involved in the aetiology of many human diseases. DDR suppresses cancer formation, by preventing mutation formation. DDR is a therapy target in cancer treatment – through radiation or chemotherapies, or more targeted precision therapies. Finally, DDR is emerging as an important tool in treatments of inherited disorders through gene editing.

Our team focuses on four lines of research that all aim to improve treatments for diseases involving DNA damage repair (DDR):

(1) identifying potential DDR targets for treating common cancers;
(2) defining DDR deficiencies that cause bone marrow failure and other childhood disorders;
(3) knowing how our cells regulate and activate DDR to prevent ageing and cancer; and
(4) creating new life-long treatments for genetic diseases using DDR gene editing therapies.

Read more about our research: https://www.svi.edu.au/laboratories/template/

A NEW METHOD FOR CRISPR-CAS9 MEDIATED GENE EDITING

Suitable for Honours or Masters

Primary Supervisor: **A/Prof Andrew Deans**
Co-Supervisor: **Dr Astrid Glaser**

For enquiries about current projects please contact: Prof Andrew Deans E: adeans@svi.edu.au, Dr Astrid Glasier E: aglaser@svi.edu.au

CRISPR-Cas9 is a game-changing gene editing tool that is likely to transform therapies for genetic disease. A programmable DNA nuclease (Cas9) is precisely guided to a specific DNA locus by a short single guide RNA (sgRNA) to elicit DNA strand breaks. Misrepair of these breaks causes gene knockouts (KOs). However, unpredictable deletions are undesirable in the context of therapeutic gene editing, where the goal is instead to precisely correct a given mutation. Precise gene editing an be accomplished by providing a DNA template flanked by homology arms resulting in precise gene correction or knock-in (KIs). A major barrier to clinical use of precise gene correction is that KOs dominate over KIs. We have discovered a novel property of Cas9 binding and cleavage that allows us to improve the rate of precise editing in vitro. By directly fusing unique enzyme activities onto Cas9 we can increase the number of KI vs KO events in cells. The student will build on these findings to generate a more precise gene editing tool, through use of novel reporter assays of KO/KI, and in systems that measure correction of disease-associated alleles. There is also an opportunity for the student to apply the technology to genes or factors associated with a genetic disorder of their own interest.

The most important outcome of this project will be a translatable application of improved gene editing for use in treatment of genetic disorders.

CANCER MUTATION PROCESSES DRIVEN BY STABILITY OF DNA:RNA HYBRIDS

Suitable for Honours or Masters

Primary Supervisor: **A/Prof Andrew Deans**
Co-Supervisor: **Sylvie van Twest**

For enquiries about current projects please contact: Prof Andrew Deans E: adeans@svi.edu.au,

Our research team has made significant progress in understanding how DNA repair factors fix DNA damage caused by stalled RNA transcription. We discovered that several cancer risk factors suppress genome instability caused by the accumulation of DNA:RNA hybrids. They enzymatically unwind RNA structures that have become trapped in the DNA duplex (see Hodson et al 2022 Cell Reports). We have now made new discoveries about the role of cancer risk factors in regulating the removal of several physiologically important R-loops. They are particularly linked to IgG class switch regions, specific promoters, splice sites, and telomeres. In cancer, these are major sites of genome instability. As part of this research program, the student will explore the basic biochemical function of enzymes that unwind DNA:RNA hybrids. They will also study the consequences of loss of these DNA interactions on genome stability in cancer pathogenesis, specifically related to mammary and blood cell development and tumour formation.

The most important outcome of this project will be a translatable application of our discovery linking tumour suppressor activity to the prevention of DNA damage caused by DNA:RNA hybrids. Because R-loops play such an important role in genome stability, they are an excellent target for new therapeutic strategies. This is especially true in tumours where normal DNA damage repair pathways are missing or mutated, or R-loop formation is high.

DNA Repair and Recombination Laboratory

Our vision is to translate basic knowledge of DNA repair pathways to treatments for cancer, bone marrow failure syndromes, and infertility.

We seek to understand the fundamentals of DNA repair pathways in both somatic and reproductive cells. Our particular focus is the Fanconi anaemia pathway, which is essential for repair of crosslinked DNA. Building on advances that we and other groups are making, we identify and characterise potential new treatments for diseases that are caused by problems of DNA repair.

Another focus of the team is how molecular pathways that maintain genome stability in somatic cells also regulate repair of double-strand breaks at meiosis. The orchestrated formation and repair of these breaks are used to generate genetic diversity and keep chromosome numbers constant from one generation to the next.

Members of our laboratory have established a support group with families affected by Fanconi anaemia (FA). The organisation, FASA, is membership-driven and aims to unite and inform the FA community in Australia, New Zealand and beyond.

Read more about our research: https://www.svi.edu.au/laboratories/dna-repair-recombination/

AUTOMATING INSIGHTS: MACHINE LEARNING ANALYSIS OF TESTES HISTOLOGY AND SPERMATOGENESIS

Suitable for Honours or Masters

Primary Supervisor: A/Prof Wayne Crismani
Co-supervisor:Dr Davis McCarthy

For enquiries about current projects please contact: A/Prof Wayne Crismani E: wcrismani@svi.edu.au

The research student project aims to harness the capabilities of machine learning to analyze histological images of testes and spermatogenesis. By employing cutting-edge deep learning techniques, the student intends to develop a robust and automated system for accurately identifying and quantifying various cellular structures and stages of spermatogenesis within testicular tissue sections. This novel approach will enable a comprehensive and efficient evaluation of sperm development, providing insights into the molecular and cellular processes underlying normal and aberrant spermatogenesis. Through the creation of an extensive annotated dataset, the student will train the machine learning model to recognize specific patterns and abnormalities associated with spermatogenic defects, contributing to advancements in male infertility diagnostics and reproductive health research. This interdisciplinary project holds great potential for unraveling the complexities of spermatogenesis and may lead to the development of targeted interventions to improve male fertility and reproductive outcomes.

AI-POWERED INSIGHT: MACHINE LEARNING ANALYSIS OF OVARIAN HISTOLOGY AND OOGENESIS

Suitable for Honours or Masters

Primary Supervisor: A/Prof Wayne Crismani
For enquiries about current projects please contact: A/Prof Wayne Crismani E: wcrismani@svi.edu.au

The research student project aims to revolutionize the study of ovarian biology by employing state-of-the-art machine learning techniques to analyze histological images of ovaries and oogenesis. Through the development of an advanced deep learning model, the student seeks to automate the identification and quantification of various cellular structures and stages of oogenesis within ovarian tissue sections. This innovative approach will provide a comprehensive and efficient assessment of oocyte development, allowing for a deeper understanding of the molecular and cellular processes underlying normal and perturbed oogenesis. By creating a well-annotated dataset, the student will train the machine learning model to detect specific patterns and abnormalities associated with oocyte maturation, offering valuable insights into female fertility and reproductive health. This transformative interdisciplinary project has the potential to advance our knowledge of ovarian biology and could lead to the development of targeted interventions to address infertility and reproductive disorders in women.

SYNAPSISENHANCE: ADVANCING MEIOTIC IMMUNOFLUORESCENCE DATA ANALYSIS WITH AN IMPROVED R PACKAGE

Suitable for Honours or Masters

Primary Supervisor: A/Prof Wayne Crismani
For enquiries about current projects please contact: A/Prof Wayne Crismani E: wcrismani@svi.edu.au

The student research project aims to enhance an existing R package – synapsis - for meiotic immunofluorescence data analysis, streamlining its functionalities and addressing user feedback to create a more efficient and user-friendly tool. By conducting an in-depth review of the current package and identifying areas of improvement, the student will work on optimizing data preprocessing steps, implementing advanced image analysis algorithms, and incorporating robust statistical methods for data quantification. Additionally, the project will focus on enhancing visualization capabilities, allowing researchers to gain better insights into meiotic events. Through rigorous testing and validation with real-world datasets, the student will ensure the package's reliability and reproducibility. By collaborating with the package's developers and actively seeking feedback from users, this research endeavor seeks to provide a valuable resource for the scientific community, enabling more accurate and comprehensive analysis of meiotic immunofluorescence data and contributing to advancements in our understanding of meiosis and genetic recombination.

UNRAVELING TUMOR SUPPRESSION WITH A NOVEL BREAST CANCER MOUSE MODEL

Suitable for Honours or Masters

Primary Supervisor: A/Prof Wayne Crismani
For enquiries about current projects please contact: A/Prof Wayne Crismani E: wcrismani@svi.edu.au

The student research project aims to establish a novel breast cancer mouse model to investigate the potential tumor suppressor role of a specific gene in breast cancer development and progression. Through genetic engineering techniques, the student will generate a cohort of mice with targeted deletion or mutation of the gene of interest within mammary epithelial cells. The resulting mouse model will be carefully characterized and monitored for the development of breast tumors and metastasis. Histopathological, molecular, and functional analyses will be conducted to assess tumor growth, cellular behavior, and the impact of the gene manipulation on tumor suppression. By elucidating the gene's potential role as a tumor suppressor in breast cancer, this project has the potential to provide crucial insights into the underlying mechanisms of tumorigenesis and may offer new opportunities for targeted therapeutic interventions.

Stem Cell Regulation Laboratory

Billions of blood cells are produced in our body each day, due to highly controlled regulation of self-renewal and differentiation processes of blood stem cells. Blood cell production predominantly occurs in the bone marrow and the non-blood cell types present in the bone marrow (collectively called the bone marrow microenvironment) are important in helping to control blood cell production from stem cells. Incomplete production or function of the different blood cell types or problems arising in the function or composition of the non-blood cells that regulate blood cell production can lead to blood cell diseases such as cancers.

The Stem Cell Regulation Unit is interested in learning how stem cells, in particular blood cell-forming stem cells, are regulated to either increase in number (by a process termed self-renewal) or produce more blood cells (a process termed differentiation). We are also interested in learning how cells of the bone marrow microenvironment (where blood stem cells normally reside) interact with blood stem cells to regulate both self-renewal of blood stem cells and blood cell production from blood stem cells. We are passionate about translational research and collaborate with a number of clinicians in the Melbourne precinct.

Read more about our research: https://www.svi.edu.au/laboratories/stem-cell-regulation/

HOW DO BONE MARROW MICROENVIRONMENTS REGULATE B LYMPHOCYTE PRODUCTION?

