2024 Parkville Precinct - Project Handbook

Honours and Master of Biomedical Sciences Projects Melbourne Medical School

August 2023
Baker Heart and Diabetes Institute

Developing platelet-derived nanoparticles for targeted thrombolysis

Project Description:

Stroke and heart attack are the leading causes of death and major morbidity worldwide. Despite this, the current thrombolytic (clot-busting) therapies remain largely ineffective and many patients are resistant to therapy. There is a need for improved thrombolytic drugs and strategies for overcoming thrombolysis resistance. One strategy for achieving this is using targeted drug delivery to deliver high local concentrations of thrombolytic drugs to the thrombus, to improve the efficacy of drug treatment. To achieve this, we propose using platelet-derived nanoparticles loaded with thrombolytic drugs to achieve targeted thrombolysis. Technologies the students will learn in this project include: Multicolour Flow Cytometry, in vitro models and animal models of thrombosis, platelet-function tests, and development of recombinant antithrombotic drugs.

Primary Supervisor: Prof Karlheinz Peter

Primary Supervisor Contact: karlheinz.peter@unimelb.edu.au

Honours places available: 0

Master of BioMed places available: 1
Immunity, Chronic Inflammation and Cardiovascular Disease

Project Description:
Our research focuses on understanding the immunological mechanisms that drive inflammation in cardiovascular diseases. In doing so, we aim to facilitate the development and implementation of effective anti-inflammatory and immune-modulating therapies for patients with cardiovascular disease. The development of novel therapies for prevention and treatment of heart attacks is one of our major goals. Technologies the students will learn in this project include: Multicolour Flow Cytometry, single-cell RNA sequencing, animal models of heart attack, immunology of inflammation and heart attack, and novel drug design.

Primary Supervisor: Prof Karlheinz Peter
Primary Supervisor Contact: karlheinz.peter@unimelb.edu.au
Honours places available: 0
Master of BioMed places available: 1

Mechanotransduction in blood cells and consequences for thrombosis and inflammation

Project Description:
This project will determine the effects of blood flow on immune cell function, and identify mechanoreceptors that control such effects and are thus novel therapeutic targets. We are seeking to prevent aortic stenosis, a highly prevalent disease. For this study, microfluidic assays, animal studies and blood samples from patients with aortic stenosis will be used. This is a highly translational and directly clinically relevant project.

Primary Supervisor: Prof Karlheinz Peter
Primary Supervisor Contact: karlheinz.peter@unimelb.edu.au
Honours places available: 0
Master of BioMed places available: 1
Novel therapies for atherosclerotic plaque stabilisation

Project Description:
Our research focuses on understanding the molecular mechanisms that drive atherosclerotic plaque formation and plaque rupture in cardiovascular diseases. We aim to characterise the fundamental molecular pathways underlying plaque formation and rupture using translational disease models and novel therapeutic agents. Technologies the students will learn in this project include: Multicolour Flow Cytometry, single-cell RNA sequencing, animal model of plaque instability, immunology of inflammation and atherosclerosis, and novel drug design.

Primary Supervisor: Prof Karlheinz Peter
Primary Supervisor Contact: Karlheinz.Peter@baker.edu.au
Honours places available: 0
Master of BioMed places available: 1
Department: Baker Heart and Diabetes Institute -Department of Cardiometabolic Health

Developing novel antithrombotic drugs without bleeding complications

Project Description:
Current antithrombotic drugs are often limited in their use by causing bleeding complications. We are designing and developing novel recombinant antithrombotic drugs that do not come with bleeding complications. Technologies the students will learn in this project include: Flow cytometry, histology, platelet-function tests, molecular biology of drug development, development of recombinant antithrombotic drugs, in vitro models and animal models of thrombosis.

Primary Supervisor: Prof Karlheinz Peter
Primary Supervisor Contact: Karlheinz.Peter@baker.edu.au
Honours places available: 0
Master of BioMed places available: 1
Department: Baker Heart and Diabetes Institute -Department of Cardiometabolic Health

Exploring innate immune memory
Immune memory is a defining feature of the adaptive immune system, but activation of the innate immune system can also result in heightened responses to re-challenge. This adaptation has been termed "trained immunity", a de facto form of innate immune memory. Studies over the past few years have pointed to the broad benefits of trained immunity for host defence but have also suggested detrimental outcomes in chronic inflammatory disease, such as atherosclerosis. By inducing metabolic and epigenetic changes in haematopoietic stem cells (HSCs), trained immunity drives myeloid cell expansion and the sustained generation of monocytes with a “proinflammatory” phenotype.