Suitable for Honours

Primary Supervisor: Prof Louise Purton
Co-supervisor:Dr Gavin Tjin

For enquiries about current projects please contact: Prof Purton E: lpurton@svi.edu.au

B lymphocytes, which are essential in eliminating pathogens such as viruses and bacteria, decline during aging, in part due to a reduced bone marrow microenvironment (the factory for B lymphocyte production). The changes that occur in the B lymphocyte factory that cause this decline are unclear and will be investigated in this project.

THE IMPACT OF CANCER THERAPIES ON THE BONE MARROW MICROENVIRONMENT

Suitable for Honours

Primary Supervisor: Prof Louise Purton
Co-supervisor:Dr Gavin Tjin

For enquiries about current projects please contact: Prof Purton E: lpurton@svi.edu.au

Cancer therapies cause profound reductions in blood cell counts in a range of patients and can affect treatment outcomes. We have shown that some of these effects are caused by damage to the non-blood cells that regulate blood cell production, which will be further investigated here.

REGULATION OF BLOOD CELL PRODUCTION BY ENDOTHELIAL CELL-DERIVED RETINOIC ACID RECEPTOR GAMMA

Suitable for Honours

Primary Supervisor: Prof Louise Purton
Co-supervisor:Dr Gavin Tjin

For enquiries about current projects please contact: Prof Purton E: lpurton@svi.edu.au

We have deleted the vitamin A receptor, retinoic acid receptor gamma, in endothelial cells in mice. The mice develop many defects in blood cell production and develop a bone marrow failure-like syndrome, which is a largely incurable blood cell malignancy. This project will further explore the phenotypes that occur in the mice, with an overall goal to understand how endothelial cells regulate blood cell production.

ROLES OF RETINOIC ACID RECEPTORS IN THE REGULATION OF HAEMATOPOIETIC STEM CELLS

Suitable for Honours

Primary Supervisor: Prof Louise Purton
Co-supervisor:Dr Gavin Tjin

For enquiries about current projects please contact: Prof Purton E: lpurton@svi.edu.au

We have previously shown that the biologically active derivative of vitamin A, all-trans retinoic acid (ATRA), regulates blood stem cell self-renewal. The effects of ATRA occur via three different retinoic acid receptors (RARs). We now have evidence that the three distinct RARs have different effects on blood-forming stem cells. This project will further investigate how the three different RARs regulate blood-forming stem cells, including exploring the use of RAR ligands for therapeutic purposes.

IDENTIFYING BETTER THERAPIES FOR PATIENTS WITH MYELODYSPLASTIC SYNDROMES

Suitable for Honours

Primary Supervisor: Prof Louise Purton
Co-supervisor:Dr Gavin Tjin

For enquiries about current projects please contact: Prof Purton E: lpurton@svi.edu.au

Myelodysplastic syndromes (MDS) are a heterogeneous group of blood cell cancers that are poorly understood and lack curative treatments. We have developed two different mouse models of MDS by differentially altering the expression of Homeobox a1 (Hoxa1) isoforms in the blood-forming cells. We have also identified that the expression of HOXA1 isoforms is dysregulated in human MDS cells. This project will further determine how dysregulated Hoxa1 expression causes MDS.

RNA & T Cell Biology Laboratory

We interrogate the genetic mechanisms that control development of the immune system, to better understand human health and disease.

The RNA & T Cell Laboratory works in two general research areas. Firstly, we are interested in the molecular mechanisms that control immune cell development. The immune system is comprised of a diverse range of cell types, and each type must be replenished continuously in appropriate numbers and with appropriate functional properties. This ensures that immunity against potential infections is maintained while inappropriate immune responses are suppressed. Any defect in this balance can result in susceptibility to infection or cancer, or the development of autoimmune disease.

Secondly, we are interested in the biogenesis and function of non-coding RNAs. We study how these RNAs are transcribed and processed so they can generate functional molecules. We are also interested in understanding the regulation of the microRNA machinery.

The following is a list of projects areas on offer. However, students are also encouraged to propose their own ideas. Projects within the general areas of Genomics, RNA biology and/or T cell biology are always a possibility, and can be adapted for PhD, Masters or Honours students.

Read more about our research: https://www.svi.edu.au/laboratories/rna-t-cell-biology/

REGULATION OF ILC FUNCTION AND INTESTINAL HOMEOSTASIS BY CORONIN 2B

Suitable for Honours or Masters

Primary Supervisor: A/Prof Mark Chong
For enquiries about current projects please contact: A/Prof Chong E: mchong@svi.edu.au

Homeostasis within intestinal tract involves complex interactions between the many resident immune cells, commensal flora, and food antigens. The immune cells must protect against infection from potentially harmful microbes while maintaining tolerance towards commensal organisms and food antigens. Innate lymphoid cells (ILCs) are particularly enriched at mucosal sites and have been shown to be critical for intestinal homeostasis. The lab is interested in understanding the molecular mechanisms that regulate the location and function of ILCs in the intestine and has identified Coronin 2B (Coro2b) as potentially important. Coro2b is a member of a family of actin cytoskeleton regulators and thus may be important for ILC localisation and function. To investigate this, we have developed Coro2b deficient mice for analysis. This project will involve the characterisation of the intestinal ILCs in these mice by flow cytometry and imaging. This project will also investigate the impact of Coro2b deficiency in colonic dyshomeostasis in the dextran sulfate sodium-induced colitis disease model.

DEVELOPMENT OF MICRORNA MACHINERY REPORTERS FOR HIGH THROUGHPUT DRUG SCREENING

Suitable for Honours or Masters

Primary Supervisor: A/Prof Mark Chong
For enquiries about current projects please contact: A/Prof Chong E: mchong@svi.edu.au

The RNase III enzymes Drosha and Dicer are best known for their roles in microRNA biogenesis. MicroRNAs are small (typically ~22nt) regulatory RNAs that modulate gene expression by inhibiting the translation and stability of protein coding RNAs. These small RNAs are derived by much longer precursor RNAs that are processed sequentially by the Drosha and Dicer. However, there is increasing evidence suggesting that these enzymes, particularly Drosha, have important functions beyond microRNA genesis. These alternate functions appear to manifest in response to various cellular stresses, such as DNA damage or viral infections. Moreover, Drosha has been shown to relocalise to alternate subcellular compartments to exert these alternate functions. To better understand the roles of Drosha in protecting against cellular stresses, we wish to develop new tools that will allow for high throughput screening of Drosha function in response to cellular challenges and drug treatments. The goal of this project is to tag Drosha in cell lines, which can then be employed in imaging approaches. This project will employ CRISPR-mediated gene targeting to insert GFP into the N- or C-terminus of the endogenous Drosha gene. These cells will then be analysed for the localisation of Drosha in response to important cellular stresses, including inflammatory stimuli, DNA damage and virus infection.

Human Immunology Laboratory

The Human Immunology laboratory is focused on the autoimmune disease type 1 diabetes. Broadly, we have two goals. The first is to understand how and why insulin-producing beta cells are attacked by the immune system's T cells – which is the ultimate cause of type 1 diabetes. Our second goal is to use this information to develop safe and effective ways to stop disease progression for people at high risk. Our long-term objective is to reverse type 1 diabetes in people who have been recently diagnosed.

Currently, the focus of our work is unravelling the specificity of the autoimmune responses that cause people to develop type 1 diabetes. We achieved a world-first when we isolated and analysed

human islet-infiltrating T cells from deceased organ donors who suffered from type 1 diabetes. This invaluable resource has allowed us to understand the 'nuts and bolts' of the autoimmune response in the part of the body that is affected. A second major focus is to develop and validate new tests that can be used to monitor the autoimmune response that causes type 1 diabetes. This works will lead us to develop safe and effective therapies for the prevention, or reversal, of type 1 diabetes.

The Human Immunology Laboratory has an array of Student projects suitable for Honours, Masters of PhD students. The projects focus on the immunology of type 1 diabetes in humans. Students interested in pursing graduate studies in the Human Immunology laboratory should have a background one or more of the following areas: biomedicine, biochemistry, genetic, pathology, physiology and Immunology. A strong background in immunology is a distinct advantage. Graduate students are integrated into the research team. They are supported by Associate Professor Mannering and all other members of the laboratory. We offer several continuing learning opportunities, including, Journal Club, Seminars, and lab meetings. Students will emerge with a strong background in contemporary immunology. They will have highly developed technical skills in their project area, a strong knowledge of immunology, autoimmunity and diabetes. Students learn to communicate their research findings in both written and oral form.

https://www.svi.edu.au/laboratories/human-immunology/

DO CD4+ T CELLS, THAT INFILTRATE HUMAN PANCREATIC ISLETS, IN TYPE 1 DIABETES RECOGNIZE ENTEROVIRUS PROTEINS?

Suitable for Honours or Masters

Primary Supervisor: A/Prof Stuart Mannering
Co-supervisor:Dr Pushpak Bhattacharjee

For enquiries about current projects please contact: A/Prof Mannering E: smannering@svi.edu.au

Type 1 diabetes (T1D) is an autoimmune disease that is caused by the T-cell mediated destruction of the pancreatic, insulin-producing, beta cells. Unusual for an autoimmune disease, T1D frequently develops in the first decades of life. Currently T1D is treated by frequent insulin injections which replaces the insulin normally produced by the beta cells. While insulin replacement has been a life-saving therapy for T1D it is not a cure and people with T1D have a shorter life expectancy than those without T1D.

The immune pathogenesis of T1D is poorly understood [1]. It is clear that both CD4+ and CD8+ T cells work together to mediate beta-cell destruction. However, it remains unknown 'how and why' the immune system targets the insulin-producing cells in people who develop T1D. Viral infections, particularly enterovirus infections, have been suggested to contribute to the onset of autoimmunity, but this remains controversial [2][3].

The goal of this project is to investigate if human islet-infiltrating CD4+ T cell recognize antigens derived from enteroviruses. We have amassed a large (100s) panel of CD4+ and CD8+ T-cell clones or T-cell receptors (TCRs) from 12 deceased T1D donors. This is a powerful resource because it allows us to scrutinise the antigen specificity of human T cells that have infiltrated the pancreatic islets, the site of autoimmunity in T1D [4]. Finding enterovirus specific CD4+ T cells within the pancreatic islets of organ donors who had T1D would be important new evidence implicating

enteroviruses in the immune pathogenesis of T1D. On the other hand, if we find that islet infiltrating CD4+ T cells don't recognize enterovirus antigens, this suggests that this virus does not play a direct role in the immune pathogenesis of human T1D.