**Primary Supervisor:** Dr Andrew Fleetwood

**Primary Supervisor Contact:** andrew.fleetwood@baker.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Baker Heart and Diabetes Institute - Department of Cardiometabolic Health

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Understanding how failures in cell metabolism and the immune system lead to heart failure following a heart attack

**Project Description:**

The heart is a highly metabolically active tissue that requires the efficient production, and ongoing supply, of energy in order to maintain optimal heart function and health. Mitochondria are the powerhouse of the cell, where declines in mitochondrial health and function caused by either genetic mutation or environmental stress, can lead to reductions in energy production and subsequently impact the functional capacity of the heart.

Indeed, one of the most common genetic conditions in humans is mitochondrial disease, which affects many tissues in the body, but often individuals suffer predominantly from heart related ailments. Unfortunately, little is known about the effects of mitochondrial dysfunction specifically in the heart, or why mitochondrial dysfunction in other tissues also leads to heart failure. Recent evidence suggests that mitochondrial dysfunction leads to activation of a specific arm of the immune system, which leads to excessive immune infiltration and subsequent heart failure. This project will use a novel mouse model exclusive to our laboratory to study the cellular and molecular drivers of mitochondrial cardiomyopathy, that may help identify new therapeutic targets, biomarkers and treatments for heart disease in humans.

**Primary Supervisor:** A/Prof Brian Drew

**Primary Supervisor Contact:** brian.drew@baker.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 0
Atrial adaptations in physiological and pathological cardiac hypertrophy

Project Description:

Atrial fibrillation (AF) is the most common rhythm disorder of the heart, and is characterised by the high frequency excitation of the atrium, leading to dyssynchronous contraction of the atria and irregular excitation of the ventricles. AF has been reported to affect 1-4% of the general population worldwide, but this is likely to be an under representation because many people remain undiagnosed. Thus, it is important to understand the underlying mechanisms of AF for further development of novel therapeutic strategies.

One of the key features of AF is atrial enlargement but the critical mechanisms are mostly unknown. Research has previously focused on understanding the growth of the ventricles, and has identified the differences between pathological and physiological ventricular growth. In contrast, differences in growth of the atria and underlying mechanisms of atrial enlargement in both pathological and physiological setting are poorly understood.

The key aim of this project is to characterise the atria from physiological and pathological cardiac hypertrophy mouse models. The characterisation will include functional, morphological, histological and molecular analyses. Results from this project are expected to lead to the identification of new drug targets and strategies for AF.

Primary Supervisor: Prof Julie McMullen

Primary Supervisor Contact: julie.mcmullen@baker.edu.au

Honours places available: 1

Master of BioMed places available: 1

Plasma lipidomic profiling in type 2 diabetes and coronary artery disease

Project Description:

The Metabolomics Laboratory uses state-of-the-art tandem mass spectrometry to obtain metabolic/lipid profiles from cell and animal models in addition to clinically relevant human samples to develop new approaches to diagnosis, risk assessment and therapy for diabetes and cardiovascular disease. Type 2 diabetes and coronary artery disease are major causes of morbidity and mortality in Australia. A number of lipids and lipoproteins have been identified as useful indicators and predictors of both type 2 diabetes and atherosclerosis (i.e. cholesterol, HDL,
triglycerides). However, these provide only a restricted picture and a limited interpretation of the disease risk/status of an individual. It is now becoming clear that many other lipid types are altered during disease onset and progression and it is likely that some/many of these are involved in disease pathogenesis. We have an ongoing program of method development and biomarker discovery to identify and validate new lipid biomarkers of disease. We hypothesise that: the major differences in the plasma lipid profiles between healthy and type 2 diabetes or coronary artery disease precede the clinical presentation and so will be useful to predict disease outcomes. The specific aims are to: Perform plasma lipid profiling on patient cohorts that have been clinically phenotyped (type 2 diabetes or coronary artery disease). Determine the plasma lipid profiles that are correlated with the burden of disease and use this to develop predictive models to identify individuals at increased risk of a disease onset and progression. This project is suitable for a PhD student and will use our laboratories novel lipidomic approach to generate lipid profiles from patient cohorts at different stages of disease to identify those lipids and lipid profiles that are specifically associated with disease onset and progression. The primary outcome of this project will be the development of a plasma lipid profiling test to enable the early detection of patients at increased risk of type 2 diabetes and coronary artery disease. In addition we will develop methods to monitor treatment. Identification of individuals prior to the development of disease will enable early intervention and will have a profound effect on the health of the Australian population.