This project will give the student an excellent training in immunology, particularly human T-cell immunology and autoimmunity. This project will make a significant contribution to understanding of the role of enteroviruses in human T1D.

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WHAT HYBRID INSULIN PEPTIDES (HIIPS) ARE RECOGNIZED BY HUMAN ISLET-INFILTRATING CD4+ T CELLS IN TYPE 1 DIABETES?

Suitable for Honours or Masters

Primary Supervisor: A/Prof Stuart Mannering
Co-supervisor:Dr Pushpak Bhattacharjee

For enquiries about current projects please contact: A/Prof Mannering E: smannering@svi.edu.au

Type 1 diabetes (T1D) is an autoimmune disease that is caused by the T-cell mediated destruction of the pancreatic. The immune pathogenesis of T1D is poorly understood. It is clear that both CD4+ and CD8+ T cells work together to mediate beta-cell destruction. However, it remains unknown 'how and why' the immune system targets the insulin-producing cells in people who develop T1D. Recently we helped to identify an entirely new class of antigen, known as Hybrid Insulin Peptides (HIPs). HIPs are neoepitopes [5] formed by the fusion of two beta-cell granule proteins and are recognized by pathogenic CD4+ T-cells in the NOD mouse and by human islet-infiltrating CD4+ CD4+ T cells [6, 7]. Currently less than 20 HIPs recognized by human CD4+ T cells have been reported. Because a HIP can be formed by fusing any two protein fragments, it has been very challenging to identify new HIPs [8].

To overcome this technical challenge, we have established an antigen screening platform that has allowed us to identify new HIPs from a library of over 4,000 candidate HIPs. The strength of our approach is that we use CD4+ T cells isolated from the pancreatic islets of deceased organ donors who had T1D [4]. This ensures that we identify antigens that are clinically relevant to the development of T1D. In our first project we used HIPs formed by the fusion of fragments of proinsulin to other proinsulin fragments (manuscript in preparation). Now we'd like to explore HIPs formed by the fusion of proinsulin with other beta-cell proteins.

The goal of this project is to apply our HIPs screening platform to identifying HIPs formed by the fusion of proinsulin with other beta cell granule proteins. This project will leverage our established optimised work-flow and our large (100s) panel of CD4+ T-cell clones from 12 deceased T1D donors [4].

This project will give the student an excellent training in T-cell immunology, particularly human T-cell immunology and autoimmunity. This project will build on our current work to further explore the array of HIPs recognized by human T cells in T1D.

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MEASURING ISLET-ANTIGEN SPECIFIC REGULATORY T-CELL (TREG) FUNCTION IN HUMAN TYPE 1 DIABETES.

Suitable for Honours or Masters

Primary Supervisor: A/Prof Stuart Mannering
Co-supervisor:Dr Matthew Lacorcia

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Type 1 diabetes (T1D) is an autoimmune disease caused by the combined action of CD4+ and CD8+ T-cell response against the insulin-secreting beta cells which are found within the islets of Langerhans in the pancreas. The adaptive immune response has many 'check and balances' that prevent, or attenuate harmful immune responses. CD4+ regulatory T cells, known as Treg, play an important role in maintaining immune tolerance and curbing undesirable immune responses. Tregs work similarly to CD4+ T helper, or effector, cells. They use their T-cell receptor (TCR) for antigen to 'recognize' peptide antigens presented by HLA-Class II. However, unlike Teff, which after TCR mediated activation secrete cytokines that 'activate' other immune cells in the vicinity, Treg actively suppress the effector function of neighbouring immune cells.

Regulatory T -cell responses are thought to play a central role in the development of autoimmune diseases, like T1D. For an autoimmune disease to manifest, the 'self' reactive immune cells must avoid, or be refractory to, the function of regulatory T cells. Boosting the number and/or the activity of autoantigen specific Treg is a promising therapeutic avenue for developing new therapies for autoimmune diseases, including T1D.

Harnessing Treg to prevent, or reverse, autoimmune diseases is hampered by difficulties in measuring the number and function of self-antigen specific CD4+ T reg. Treg function can be measured in vitro using purified cell populations, stimulated with an anti-CD3 mAb. Anti-CD3 stimulates all T cell irrespective of their antigen specificity. However, it has proven to be much more difficult to measure antigen specific Treg function. In our work to address this problem we have recently acquired data that suggests that we may be able to measure the function of human beta cell antigen specific Treg.

Hence, the aim of this project is two-fold. First to validate that the responses we are seeing are CD4+ regulatory T-cell responses. The second aim is to dissect the mechanism by which this Treg functions mediated.

This project will give the student an excellent training in immunology, particularly human T-cell immunology and autoimmunity. In the longer term this work will contribute to understanding of human Treg function, which has very important implications for both the diagnosis and developing new antigen specific therapies to prevent T1D.

Immunology Laboratory

We study the precise mechanisms by which T cells destroy beta cells – the ultimate cause of type 1 diabetes – and test ways to prevent this from happening.

In type 1 diabetes, insulin-producing beta cells (arranged in clusters called islets) are destroyed by immune mechanisms. The major immune cell type involved is the CD8+ cytotoxic T lymphocyte (CTL) that directly recognises short peptides derived from proteins like insulin presented by major histocompatibility complex class I proteins on the surface of beta cells.

We study the precise mechanisms by which T cells destroy beta cells, and test ways to prevent this from happening. Much of our work is based on the NOD mouse model that develops diabetes in a similar manner to humans. We also have several transgenic mice that express particular T cell receptors that are able to cause rapid diabetes. We use these mice, and our expertise in flow cytometry, immunohistochemistry and molecular biology, to study the role that cytokines, death-receptor molecules and perforin/granzymes play in the development of diabetes.

The major questions we are studying are the use of immune tolerance to insulin as a way of arresting diabetes, and also how CTL differentiate into fully effective cytotoxic T cells.

Read more about our research: https://www.svi.edu.au/laboratories/immunology/

CLINICAL RESEARCH USING DATA AND SAMPLES FROM CLINICAL TRIALS

Suitable for Honours or Masters

Primary Supervisor: **Prof Tom Kay**
Co-supervisors: **Dr Michelle So, Dr Michaela Waibel**

For enquiries about current projects please contact: Prof Kay E: tkay@svi.edu.au

We have just completed the Bandit trial, a placebo-controlled trial to investigate the safety and efficacy of baricitinib in individuals with recent-onset type 1 diabetes. The primary objective to determine if baricitinib can reduce the loss of meal-stimulated C-peptide, a measure of beta-cell function, was met. This trial will be followed by other trials of JAK inhibitors if it is successful and also by trials of other therapies. Trials like Bandit produce large amounts of patient data with numerous immunological and metabolic parameters and numerous aliquots of plasma and peripheral blood mononuclear cells, the term used for preparations of lymphocytes and monocytes isolated from blood. Some of the challenges we recognise include being able to measure disease activity in order to titrate immunotherapy or add new agents in the event of a flare of disease. Are

there cellular patterns or cytokine levels in blood that can guide this in the absence of clinical features that indicate disease activity in other autoimmune diseases. Does a concurrent medical event like the Covid-19 pandemic affect a trial. These are the kinds of questions that can be tested.

IMPACT OF JAK INHIBITORS ON T-CELL EXHAUSTION AND OTHER IMMUNE REGULATORY MECHANISMS

Suitable for Honours or Masters

Primary Supervisor: Prof Tom Kay
Co-supervisor:A/Prof Bala Krishnamurthy

For enquiries about current projects please contact: Prof Kay E: tkay@svi.edu.au

We do not know whether JAK inhibitors would increase or decrease the development or impact of T-cell exhaustion and whether these two approaches would make a possible future combination treatment. JAK inhibitors might block the effect of cytokines produced in the islet that we have suggested sustain the reservoir of precursor exhausted T cells in the islets. Or do Jak inhibitors reduce the expression or effect of cytokines like IL-10 that may contribute to the impact of T-cell exhaustion. This study will utilise the NOD mouse model and our previously produced models of T-cell exhaustion to explore this question.

MECHANISMS OF REGULATORY T CELL ACTION IN TYPE 1 DIABETES

Suitable for Honours, Masters or PhD

Primary Supervisor: Dr Andrew Sutherland
For enquiries about current projects please contact: Dr Sutherland, E: asutherland@svi.edu.au

Type 1 diabetes (T1D) is a human disease involving progressive autoimmune destruction of the b-cells in the pancreatic islets. Regulatory T cells including FoxP3+ Tregs and Type 1 regulatory (Tr1) cells can play important roles in the progression of autoimmune diseases by suppressing pathogenic autoimmune responses, however their precise mechanisms of action in T1D pathogenesis remain unclear. A clearer understanding of these processes will provide better opportunities for therapeutic intervention in human T1D patients. This project seeks to identify novel mechanisms of regulatory T cell differentiation and function in T1D, with a specific focus on cytokine regulated pathways and interactions with gut microbiota. The project will make use of both mouse and human systems including newly developed gene knockout NOD mice, CRISPR/Cas9 gene editing, cellular and molecular immunology techniques, pancreatic islet isolation, RNA-seq and flow cytometry.

UNDERSTANDING THE FUNCTIONS OF IL-17 FAMILY RECEPTORS IN TYPE 1 DIABETES

Suitable for Honours, Masters or PhD

Primary Supervisor: Dr Andrew Sutherland
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Type 1 diabetes (T1D) is a human disease involving progressive autoimmune destruction of the b-cells in the pancreatic islets. Inflammatory cytokines are important regulators of T1D, however their

precise mechanisms of action in T1D pathogenesis remain unclear. A clearer understanding of these processes will provide better opportunities for therapeutic intervention in human T1D patients.

Recent findings in our laboratory indicate that IL-17 receptors control the development of T1D in animal models. This project seeks to identify the underlying immune mechanisms of T1D protection and test the therapeutic effects of immune inhibitors targeted against these pathways. The project will make use of both mouse and human systems including newly developed gene knockout NOD mice, immune inhibitors, CRISPR/Cas9 gene editing, cellular and molecular immunology techniques, pancreatic islet isolation, RNA-seq and flow cytometry.