**Primary Supervisor:** Prof Peter Meikle

**Primary Supervisor Contact:** peter.meikle@baker.edu.au

**Honours places available:** 0

**Master of BioMed places available:** 1

**Department:** Baker Heart and Diabetes Institute -Department of Cardiometabolic Health

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**Exploring the contribution of intrinsic lipids to immune cell development and function**

**Project Description:**

This project is focused on exploring how unique lipid signatures (lipidomes) of immune cells influence their function and/or development. The overarching goal is to identify ways to manipulate specific lipids to alter cell function in disease.

Over the past few years we have generated a new and exciting data set profiling the lipid compositions (lipidome) of 16 different human immune cells and the major mouse immune cell equivalents. This revealed striking diversity between various immune cells, particularly between the innate and adaptive immune system.

We are now exploring two overall questions: 1. Do specific lipids drive immune cell function? 2. How do the lipidomes of immune cells form as they develop from stem cells.

The specific project can be focused on either of the two questions above.
Project 1: Exploring the contribution of lipids sensitive to peroxidation which confer susceptibility to a specific form of cell death known as ferroptosis.

Hypothesis: Immune cells enriched in lipids that are sensitive to peroxidation undergo ferroptosis when exposed to ferroptotic agonists, while immune cells devoid in these lipids will be resistant.

This project will involve manipulating human and mouse immune cells in culture. Techniques to explore this question will be cell death assays via flow cytometry and assessment of lipid peroxidation by mass spectrometry. Mouse models will also be used to test this hypothesis in vivo and depending on the applicant (hons/PhD) will use mouse models to genetically modify the lipid composition or ferroptotic pathway of specific immune cells.

Project 2: Determining the contribution of particular lipids to immune cell development.

Hypothesis: Specific lipids are critical to the development of immune cells.

This project will determine the lipidomes of haematopoietic stem cells and how they change as these cells mature down specific lineages to form mature immune cells. Given we have identified a very unique signature in blood neutrophils (i.e. an enrichment in ether lipids), this project will first explore what happens when we delete an enzyme called glyceronephosphate O-acyltransferase (GNPAT – rate limiting enzyme for the production of ether lipids) specifically in stem cells and explore the neutrophil maturation pathway in the bone marrow and blood. We will also explore some functional properties of neutrophils such as inflammatory signalling in response to bacterial stimuli and phagocytosis. These experiments will be conducted in mice using flow cytometry to quantify cell population and examine the functional readouts.

Primary Supervisor: Prof Andrew Murphy

Primary Supervisor Contact: andrew.murphy@baker.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Baker Heart and Diabetes Institute -Department of Cardiometabolic Health

Activated platelets targeted drug therapy

Project Description:

Developing a novel targeted fibrinolytic drug that is directed against activated platelets. Fibrinolysis is a valuable alternative for treating myocardial infarction when an invasive/surgical procedure is not available in a timely fashion.

Primary Supervisor: Dr Xiaowei Wang

Primary Supervisor Contact: xiaoweiw@unimelb.edu.au

Honours places available: 1
Master of BioMed places available: 1
Department: Baker Heart and Diabetes Institute -Department of Cardiometabolic Health

Developing nanoparticles for targeted theranostics delivery of drug and gene therapeutics

Project Description:
Research in the Molecular Imaging and Theranostics lab focus on translational research that links the findings from basic science to the practical applications that enhance human health and well-being in clinical settings. Developing new bio-compatible nanoparticles that can be used for targeted delivery and localize the drugs/genetic therapy to the site of disease, thereby eliminating reduce side effects.