USING JAK INHIBITORS TO ATTENUATE SELF-REACTIVE MEMORY T CELLS IN AUTOIMMUNE DIABETES

Suitable for Honours

Primary Supervisor: Prof Helen Thomas
Co-supervisor:Dr Prerak Trivedi

For enquiries about current projects please contact: Prof Helen Thomas, E: hthomas@svi.edu.au

Type 1 diabetes results from destruction of insulin producing beta cells by self-reactive T cells. Persistence of self-reactive memory T cells that can give rise to effector cells is a major hurdle to preventing beta cell destruction. Differentiation and survival of memory T cells require signalling through both T cell receptors and pro-inflammatory cytokines that signal via the JAK-STAT pathway. We have previously shown that blocking cytokine signalling using a JAK inhibitor can impede the function of self-reactive effector T cells and hence prevent diabetes. However, quiescent self-reactive memory T cells have reduced dependence on cytokines and can possibly escape JAK inhibitor treatment. We propose that modulating T cell receptor signalling will make memory T cells more dependent on cytokines, allowing JAK inhibitors to permanently disarm self-reactive T cells. We will test this in NOD mice. Anti-CD3 therapy with teplizumab has shown promising results in delaying type 1 diabetes onset in clinical trials and we are currently testing the efficacy of the JAK inhibitor baricitinib in recent onset type 1 diabetic patients. This work will provide rationale for combing these two therapies in future clinical trials to prevent type 1 diabetes.

USING JAK INHIBITORS WITH LOCALLY DELIVERED IMMUNOSUPPRESSION TO TARGET ISLET GRAFT REJECTION

Suitable for Honours or Masters

Primary Supervisor: Prof Helen Thomas
Co-supervisor:Prof Thomas Kay

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Beta cell replacement offers the opportunity to cure type 1 diabetes. However, due to a shortage of suitable organ donors, replacement beta cells are likely to be stem cell derived. These cells will need to be protected from allogenic rejection and recurrence of autoimmunity. In this project we will test whether JAK inhibitors, that block cytokine signalling pathways, together with antibodies that target memory T cells, will prevent loss of grafted beta cells. We will do this using the NOD mouse model

of spontaneous autoimmune diabetes. Methods include islet grafting, flow cytometry, imaging and single cell RNAseq.

INDUCING T-CELL EXHAUSTION TO PREVENT TYPE 1 DIABETES

Suitable for Honours

Primary Supervisor: Dr Bala Krishnamurthy
Co-supervisors: Dr Gaurang Jhala, Prof Helen Thomas

For enquiries about current projects please contact: Dr Krishnamurthy E: bmurthy@svi.edu.au or Prof Helen Thomas, E: hthomas@svi.edu.au

Immune therapies that target beta-cell antigen-specific T cells are needed to prevent type 1 diabetes. T-cell exhaustion is a state of cellular dysfunction with decreased cytokine production, effector function and self-renewal capacity. Understanding T-cell exhaustion is an emerging area of research in chronic infection, cancer immunotherapy, and more recently, autoimmunity. While deleterious in the context of cancer, T-cell exhaustion would be desirable in autoimmune diseases like type 1 diabetes. High and persistent antigen exposure is important driver of T-cell exhaustion. However, despite chronic exposure to beta cell antigen, T cells go on to destroy beta cells in type 1 diabetes indicating retain cytotoxic function and self-renewal capacity of the T cells. To understand this paradox, we have generated powerful animal models to test methods to induce T-cell exhaustion to prevent type 1 diabetes. We will study the number, function and exhausted phenotype of beta cell specific T cells in transgenic mice and their capacity to induce diabetes. We will also gain detailed mechanistic insight at the single cell level using transcriptomic profiling of islet reactive T cells. Our studies will lay the groundwork for developing future clinical studies.

CONCURRENT ANALYSIS OF T-CELL EXHAUSTION IN ISLET AND TUMOUR MICROENVIRONMENTS IN A NOVEL TUMOUR MODEL IN NOD MICE.

Suitable for Honours or Masters

Primary Supervisor: Dr Gaurang Jhala
Co-supervisor:Dr Bala Krishnamurthy

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Chronic exposure to tumour antigens in cancer and organ-specific antigens in autoimmune diseases such as type 1 diabetes (T1D) drives T cell exhaustion. T cell exhaustion reduces the effectiveness of T cells to control the tumours allowing cancer to progress, but paradoxically islet reactive T cells showing features of exhaustion continue to destroy beta-cells in T1D. Our work is focused on understanding how the exhausted T cells in the tumour environment are different to those developing in the autoimmune islet environment. Understanding this will allow us to exploit processes that make T-cells causing T1D more exhausted like those in cancer and prevent T1D. To do this we have developed a novel transplantable tumour cell line expressing islet antigen(s). We will transplant tumours expressing islet antigens in the non-obese diabetic (NOD) mouse model of T1D and study the difference in the exhaustion program of islet antigen-specific T cells developing

in the transplanted tumour and host islet microenvironment. We hypothesize that islet antigen-specific T cells infiltrating the tumour will undergo severe T cell exhaustion. To examine how exhausted islet-specific T cells regulate the other effector T cells in NOD mice we will remove the tumour and follow the NOD mice to see if they are protected from diabetes.

Diabetes & Metabolic Disease Laboratory

Metabolic diseases such as obesity and diabetes are major health concerns worldwide, with Australia being one of the most affected countries. Diabetes increases cardiovascular risk at least three-fold, it is associated with accelerated atherosclerosis and linked to premature mortality. We are interested in studying the underlying mechanisms that contribute to the development of these metabolic disorders. Further understanding of the pathophysiology of obesity, diabetes and atherosclerosis will help us develop more effective therapeutic approaches for these diseases.

Specifically, our research program focuses on the discovery and fundamental biology of several key molecules – including Salt-inducible kinase 3 (SIK3), Neuropeptide Y (NPY) and AMP-activated protein kinase (AMPK) – that play crucial roles in the regulation of energy homeostasis, beta-cell biology, glucose and lipid metabolism. These molecules are currently being pursued across the pharmaceutical sector as promising drug targets for chronic diseases such as diabetes, obesity and cardiovascular disease.

We have developed a sophisticated suite of research tools, such as several novel transgenic mouse models, to determine the precise role of these molecules in metabolic regulation. We aim to clarify the exact contribution these molecules make to the development of metabolic diseases – such as obesity, diabetes and atherosclerosis – to find new and more effective treatments.

https://www.svi.edu.au/laboratories/diabetes-metabolic-disease/

INVESTIGATING A NOVEL MECHANISM FOR IMPROVING BETA-CELL FUNCTION IN TYPE 2 DIABETES

Suitable for Honours or PhD

Primary Supervisor: Dr Kim Loh

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We aim to investigate whether pharmacological inhibition of SIKs signalling will enhance β-cell function and improve glucose homeostasis in type 2 diabetes.

Current efforts to enhance β-cell function focus mostly on the pathways that stimulate insulin release, very little is known about the inhibitory mechanisms that terminate insulin secretion. Improving β-cell function by inhibiting the counter-regulatory pathway that suppresses the release of insulin remains largely unexplored as a therapeutic option. Peptide YY has been shown to activate neuropeptide Y1 receptor to attenuate insulin secretion in mouse pancreatic islets.

We have identified that the neuropeptide Y1 receptor is also expressed in the β-cells in humans. Our recent published studies (Loh et.al, 2017, Nature Communications) have shown that pharmacological inhibition of this receptor using a Y1 receptor specific antagonist, BIBO3304,

significantly enhanced β-cell function in human islets. Despite this, the beneficial effects of Y1 inhibition in improving β-cell function and glycaemic control in type 2 diabetes remain to be examined. We will now extend our published work with a detailed exploration of Y1 receptor inhibition in type 2 diabetes models. We aim to investigate whether pharmacological inhibition of Y1 receptor signalling will enhance β-cell function and improve glucose homeostasis in type 2 diabetes.

As part of our laboratory, you will receive multi-disciplinary training from experts in biochemistry, cell biology, x-ray crystallography and mass spectrometry. The team adopts a highly collaborative approach, with studies regularly published in high impact journals.

Metabolic Signalling Laboratory

Te Metabolic Signalling Laboratory conducts research on kinase signalling networks that control cellular metabolism. These networks become dysfunctional in metabolic diseases such as insulin resistance, type 2 diabetes and cardiovascular disease, and also represent vulnerabilities in cancer cells that can be targeted to prevent tumour growth and metastasis.

Our principal focus is the cellular fuel gauge AMP-activated protein kinase (AMPK) which detects when energy in the cell is low and co-ordinates multiple pathways to counter energy imbalance (e.g. fat burning, protein synthesis, autophagy). AMPK is also a key regulator of appetite and muscle adaption to exercise. Other metabolic enzymes of interest include CaMKK2, a driver of prostate and ovarian cancers and metabolic disorders, and DRP1, important for mitochondrial health and heart function.

We apply biochemistry, cell biology, microscopy, structural biology, mass spectrometry and animal models to gain insight on the roles of these important enzymes and how they are regulated, with the aim of developing new, effective and safe strategies to unlock their therapeutic potential.

Read more about our research: https://www.svi.edu.au/laboratories/metabolic-signalling/

HOW DOES FAT REGULATE MITOCHONDRIAL DYNAMICS?

Suitable for Honours or Masters

Primary Supervisor: A/Prof. Jon Oakhill
Co-supervisor:Dr Naomi Ling

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Mitochondria are organelles that provide cells with the energy they need to survive and grow. Mitochondrial health is crucial for cell function and is partly controlled by the enzme DRP1 - a promising drug target for various neurological, oncological and cardiovascular disorders (Rosdah et al, doi: 10.1016/j.pharmthera.2020.107594). DRP1 is regulated by phosphorylation events and we have recently discovered that DRP1 is activated by long chain fatty acid CoA esters (LCFA-CoAs) such as palmitoyl-CoA. We hypothesise that DRP1-regulating kinases in the Ras-Raf-MEK-ERK pathway are also regulated by endogenous LCFA-CoAs, revealing a co-ordinated, metabolite-sensing capacity linking cellular nutrient availability to mitochondrial function. Using a combination of biochemistry, cell biology, mass spectrometry and microscopy in a supportive and well-equipped environment,

this exciting Honours project will generate new knowledge on metabolite sensing by central and fundamental signalling pathways. Applicants considering this project will need to be motivated and curious.

EXAMINING STRUCTURE AND FUNCTION OF THE MAJOR DRUG TARGET AMPK IN MUSCLE

Suitable for Honours or Masters

Primary Supervisor: A/Prof. Jon Oakhill
Co-supervisor:Dr Ash Ovens

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AMP-activated protein kinase (AMPK) is a critical regulator of cellular energy metabolism that controls many of the acute and adaptive effects of exercise in skeletal muscle (Kjøbsted et al, doi: 10.1096/fj.201700442R). As such, AMPK in skeletal muscle is an important drug target for Type 2 Diabetes, sarcopenia, cachexia, muscular dystrophy etc. Skeletal muscle is the only organ in humans to express the regulatory AMPK γ3 isoform, which is differentiated from the other γ isoforms 1 & 2 by a unique N-terminal domain (NTD). Our extensive preliminary data has revealed an unexpected regulatory role for the γ3 NTD that could be exploited for muscle-specific AMPK activation, a major aim of big pharma. Using a combination of biochemistry, cell biology, mass spectrometry and structural biology in a supportive and well-equipped environment, this exciting Honours project will generate new knowledge on the structure and function of AMPK γ3. Applicants considering this project will need to be motivated and curious.

Structural Biology Laboratory

We determine the three-dimensional atomic structures of proteins involved in disease, with a focus on neurodegenerative diseases and cancer. These structures help us to explore protein function, as well as to discover new drugs.

The work of the Structural Biology Laboratory is internationally recognised. Our work has defined more than 200 crystal structures and more recently, structures derived from cryo-election microscopy – including those of membrane-associating proteins, detoxifying enzymes and protein kinases. This work has provided insights into cancer, bacterial and viral infections, and neurological diseases such as Alzheimer's disease.

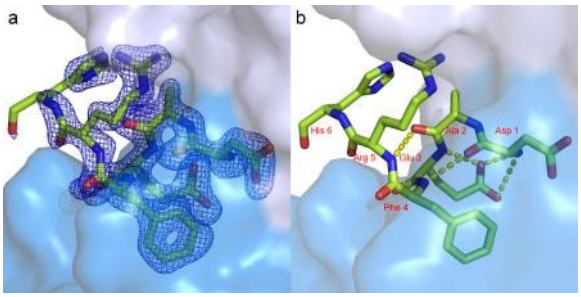
In recent years, we have emphasised the translational aspects of our work, with increasing focus on structure-based drug discovery. This focus has been underpinned by development of virtual screening and fragment screening platforms in-house, by funding from the Australian Cancer Research Foundation, and partnerships with biotechnology companies including CSL Limited and Janssen.

Read more about our research: https://www.svi.edu.au/laboratories/structural-biology/

STRUCTURAL BIOLOGY OF PROTEINS INVOLVED IN MENTAL ILLNESSES

Suitable for Honours, Masters or PhD

Primary Supervisor: Prof Michael Parker
Co-supervisor:Dr Stefan Hermans



For enquiries about current projects please contact Prof Parker Email: mwp@unimelb.edu.au

We are focused on understanding the molecular bases of a range of neurodegenerative diseases and to develop much needed treatments. One area of focus is Alzheimer's disease (AD) which is the fourth biggest killer in developed countries. Amyloid precursor protein (APP) plays a central role in the development of AD. Here we will use biophysical approaches to probe APP function together with X-ray crystallography at the Australian Synchrotron and cryo electron microscopy to determine the 3D atomic structures of APP and of potential therapeutic antibodies and diabodies bound to parts of APP. The latter project allows us to rationally engineer more potent antibodies and diabodies as treatments for AD. Toxic molecules associated with neurodegenerative diseases are disposed of by the brain's immune cells called microglia. We are investigating the structure and function of key protein receptors found on the surface of microglia cells as a basis for the discovery of drugs to treat a range of neurodegenerative diseases including AD, ALS, Motor Neuron Disease and Parkinson's Disease.

Structural Immunobiology Laboratory

We aim to reveal the way immune cells – with particular emphasis on 'natural killer' cells – communicate with their environment. We wish to harness this information to improve diagnosis and treatment of diseases such as leukaemia, HTLV1 infection, multiple sclerosis and psoriasis.

Our lab is interested in cellular immunity and the interplay between cell surface receptors that drive the function of these cells. A focus of the lab is Natural Killer (NK) cells that keep constant watch over the body and detect and directly kill cells that have been transformed by viral infection or malignancy (cancer). Without NK cells, viral and tumour burdens are higher and progress more quickly.

We make use of protein chemistry, protein engineering and structural biology techniques to unravel the mechanisms of receptor/ligand specificity and how this regulates NK cell fate and function. Our goal is to improve the clinical application of NK cells to:

(1) understand susceptibility to disease and
(2) develop the next generation of immune-based therapies.

https://www.svi.edu.au/laboratories/structural-immunobiology-laboratory/

MOLECULAR IMMUNOLOGY

Suitable for Honours or Masters

Primary Supervisor: Dr Julian Vivian

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Projects are available that centre on understanding immune receptor recognition of tumours and viruses. The primary techniques employed focus on structural biology, inlucding X-ray crystallography and electron microscopy. These techniques will be complemented with cellular and biophysical techniques including surface plasmon resonance. The ultimate goal of these projects is to advance cellular immunotherapies and ultimately enhance human health.

O'Brien Institute Research Projects (Department of St Vincent's Institute)

TISSUE ENGINEERING OF 3D SOFT TISSUES AND ORGANS FROM STEM CELLS

Note: This is not a specific project being offered, but it is an introductory overview of the Tissue Engineering Programs at the O'Brien Institute. Specific projects are listed after this. Students are generally enrolled through the Department of Surgery.

Tissue engineering is the creation of new body parts from the building blocks of cells, a matrix and a blood supply. The cells may be autologous or foreign and they may be differentiated to stem cells. These may be adult, embryonic or sourced from cord blood. The exciting new field of iPS cells offers the hope of individualized tissue without rejection.

- Matrix – the matrix environment influences cell behaviour. These matrices may be synthetic or biologically derived, rigid, biodegradable or hydro gels.
- Blood supply – we have developed a chamber model of in vivo tissue engineering where the blood supply is created by microsurgical means (AV loop) and when inserted into a closed chamber induces intense angiogenesis. In this environment, cells are attracted to the chamber and the fibrin matrix and a fibrous tissue organoid develops spontaneously.
- Cell manipulation – we can influence the specific tissue type that forms by seeding the chamber with cells, which can survive, and differentiate according to the environment created within the chamber. Using this technique we have been able to create skeletal muscle, fat and bone, as well as heart, pancreas, thymus, liver and growth hormone secreting organs.

By implanting a vascularized pedicle, containing a small amount of fat in the chamber, spontaneous growth of the fat occurs to fill the chamber space. In rats, rabbits and pigs we have tested this phenomenon and have been able to fill an 80mm chamber. This offers the potential to grow tissue for breast reconstruction.

Why does tissue grow within the chamber? We believe one of the critical factors in the growth observed is the creation of a space, which influences the forces transmitted through the cells. In general, tension results in cell proliferation and migration, while relaxation results in cell growth arrest, differentiation or apoptosis. Most recently, we have grown beating cardiac tissue in rat chambers from implanted cardiomyocytes and this tissue responds to cardiogenic drugs and to pacing.

This exciting field offers the possibility for a number of projects related to tissue engineering including microsurgery, angiogenesis, lymphangiogenesis, stem cell biology, mechanotransduction, cytoprotection and biomaterials (collaboration with The University of Melbourne Department of Bioengineering).

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Cardiac Regeneration Laboratory

As part of the Institute's O'Brien Department, we use human stem cells to engineer beating heart tissue on a lab dish to develop effective and translatable treatments for heart disease.

Heart disease continues to be the leading cause of death worldwide. However, our understanding of this disease remains limited because human heart tissues are hard to come by. Human heart cells generated from stem cells can be used to grow human heart tissues in a lab dish. This pre-clinical human heart model has allowed us to test new drugs with the potential to protect the heart from injury, as well as to study genetic mutations that can cause heart disease.

https://www.svi.edu.au/laboratories/cardiac-regeneration/

INVESTIGATING CARDIOMETABOLIC DISEASE USING HUMAN INDUCED PLURIPOTENT STEM CELLS

Suitable for Masters in Biomedical Science

Primary Supervisor: A/Prof Shiang (Max) Lim
Co-supervisor:Dr Jarmon Lees

For enquiries about current honours and PhD projects please contact: A/Prof Lim on E: maxlim@unimelb.edu.au or mlim@svi.edu.au OR Dr Lees on E: jlees@svi.edu.au

This project aims to generate patient-specific cardiovascular cells from induced pluripotent stem cells to establish human models of cardiometabolic diseases

The knowledge and skills involved in this project are suitable for students who are interested in stem cell biology, cardiovascular disease, and mitochondrial biology. A student working on this project will have the opportunity to learn various experimental skills, including; cell culture, protein and gene analysis, histology and mitochondrial assays.

DEVELOPING NOVEL BIOMARKER FOR FRIEDREICH ATAXIA HEART DISEASE

Suitable for Masters in Biomedical Science

Primary Supervisor: A/Prof Shiang (Max) Lim

Co-supervisor:Dr Jarmon Lees

For enquiries about current honours and PhD projects please contact: A/Prof Lim on E: maxlim@unimelb.edu.au or mlim@svi.edu.au OR Dr Lees on E: jlees@svi.edu.au

Friedreich ataxia is a fatal genetic disorder that causes progressive damage to the nervous system, muscle and heart tissue. Heart disease is the leading cause of premature death in Friedreich ataxia patients. Unfortunately, heart disease specific to Friedreich ataxia patients cannot currently be reliably diagnosed and monitored. The objective of this project is to establish a new blood test to monitor the onset, progression and severity of heart disease in Friedreich's ataxia patients.