Primary Supervisor: Dr Xiaowei Wang

Primary Supervisor Contact: xiaoweiw@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1
Department: Baker Heart and Diabetes Institute -Department of Cardiometabolic Health

Molecular Imaging and Theranostics

Project Description:
The use of small recombinant antibodies for diagnostic molecular imaging and targeted drug delivery is well-established in our lab. Magnetic resonance imaging (MRI) offers significant advantages: it is already a well-established clinical imaging technique and the equipment required is already available in most hospitals. MRI avoids the radiation associated with CT and PET imaging; it is thus an ideal technology for longitudinal studies and multiple follow-ups. MRI can provide whole-body imaging at a very high spatial resolution and has the capacity for accurate tissue characterisation, which is useful for accurate thrombus/inflammation imaging. This project would focus on small recombinant antibodies that binds to the activated platelets on thrombi and/or vascular cell adhesion molecule-1, which is one of the endothelial surface molecules most strongly and specifically up-regulated in inflammation. We propose to conjugate these antibodies to MRI contrast agents for molecular imaging. By adding drugs to the contrast agents, we will also be able to provide site-specific therapy. We would therefore use this recombinant antibody for diagnosis imaging and targeted delivery of pharmacological treatment.

Primary Supervisor: Dr Xiaowei Wang
mRNA therapy for cardiovascular diseases

Project Description:

mRNA therapy has attracted major interest after the success of COVID-19 vaccination; we are designing and testing new mRNA therapeutics to be delivered via lipid nanoparticles for the transfection of endothelial cells and thus the treatment of cardiovascular diseases.

Primary Supervisor: Dr Xiaowei Wang
Honours places available: 1
Master of BioMed places available: 1
Department: Baker Heart and Diabetes Institute -Department of Cardiometabolic Health

Using molecular MRI to diagnose and treat thrombotic and inflammatory diseases

Project Description:

The use of small recombinant antibodies for diagnostic molecular imaging and targeted drug delivery is well-established in our lab. Magnetic resonance imaging (MRI) offers significant advantages: It is already a well-established clinical imaging technique and the equipment required is already available in most hospitals. It avoids the radiation associated with CT and PET imaging, and is thus an ideal technology for longitudinal studies and multiple follow-ups. MRI can provide whole-body imaging at a very high spatial resolution and has the capacity for accurate tissue characterisation, which is useful for accurate thrombus/inflammation imaging. This project would focus on small recombinant antibodies that bind to the activated platelets on thrombi and/or vascular cell adhesion molecule-1, which is one of the endothelial surface molecules most strongly and specifically up-regulated in inflammation. We propose to conjugate these antibodies to MRI contrast agents for molecular imaging. By adding drugs to the contrast agents, we will also be able to provide site-specific therapy. Therefore, we would use these recombinant antibodies for diagnosis imaging and targeted delivery of pharmacological treatment.

Primary Supervisor: Dr Xiaowei Wang
Unravelling the role of breast milk ether lipids in modulating immune function in early life

Project Description:

Breastfeeding, the biological norm of feeding babies, provides numerous health benefits to babies. Infant-formula-feeding is thought to be inferior to breastfeeding because human milk provides specific and non-specific factors that have long-term consequences for early metabolism and the development of diseases (1). However, the 20th century witnessed an increase in formula feeding. Currently, only 35% of infants are exclusively breastfed in the first six months of their life. Lipids make up 3-5% of the composition of human breast milk. Besides providing energy, breast milk lipids are also necessary for the infant growth and development (2). We have recently performed the largest plasma lipidomic profiling study of mothers and infants from the Barwon Infant Study (BIS) and observed that ether lipid species were markedly elevated in infants who were breastfed compared to those who were not. We have also profiled breast milk samples available from BIS and several infant formulae and found that breast milk has a clearly distinct lipidome compared to infant formulae. In particular, breast milk has significantly higher ether lipid content compared to infant formulae. Ether lipids are a class of lipids with unique structural feature and are thought to have anti-oxidant, anti-inflammatory and immunomodulatory properties (3). We hypothesise that breast milk ether lipids can modulate immune cell function and thereby help in the development of immunity in infants. The aim of this project is to determine the effects of modifying the ether lipid content of milk (a) on the immune cell lipidomes and (b) on the susceptibility of these immune cells to pathogenic stimuli such as oxidative stress and inflammation in a murine model. We will generate a unique genetically modified mouse model to deplete the content of ether lipids in mouse milk. We will also supplement pregnant and lactating mice with alkylglycerols (naturally occurring precursors that can be metabolised into endogenous ether lipids) to modify the milk ether lipid content in different magnitudes. We will characterise the milk samples using our state of the art liquid-chromatography mass spectrometry based lipidomics method to confirm the modification of ether lipid content in mouse milk. We will also characterise the lipidomes of plasma, different immune cell types and several tissues of newborn mouse pups (before they transition onto solid food) to examine how modification of ether lipid content in milk affects pups’ endogenous lipidomes. We will also examine the susceptibility of different immune cell sub-types from newborn pups exposed to different levels of milk ether lipids to oxidative cell death and inflammation. In this project we will combine our lipidomics expertise with our unique mouse models of ether lipid modification to define the role of breast milk ether lipids in modulating immune function in infants. References: 1. Jackson KM, Nazar AM. Breastfeeding, the immune response, and long-term health. The journal of the American osteopathic association. 2006;106(4):203-7. 2. Ballard O, Morrow AL. Human milk composition: Nutrients and bioactive factors. Paediatric clinics of North America. 2013;60(1):49-74.