TREATING CARDIAC VASCULAR DYSFUNCTION IN FRIEDREICH ATAXIA USING HUMAN IPSC-DERIVED MULTICELLULAR CARDIAC ORGANOIDS

Suitable for Masters in Biomedical Science

Primary Supervisor: Dr Jarmon Lees

Co-supervisor:A/Prof Shiang (Max) Lim

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Friedreich ataxia is an autosomal recessive neuromuscular disease and the most common inherited ataxia. Cardiomyopathy is the leading cause of premature death in Friedreich ataxia patients. Clinical reports indicate that the cardiomyopathy may be associated with abnormalities of the small coronary arteries. We have recently discovered multiple genes which may be involved in the disease pathogenesis. This project will knockdown key genes in the cardiac vascular system to determine their role in Friedreich ataxia cardiomyopathy using a cutting-edge 3D multicellular human cardiac organoid model. The knowledge and skills involved in this project are suitable for students who are interested in stem cell biology, metabolic and mitochondrial diseases, and heart disease.

MODELLING DIABETIC-INDUCED CARDIOMYOPATHY USING HUMAN CARDIAC ORGANOIDS

Suitable for PhD or Masters

Primary Supervisor: A/Prof Shiang (Max) Lim
Co-supervisor:Dr Jarmon Lees

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This project aims to construct a multicellular cardiac organoid model using cardiomyocytes and non-myocyte cell populations derived from human induced pluripotent stem cells to study heart disease.

Heart disease continues to be the leading cause of death worldwide. Development of specific and effective new drug candidates has been severely limited and a more detailed characterisation of human heart disease is urgently needed. However, this has been largely impeded by the limited access to viable human heart samples and by the cellular diversity of heart tissue. Our lab has recently established a novel proprietary cardiac organoid model that contains heart cells, blood vessels and autonomic neurons completely derived from human induced pluripotent stem cells. This project aims to use this new pre-clinical human model to study the pathophysiology of heart disease caused by ischaemia-reperfusion injury, diabetes and chemotherapy.

The knowledge and skills involved in this project are suitable for students who are interested in stem cell biology, organoid research, cardiovascular disease and diabetes. A student working on this project will have the opportunity to learn various experimental skills, including: cell culture, protein and gene analysis, histology, electrophysiology and tissue engineering.

Lymphatic, Adipose & Regenerative Medicine Laboratory

As part of the Institute's O'Brien Department, we investigate and seek new treatments for Radiation Injury Bystander Effect (RIBE) in cancer patients and for lipoedema, a condition often misdiagnosed as obesity.

The range of cancers for which radiotherapy is being used is ever expanding. There is an unavoidable dose exposure that occurs in surrounding normal cells. This radiation exposure does not have the effect of simply killing normal cells but elicits a permanent damage or injury profile that persists and continues to evolve throughout the life of the patient. This is known as Radiation Injury Bystander Effect (RIBE). These changes result in ongoing tissue contracture, immense pain, soft tissue swelling, and tissue breakdown; in turn leading to significant disability, recurrent infection, impairment of quality of life, and potentially life-threatening exposure of vital structures such as the heart.

Lymphoedema is a debilitating soft tissue disease caused by an impairment of the lymphatic system, which leads to fluid build-up in the surrounding interstitial tissue. The lymphatic system is a network of thin-walled vessels – comprised of lymphatic endothelial cells-that is integral to fluid homeostasis, immune cell surveillance and absorption of dietary fat. Lymphoedema can be an inherited disorder, such as Milroy's disease, but in some individuals it is acquired following a trauma such as surgery, infection or radiation therapy. Approximately 20% of breast cancer patients undergoing radiotherapy and/or surgical resection of lymph nodes will develop lymphoedema. Currently, there are no therapeutic treatments available.

To understand the genetic basis and signalling pathways activated in individuals with trauma induced lymphoedema, we have developed in vitro and in vivo models of lymphoedema that mimic clinical radiation dosage regimes and surgical treatments, specifically focussing on the cell types that occur in the affected lymphoedematous tissue: adipocytes, endothelial cells, immune cells and adipose-derived mesenchymal stem cells that comprise the skin architecture. We performed a raft of functional bioassays to specifically interrogate the key functions of each cell type during the course of radiation-induced lymphoedema and have developed genomic, proteomic and metabolic platforms to understand the key signalling and communication pathways between lymphatic endothelial cells and other key cells within their microenvironment. This knowledge will enable development of therapeutic agents that may treat aspects of this disease such as tissue swelling, tissue fibrosis and pain, as well as agents that promote tissue regeneration.

https://www.svi.edu.au/laboratories/lymphatic-adipose-regenerative-medicine/

UNDERSTANDING THE EPIGENETIC REGULATION SPHK2 IN FAT DEVELOPMENT AND METABOLIC DISEASE

Suitable for Honours or Masters

Primary Supervisor: Dr Tara Karnezis
Co-supervisor:Dr Nadeeka Bandara

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Metabolic disease including obesity and diabetes is fast becoming one of the major health issues affecting human health to date. We have shown that SphK2 is an epigenetic regulator of fat formation when adipose derived stem cells are activated to become adipocytes, the major cellular component of adipose (fat) tissues, in both embryonic development and metabolic disease. We wish to further characterise this novel mechanism by understanding the interaction between SphK2 and the chromatin in adipose derieved stem cells to equistately control downstream expression of target genes that are responsible for many aspects of fat development in mouse and human tissue.

UNDERSTANDING THE GENETIC BASIS OF LIPEDEMA

Suitable for PhD or Masters

Primary Supervisor: Dr Ramin Shayan
Co-supervisor:Dr Tara Karnezis

For enquiries about current honours and PhD projects please contact : tkarnezis@svi.edu.au or rshayan@svi.edu.au

Lipedema is a debilitating disease caused by excessive accumulation of fat in arms and lower extremities, affecting women at the onset of puberty. There is no known cure. Often, there is a lymphodema component associated with this disease but the precise role of lymphatics in disease pathology is unclear. This project will initiate a genetic screen of affected individuals and their families in order to identify genes that may be affected in these patients. This project will utilise microarray platforms, immunohistochemistry of human specimens, metabolomics, bioinformatics and the generation of animal models using CRISPR technology to determine whether there is a mutation within a specific gene of affected individuals that leads to Lipedema.

This project is conducted in St Vincent's Institute of Medical Research, Lympathic and Regenerative Surgery Group, (O'Brien Institute Department of SVI).

Vascular Biology Laboratory

As part of the Institute's O'Brien Department, our main research focus is generating human blood vessels for integration in various human tissues grown in the laboratory, including human skin and small pieces of human liver (liver organoids). We also study the structure and function of these lab-generated human tissues.

Research in the Vascular Biology Laboratory focuses on creating small blood vessel networks for tissue regeneration, both in tissue engineering of new organs or tissues, or as part of a skin wound-healing response.

The team's work originally focused on the spontaneous formation of capillary networks that sprout from large blood vessels isolated in a tissue engineering chamber in an animal. This chamber model has grown cardiac muscle, fat, pancreatic islets and liver tissue. More recently, the team has focused on growing capillary networks in the laboratory that are incorporated into engineered tissues, or organs such as skin tissue or liver organoids.

A major problem in assembling three-dimensional engineered tissues and organs is providing an interconnected blood vessel network throughout the engineered tissue. When transplanted into living tissue, this enables structural and functional linking to host blood vessels. If this union of lab-grown small blood vessels to host tissue blood vessels can occur, then a rapid blood flow will be supplied to the lab-grown tissues – enabling their survival and function in the host.

https://www.svi.edu.au/laboratories/vascular-biology/

STEM CELL-DERIVED HUMAN LIVER ORGANOIDS FOR REGENERATIVE MEDICINE

Suitable for Honours

Primary Supervisor: Dr Kiryu Yap
Co-supervisor:A/Prof Geraldine Mitchell

For enquiries about the current projects please contact: Dr Kiryu Yap, E: kiryu.yap@unimelb.edu.au

The Vascular Biology Group has developed liver organoids from human induced pluripotent stem cells (hiPSC). These complex structures contain several different cell types, including hepatocytes, cholangiocytes, and endothelial cells. As a next step, various aspects of advancement of this technology are available, suitable for an Honours or PhD project. This includes the characterisation of bile ducts produced within organoids, or the incorporation of additional elements, including liver-specific stromal cells (stellate cells) and immune cells (macrophages), all derived from hiPSC. Techniques used include stem cell and organoid culture, histology, microscopy (including confocal and light-sheet microscopy), and molecular biology methods (qPCR, ELISA, western blot). Different methods of liver organoid transplantation are also being trialed in mouse models of liver disease, to determine clinically-suitable methods for organoid delivery.

Ophthalmology, Department of Surgery/ Centre for Eye Research Australia (CERA) Research Projects

Ophthalmology research at the Centre for Eye Research Australia (CERA) has a strong reputation for its clinical and translational focus. Ranked amongst the top five ophthalmology research groups globally, its ultimate goal is to find solutions for the three major blinding eye diseases that affect Australians – macular degeneration; glaucoma and diabetic eye disease and to pioneer vision regeneration programs to give hope to people who have lost their sight.

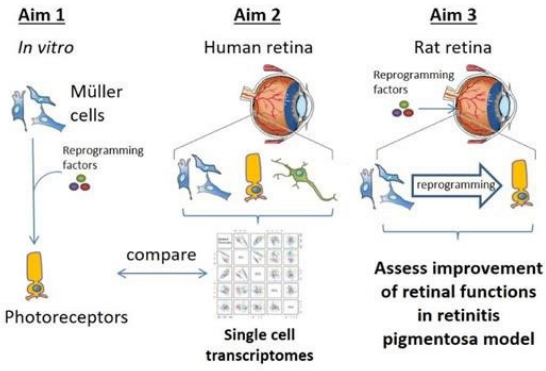
https://medicine.unimelb.edu.au/school-structure/surgery/about-us/department-precincts/ophthalmology

https://www.cera.org.au/

Cellular Reprogramming Unit

Group Leader: Dr Raymond Wong

Email: wongcb@unimelb.edu.au



The Cellular Reprogramming unit aims to harness the medical potential of cellular reprogramming and stem cells to study and treat ocular diseases. Our research focuses on developing novel cellular reprogramming technologies to regenerate retinal cells, as well as stem cell technology to generate retinal cells. Our research utilises cutting-edge techniques that includes direct reprogramming/ induced pluripotent stem (iPS) cell technology, single cell transcriptomic analysis and the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) systems.

Prospective students should contact the Research Group Leader in the first instance to discuss potential graduate research opportunities.

Ophthalmic Genetics

Group Leader: Prof Alex Hewitt

The Ophthalmic Genetics group is interested in understanding the genetics and molecular mechanisms underlying inherited eye diseases. We utilise genetic tools such as whole exome/genome sequencing, genome-wide association studies and more recently CRISPR/Cas to decipher genes which may be responsible for causing disease. The ultimate aim of our research is to contribute to the development of future treatments and therapies for patients with the hope to prevent and/or cure blindness in these patients.

Prospective students should contact the Research Group Leader in the first instance to discuss potential graduate research opportunities.

Clinical Trials Research Centre

Group Leader: A/Prof Lyndell Lim
Email: limllp@unimelb.edu.au

A/Prof Lyndell Lim, a Uveitis and Medical Retina Subspecialist, leads the Clinical Trials Research Centre at the Centre for Eye Research Australia. A/Prof Lim is largely involved in clinical studies, particularly in the field of uveitis and ocular immunology, and diabetic retinopathy. Her team runs both investigator initiated and sponsored clinical trials that aim to investigate new treatments in a variety of ophthalmic diseases.

Current projects include prospective randomised clinical trials in diabetic macular oedema, the major cause of visual loss in diabetic retinopathy, and chronic non-infectious uveitis, a form of blinding auto-immune disease of the eye.

Ophthalmic Neuroscience Unit

Group Leader: A/Prof Peter van Wijngaarden

The Ophthalmic Neuroscience Unit is focused on the discovery of novel imaging biomarkers of retinal and central nervous system diseases. The research combines state-of-the-art imaging with advanced image analysis methods including a range of artificial intelligence approaches.

***SATELLITE IMAGING TECHNOLOGY TO DETECT THE EARLY SIGNS OF GLAUCOMA AND ALZHEIMER'S DISEASE IN THE RETINA**

Suitable for PhD

Supervisor: A/Prof Peter van Wijngaarden
Email: peterv@unimelb.edu.au

We aim to be the first group in the world to bring hyperspectral imaging, based on NASA satellite technology, to the clinic to improve the care of Australians with Alzheimer's disease, glaucoma and a range of retinal diseases. 400,000 Australians live with dementia and most have Alzheimer's disease. Abnormal proteins accumulate in the brain and retina for 10-20 years before memory impairment, providing an opportunity for early detection and treatment. There are no screening tests for the earliest stages of the disease. Similarly, glaucoma is a leading cause of vision loss affecting 300,000 Australians. Early treatment can save vision, but late diagnosis is typical. The deposition of abnormal proteins in the retina in Alzheimer's disease and structural changes in the nerve cells affected by glaucoma scatter light in characteristic ways which we can detect during

the early stages of disease. This project combines clinical imaging with advanced image analysis methods, including deep learning approaches.

Glaucoma Research Laboratory

*TAKING THE "GUESSWORK" OUT OF GLAUCOMA CLINICAL MANAGEMENT WITH NOVEL IMAGING

Suitable for PhD

Primary Supervisor: Dr Zhichao Wu
Email: wu.z@unimelb.edu.au

The clinical management of glaucoma seeks to prevent patients from experiencing visual disability from the progressive degeneration of retinal ganglion cells. This task is especially difficult by the lack of effective methods to detect and characterise disease progression accurately and meaningfully. Current clinical tests are currently so variable that clinicians are often left with a great deal of "guesswork" in the clinical management of glaucoma. Optical coherence tomography is a modern clinical imaging technique that could accurately detect disease progression and predict long-term outcomes, given its ability to non-invasively visualise the retina three-dimensionally at near-cellular resolution. This powerful technology could be exploited to transform the clinical management of glaucoma patients.

This project will involve development of this imaging technique and analytical methods and understanding its relation to patient-reported measures of visual disability to understand the clinical relevance of its results.

*EVIDENCE-BASED PRACTICE IN THE MANAGEMENT OF GLAUCOMA SUSPECTS

Suitable for PhD or MPhil

Supervisors: Dr Zhichao Wu, Dr Laura Downie

For enquiries about current honours and PhD projects please contact: Dr Wu at E: wu.z@unimelb.edu.au OR Dr Downie at E: ldownie@unimelb.edu.au

Glaucoma is a leading cause of irreversible vision loss in Australia and worldwide, with half of those with this condition being undiagnosed. Approximately one in ten Australians over 50 years old would fit the criteria for being a glaucoma suspect, but there is limited evidence about how to identify those at high-risk of developing glaucoma and who prophylactic treatment is warranted for. The main evidence guiding the management of glaucoma suspects is based on two trials for those with ocular hypertension (i.e. raised intraocular pressure) from over 20 years ago, and individuals with ocular hypertension make up less than a half of those with suspected glaucoma.

This project will thus involve synthesising and critically appraising the evidence currently available, as well as obtaining prospective data on current practice patterns on the management of glaucoma suspects, so as to provide evidence-based guidance and identify key knowledge gaps that requires robust, prospective studies to address.

Macular Research Unit

Group Leader: Prof Robyn Guymer

The Macular Research Unit at the Centre for Eye Research Australia (CERA) is a leading research team focusing on the most common cause of vision impairment in people aged over 50 years in Australia – Age-related macular degeneration (AMD). The group is headed by Prof Robyn Guymer, an internationally renowned medical retinal ophthalmologist and clinician. Prof Guymer's research is focused on finding novel ways to assess, monitor and treat this devastating eye disease. She also collaborates to investigate underlying mechanisms involved in disease pathogenesis.

OCT-ANGIOGRAPHY STUDY OF RETINAL VASCULAR AUTOREGULATION IN AMD

Suitable for Honours or Masters

Primary Supervisor: **Dr David Sousa**
Co-supervisors: **A/Prof Robyn Guymer, A/Prof Chi Luu**

For enquiries about current honours and PhD projects please contact Dr David Sousa at E: davidscsousa@gmail.com

Age-related macular degeneration (AMD) is a leading cause of central vision loss in people over 50 years of age.

*ENABLING TREATMENT TRIALS OF ATROPHIC AGE-RELATED MACULAR DEGENERATION

Suitable for PhD

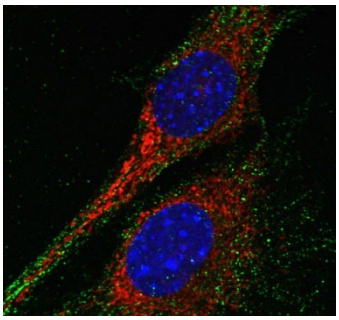
Primary Supervisor: **Dr Zhichao Wu**
Co-supervisors: **Prof Robyn Guymer**

Email: wu.z@unimelb.edu.au

Although treatments currently exist for the acute, neovascular complications of age-related macular degeneration (AMD), individuals that develop atrophic complications currently face an inevitable future of progressive central vision loss since no effective treatments are available to prevent or slow the unrelenting degeneration of the retina. Although many clinical trials are now underway for atrophic AMD, a significant barrier to their success is the lack of precise clinical measures to determine their efficacy. Furthermore, trials evaluating novel treatments for the atrophic complications of AMD may be evaluated in eyes where the disease is already too advanced.

This project will involve developing novel visual function techniques tailored for the specific stages of the atrophic disease process, especially for the early stages of the atrophic process where no outcome measures have yet been established. This will provide the necessary tools needed as a catalyst for the discovery of interventions for the debilitating complications of atrophic AMD.

Mitochondria and Neurodegeneration Unit



Group Leader: A/Prof Ian Trounce

Email: i.trounce@unimelb.edu.au

The Mitochondria and Neurodegeneration group investigates how mitochondrial dysfunction can lead to neurodegenerative processes, in particular glaucoma, Leber's hereditary optic neuropathy, Parkinson's and Alzheimer's disease, to identify novel therapeutic targets to prevent neuronal and vision loss.

Prospective students should contact the Research Group Leader in the first instance to discuss potential graduate research opportunities.

Mitochondrial Biology and Disease

Group Leader: **Dr Isabel Lopez Sanchez**

Our research suggests that the mitochondria – the batteries that supply the cells with energy – play a critical role in neurodegenerative diseases such as glaucoma, Parkinson's disease and Alzheimer's disease. The mitochondrial DNA that we inherit was 'matched' in ancient humans with the nuclear genes needed for optimal mitochondrial function. We hypothesise that in modern humans, a 'mismatching' of the two genomes can contribute to age-related neurodegenerative diseases such as glaucoma and Parkinson's disease. Our team has specialist expertise in the analysis of mitochondrial function, together with unique expertise in mitochondrial transfer between cells (cybrid cells). This allows us to determine nuclear and mitochondrial DNA gene effects independently. Along with ageing diseases, our researchers are investigating Leber's hereditary optic neuropathy (LHON), working to discover how defects in mitochondrial metabolism contribute to this rare inherited disease.

Our research in glaucoma will help determine if new treatment approaches that target mitochondrial function – rather than focusing on eye pressure – can help slow disease progression. By studying the cellular and molecular changes that occur in LHON, we hope to make discoveries that will lead to treatments to prevent or treat this devastating condition.

Retinal Gene Therapy

Group Leader: **Dr Thomas Edwards**

CERA is at the forefront of gene therapy research for eye disease and is striving to establish a Melbourne Centre for Excellence in Ocular Gene and Cell Therapy to continue advancing this exciting field. The Retinal Gene Therapy group aims to develop novel gene therapies to halt the progression and find a cure for inherited retinal diseases. Our scientists are devoted to investigating gene therapies that could halt the progression of specific inherited retinal diseases, or even partially reverse the damage. This is done by identifying a defective gene which causes vision loss, producing a correct copy of the gene in the lab and reintroducing this copy back into the retinal cells, using a specially-engineered virus. In the glaucoma research unit, our researchers are investigating a number of strategies including gene therapy to enhance optic nerve regeneration.

Surgical Research Unit

Group Leader: Prof Mark Daniell

The Surgical Research Unit at CERA conducts two main streams of research: corneal disease research and surgical research into corneal transplantation and intra ocular lens implants.