**Primary Supervisor:** Prof Peter Meikle

**Primary Supervisor Contact:** peter.meikle@baker.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Baker Heart and Diabetes Institute - Department of Cardiometabolic Health

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**Identification of additional markers of ferroptosis using mass spectrometry**

**Project Description:**
Ferroptosis is a specific form of cell death mediated by the accumulation of oxidised lipids. Several studies have highlighted this important process in relation to multiple diseases including cancer and neurodegeneration. While the biological mechanisms of lipid oxidation have been demonstrated to be a key factor, measurement of these lipid species is complicated in an in vivo setting. This project aims to identify and develop new ways of measuring molecules related to ferroptosis, using a combination of controlled in cell culture experiments and mass spectrometry assays. The assays developed will then be used to interrogate the role of ether lipids (with antioxidant properties) in ferroptosis and their potential to mediate and regulate the process in various biological settings.

**Primary Supervisor:** Prof Peter Meikle

**Primary Supervisor Contact:** peter.meikle@baker.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Baker Heart and Diabetes Institute - Department of Cardiometabolic Health

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**Validation of 4D Flow with Exercise using CMR**

**Project Description:**
Cardiac magnetic resonance imaging (CMR) is a powerful tool for assessing heart function. Advanced CMR techniques include functional assessment during exercise, and three dimensional flow assessment over the cardiac cycle. We aim to assess the validity of 4D flow during exercise, at low, medium and high intensity in a group of trained athletes.
Primary Supervisor: Dr Ben Costello

Primary Supervisor Contact: ben.costello@baker.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Baker Heart and Diabetes Institute - Department of Cardiometabolic Health

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Targeting Pyroptosis to improve diabetic cardiovascular disease.

Project Description:

Cardiovascular complications associated with Type 2 diabetes (T2D) lead to significant morbidity and mortality, for which standard treatment options are insufficient to halt or reduce this clinical burden. Recent clinical evidence from the successful CANTOS trial suggests that targeting the cytokine IL-1β lessens inflammation and reduces the burden of cardiovascular disease. IL-1β is matured on the NLRP3-inflammasome along with IL-18 and GasderminD, the pyroptosis (a specific form of cell death) regulating protein. Pyroptosis and release of detrimental cytokines is hypothesized to propagate cardiovascular disease. This proposal will investigate the role of pyroptosis in mediating diabetes-driven cardiomyopathy.

Primary Supervisor: Prof Judy de Haan

Primary Supervisor Contact: judy.dehaan@baker.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Baker Heart and Diabetes Institute - Department of Cardiometabolic Health

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Developing unique gene therapy tools to treat the failing heart

Project Description:

This project will take advantage of new technologies that have enabled the rapid development of new therapeutic techniques to treat chronic conditions using gene therapy. This includes technologies such as mRNA therapeutics, lipid nanoparticles and CRISPR. This project will focus on the use of these technologies to treat myocardial infarction and heart failure.