The clear, protective layer at the front of the eye, called the cornea, can be damaged through disease, infection or injury that can block or distort vision. CERA's Surgical Research Unit carries out clinical research into new and more effective therapies for corneal diseases such as keratitis, keratoconus and ocular surface disorders. This includes projects with biochemical engineers and pharmacologists to produce an engineered corneal transplant from stem cells and an ideal biomaterial.

The Surgical Research Unit also includes clinical trials into the efficacy and safety of surgical therapies such as corneal transplants, cataract surgery and laser surgery. The ultimate aim of corneal transplantation research is to develop an artificial cornea or grow corneal cells in the laboratory to prevent problems with rejection. The team is also looking at cellular responses to infection in the cornea.

The group is also interested in COVID-19 related pharmacological research and ApoE, IP and TP receptor mechanisms.

REDUCING CORNEAL SCARRING IN EPIDERMOLYSIS BULLOSA WITH A NOVEL FACTOR

Suitable for Honours or Masters

Supervisor: **Dr Gink Yang**
Co-Supervsior: **Prof Mark Daniell**

Email: gyang@cera.org.au

Epidermolysis bullosa (EB) is an inherited blistering disease of the skin and mucous membranes, including the cornea. Living with this disease is like living with third degree burns. An international patient survey on EB in 2020 reported patients expressing that corneal erosions ''usually completely shut down my life'' and ''are one of the worst secondary issues associated with EB, if not the most painful.'' Corneal erosions cause acute eye pain and need prompt treatment to alleviate symptoms.

Clinical treatments including contact lenses and antibiotics are often used to minimise further damage to the eye. However, these approaches do little to improve corneal wound healing or reduce scarring. An anti-scarring treatment to prevent vision loss is currently lacking for EB patients with corneal erosions. We have identified an anti-scarring factor and aim to validate the efficacy of this factor via models of recessive dystrophic EB and Junctional EB in human corneal cells.

COMPREHENSIVE INVESTIGATION OF KERATOCONUS: RISK FACTORS, EPIDEMIOLOGICAL ASPECTS, GENETICS, AND ARTIFICIAL INTELLIGENCE MODELS

Suitable for Honours or Masters

Primary Supervisor: Dr Srujana Sahebjada
Co-supervisor:Prof Mark Daniell

Email: Srujana.sahebjada@unimelb.edu.au

Keratoconus is a progressive eye disorder characterized by corneal thinning and bulging, resulting in visual impairment. To gain a comprehensive understanding of this complex condition, a multi-faceted research project will be conducted. This project aims to investigate various aspects of keratoconus, including risk factors, epidemiological patterns, genetic influences, and the application of artificial intelligence models for enhanced diagnosis and prediction.

*GENOME-WIDE EXPRESSION PROFILING OF KERATOCONUS AND NON-KERATOCONUS CORNEAS

Suitable for Masters by Research

Primary Supervisor: Dr Srujana Sahebjada
Co-supervisors: Prof Paul Baird and Prof Mark Daniell

Email: Srujana.sahebjada@unimelb.edu.au

Keratoconus is a potentially blinding eye disease of the cornea. Typically, it occurs in childhood and various intervention measures are currently used to slow its progression but there is no cure. While its aetiology is due to genes and environment, the involvement of these factors is still poorly understood. In this proposal we will greatly advance our understanding of disease through genetic analysis of this disease. The project will involve undertaking RNA sequencing from the 3 different layers (epithelium, stroma and endothelium) of the cornea to assess what changes occur in gene expression from these corneal tissues collected from keratoconus cases compared to corneas from living (non-keratoconus) donors through enucleation as well as corneas collected through an EyeBank. Our preliminary analysis of RNASeq data have indicated that different analysis programs can lead to different outcomes in terms of which genes/pathways are identified and we would like to look further into this issue to determine the factors driving these outcomes. The student will be involved in analysis of RNASeq data and pathway analysis to better understand these findings.

Students with backgrounds in Bioinformatics, Genetics, Computer science and/or optometry and visual science are welcome to apply.

***REPAIR OF THE CORNEA TO RESTORE VISION: TRANSLATION TO SURGICAL REPAIR DEVICE**

Suitable for PhD

Supervisors: Dr Karl Brown, Prof Greg Dusting and Prof Mark Daniell

Email: g.dusting@unimelb.edu.au

Severe burns and corneal disease leads to vascularisation and ulceration of the corneal surface, which is currently treated by corneal transplants and lifelong anti-rejection drugs. Many countries in the world do not have sufficient donors to meet the increasing demand for this procedure. At CERA we work closely with chemical engineers and veterinary scientists at the University of Melbourne to develop engineered constructs to replace the damaged corneal endothelium. Materials and procedures have been patented, and one is under commercial development.

The current project is to develop a source of corneal endothelium from human induced pluripotent stem cells (iPS cells) and grow these on patented hydrogel films to replace damaged endothelium. Alternatively, the reprogramming of appropriate cells from patient donors direct to corneal endothelium will be explored. Mechanisms of adhesion and proliferation of these cells will be examined, and preclinical transplantation studies will be carried out in sheep in the veterinary facility.

This project would be suitable for biomedical science students with an interest in cell biology, pharmacology or ophthalmology to work towards clinical application of this novel technique with an ophthalmologist, stem cell scientist, veterinary scientists and other cell biologists. It can be adapted for Honours, Masters or PhD students, working alongside scientists and clinicians.

Ocular Fibrosis Unit

Group Leader: Dr Jennifer Fan Gaskin

The Ocular Fibrosis Unit at CERA develops approaches to improve treatment and outcomes for patients with ocular diseases. The key area of research is to investigate ocular inflammation and fibrosis/ scarring after glaucoma surgery and chemical burn injuries in the eye. We are interested in translational approaches that include investigating the therapeutic potential of novel drugs and compounds using various preclinical models, molecular techniques, cell culture-based experimentation and analysing patient-derived materials.

DEVELOPING A TARGET SPECIFIC FIBROSIS TREATMENT USING GENE THERAPY.

Suitable for Honours or Masters

Primary Supervisor: Dr Jennifer Fan Gaskin
Co-supervisor:Dr Elsa Chan

For enquiries about current honours and PhD projects please contact: Dr Jennifer Fan Gaskin
E: fan.j@unimelb.edu.au or Dr Chan E: elsa.chan@unimelb.edu.au

Ocular fibrosis occurs in a variety of eye disorders including aged-related macular degeneration, glaucoma and corneal injury. Safe and effective treatment is lacking for this blinding condition. The

overall aims of this project are to identify potential target for controlling fibrosis and to develop a new therapy using genetic approach.

Ophthalmic Epidemiology

Group Leader: Prof Mingguang He

Prof. Mingguang He is a global expert in vision-related clinical and epidemiologic research. Prof He currently leads the Ophthalmic Epidemiology group at the University of Melbourne and Centre for Eye Research Australia and is the Director of WHO Collaborating Centre for Prevention of Blindness (Australia). The Ophthalmic Epidemiology group is comprised of eye disease researchers, public health specialists, epidemiologists, data scientists and Artificial Intelligence (AI) professionals. The team focusses on clinical and epidemiological research, randomised clinical trials, twin studies, imaging technology, AI and big data research. The studies explore integrating AI and eye disease screening in different area and clinical setting, which facilitates the application of new technology to improve healthcare efficiency and productivity.

***IMPROVED EARLY DIAGNOSIS OF EYE DISEASES BY INTEGRATION OF RETINAL PHOTOGRAPHY AND ARTIFICIAL INTELLIGENCE TO BUILD AN OPPORTUNISTIC SCREENING SERVICE IN METRO, REGIONAL AND REMOTE PRIMARY CARE SETTINGS**

Suitable for Masters or PhD

Supervisor: Prof Mingguang He
Email: mingguang.he@unimelb.edu.au

This project will be based on Professor He's current AI-based fundus image diagnosis system, a do-it-yourself (DIY) screening system that is less dependent on technicians for image acquisition, and less dependent on eye care professionals in the interpretation of clinical images. The aim of the study is to understand the needs, develop the prototype and evaluate the usability of this DIY system, in real-world clinical setting of GP and endocrinology clinics and Aboriginal Medical Services. This DIY screening system is anticipated to allow non-eye professionals to perform eye disease screening that would improve acceptability, accuracy, accessibility and cost-efficiency of eye care delivery.

Visual Neurovascular Research

Group Leader: Dr Luis Alarcon-Martinez

When our vision works correctly, light is picked up in the retina at the back of the eye and turned into electrical signals which are transmitted to the brain by millions of retinal ganglion cells. To function properly, retinal ganglion cells require an adequate supply of oxygen and nutrients from surrounding blood vessels. Inadequate blood supply can damage these cells and lead to vision loss. Our visual neurovascular team aims to gain a better understanding of how exactly blood is distributed in the retina in order to prevent damage and preserve sight. The team uses cutting-edge two-photon microscopy to investigate the dynamics between retinal cells, blood vessels and very thin nanotubes that help cells communicate with one another. The hope is to help develop strategies to prevent or treat retinal neurodegenerative diseases.

DOES AN EXCEEDED AMOUNT OF WASTE DEPOSITS PLAY A ROLE IN NEURONAL DEGENERATION DURING GLAUCOMA?

Suitable for Masters

Primary Supervisor: Dr Luis Alarcon-Martinez
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Glaucoma is the leading cause of irreversible blindness worldwide, characterized by damage to the retinal nerve cells or neurons and their projections to the brain, which form the optic nerve. The precise mechanism behind vision loss in glaucoma is not entirely understood. Although high intraocular pressure (IOP) is an important symptom, half of the patients present normal IOP (i.e., normal-tension glaucoma, NTG). Thus, it is urgent to study IOP-independent mechanisms related to the development of glaucoma. The cytotoxic theory of glaucoma suggests that the accumulation of debris or toxic compounds contributes to neuronal loss. Thus, the retina generates a significant amount of waste deposits, which must be cleared to prevent neuronal death. Nevertheless, how the retina removes this debris is not fully understood. Here, we will study whether an exceeded amount of waste deposits plays a role in neuronal damage during glaucoma.

Contact us for all enquiries: easternhill-gr@unimelb.edu.au