Primary Supervisor: A/Prof Brian Drew

Primary Supervisor Contact: brian.drew@baker.edu.au
A novel approach in improving lipidomics throughput for population profiling

Project Description:

Lipids are key biological molecules essential to life. Lipidomics is the characterisation and study of the complete lipidome of a biological system (fluid, cell, tissue, organism). In humans, plasma is an easy to obtain bio-fluid where lipids have been demonstrated to be perturbed in various disease settings. Diseases can affect everyone differently, in order better understand the relationship between lipids and disease, larger population studies are needed. Clinically related studies in the field have been limited, owing to the limitations in the rate where plasma samples can be profiled in a comprehensive manner. This study aims to generate a novel approach in comprehensive lipidomic profiling using high resolution mass spectrometry approaches in conjunction with computational biology. Students should be technology/computation oriented.

Primary Supervisor: Prof Peter Meikle

Primary Supervisor Contact: peter.meikle@baker.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Baker Heart and Diabetes Institute -Department of Cardiometabolic Health

Development and validation of a high throughput clinical lipidomics platform

Project Description:

The Metabolomics Group at the Baker Institute studies the role of lipid metabolism dysregulation in the development and progression of diseases such as type 2 diabetes, cardiovascular disease and Alzheimer’s disease. To enable this work, we have developed world-class technology which allows us to measure hundreds of different lipids within biological samples through the use of HPLC and tandem mass spectrometry. We are now in the process of translating these research-based protocols for use in a clinical setting, forming the Clinical Lipidomics Platform. The Clinical Lipidomics Platform will comprise two recently developed research capabilities working in concert and translated to a clinical setting. Firstly, from a single blood spot or plasma sample, currently available liquid chromatography-mass spectrometry (LC-MS) technology will be employed to measure the concentration of several hundred clinically relevant lipid biomarkers in the patient’s blood; those
found to be closely associated with disease outcomes. Secondly, using the resultant data, artificial intelligence (AI) based statistical modelling will be employed to determine the patient’s overall metabolic health, presented as a series of easily interpreted Metabolic Risk Scores, and subsequently used by clinicians and patients to predict future disease (Figure 1). Translating our current research protocols for the clinical platform will require the development of several different components, including a sample collection pipeline, robotic automation of sample processing, LC-MS/MS method development, automation of data collection and analysis, artificial intelligence and statistical modelling as well as a clinical interface to communicate results effectively with clinicians. Once established we will validate the platform using population and clinical cohorts as well as real-time testing of patients attending cardiac clinics. This project is suitable for a PhD or Masters student, who will work within the Metabolomics Group to help adapt our mass-spectrometry technology for a clinical setting.

**Primary Supervisor:** Prof Peter Meikle

**Primary Supervisor Contact:** peter.meikle@baker.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Baker Heart and Diabetes Institute - Department of Cardiometabolic Health

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**Integration of population level 'omics' data to target cardiometabolic disease**

**Project Description:**

Cardiometabolic diseases represent the number one cause of death in the world, encompassing cardiovascular disease (CVD), type 2 diabetes (T2D), non-alcoholic fatty liver disease (NAFLD), chronic kidney disease, and others. Dysregulation of lipid metabolism is intimately linked to the aetiology, progression, and sequelae of this collection of diseases. The Metabolomics Laboratory, at Baker Heart and Diabetes Institute, has developed a state-of-the-art lipid profiling methodology. Capable of measuring over 800 lipid species from less than a drop of blood, our lipid profiling has been used to improve the detection of people at risk of a large spectrum of conditions, including CVD, T2D, cancer, and Alzheimer’s disease. To further drive innovation in the field, we are integrating lipidomic and genomic data. Using novel statistical techniques, we aim to identify and evaluate the causal role of lipid metabolic pathways in cardiometabolic disease. With over 50,000 clinically relevant human samples already profiled, an exciting opportunity exists to identify new targets to prevent cardiometabolic diseases. This project is suitable for an Honours or PhD student and will focus on bioinformatic/statistical modelling with human clinical/population cohorts to investigate the relationship between lipid metabolism and cardiometabolic diseases.

**Primary Supervisor:** Prof Peter Meikle

**Primary Supervisor Contact:** peter.meikle@baker.edu.au

**Honours places available:** 1
Plasmalogen modulation as a therapeutic approach for fatty liver disease

Project Description:

Plasmalogens are glycerophospholipids that are present in numerous mammalian tissues and can act as a natural antioxidant (1). Lipidomic profiling of multiple populations and clinical cohorts has identified decreased levels of plasmalogens to be associated with aging and obesity (2) as well as prediabetes and type 2 diabetes (3). Modulation of plasmalogens can be achieved by oral administration of their metabolic precursors, naturally occurring compounds known as alkylglycerols or by suppressing the activity of plasmalogen catabolising enzyme, TMEM86B. Plasmalogen modulation has reported to suppress diseases related to oxidative stress such as atherosclerosis (4). However, the capacity of plasmalogen modulation to attenuate different aspects of metabolic disease is not fully defined and our understanding of the mechanisms involved is limited. Fatty liver diseases are closely associated with metabolic diseases and involve dysregulation of lipid metabolism, heightened oxidative stress and chronic inflammation. We hypothesise that upregulation of plasmalogens will reduce the pathologies association with fatty liver disease by their multifaceted roles in lipid metabolism, oxidative stress, and inflammation. The specific aims are to: 1) Define the potential of plasmalogen upregulation as a therapeutic approach against fatty liver diseases. 2) Identify the underlying mechanisms for the therapeutic potential of plasmalogen modulation against fatty liver diseases. In this project we will combine our lipidomics expertise with our unique mouse models of plasmalogen modification as well as established mouse models of fatty liver diseases to define the therapeutic potential of plasmalogen modulation against fatty liver diseases. Identification of the mechanisms operating to attenuate disease pathogenesis will provide a clear rationale for the subsequent translation and commercialisation of this new prophylactic therapy. References: 1. Paul S, Lancaster GI, Meikle PJ. Plasmalogens: A potential therapeutic target for neurodegenerative and cardiometabolic disease. Progress in lipid research. 2019;74(9):186-95. 2. Weir JM, Wong G, Barlow CK, Greeve MA, Kowalczyk A, Almasy L, et al. Plasma lipid profiling in a large population-based cohort. Journal of lipid research. 2013;54(10):2898-908. 3. Meikle PJ, Wong G, Barlow CK, Weir JM, Greeve MA, Macintosh GL, et al. Plasma lipid profiling shows similar associations with prediabetes and type 2 diabetes. PloS one. 2013;8(9):e74341. 4. Rasmiena AA, Barlow CK, Stefanovic N, Huynh K, Tan R, Sharma A, et al. Plasmalogen modulation attenuates atherosclerosis in ApoE-and ApoE/GPx1-deficient mice. Atherosclerosis. 2015;243(2):598-608.
Do short chain fatty acids prevent gut leakiness and enhanced haematopoiesis induced by a high salt diet?

Project Description:
Our laboratory has discovered that a high salt diet promotes a breakdown of the intestinal barrier in the gut which causes activation of the immune system and changes within the bone marrow microenvironment, altering blood production. This project will explore the hypothesis that supplementation of butyrate, an anti-inflammatory short chain fatty acid, will prevent high salt diet-induced gut leakiness, immune cells activation and protect the bone marrow microenvironment from being destructed. This will allow for the retention of haematopoietic stem cells and normal blood production. This project will employ a variety of assays and experimental readouts to address this hypothesis and give the student a valuable insight into immune and stem cell biology within a highly successful world class research laboratory.

Primary Supervisor: Prof Andrew Murphy
Primary Supervisor Contact: andrew.murphy@baker.edu.au
Honours places available: 1
Master of BioMed places available: 1
Department: Baker Heart and Diabetes Institute -Department of Cardiometabolic Health

Exploring how a high salt diet promotes bone destruction through immune cell activation

Project Description:
Diets rich in salt have been linked to bone pathologies. This has generally been attributed to mineral exchange, causing weaker bones. However, our group hypothesized that this process is biologically driven. We have made initial discoveries to show that specific immune cells are produced and activated by a high salt diet that is linked with bone destruction. This project will focus on the novel mechanisms contributing to this discovery. Specifically, this project will determine how the immune cells interact and activate osteoclasts within the bone and will explore where these immune cells are first activated. We anticipate these findings being important across several age groups and will explore ways to offset these detrimental effects of high salt intake. The student will be exposed to a world class research environment and cutting-edge techniques, with excellent supervision. Techniques will include flow cytometry, sectioning of tissues (including bones), immunofluorescence, micro CT and multiphoton microscopy.

Primary Supervisor: Prof Andrew Murphy
Primary Supervisor Contact: andrew.murphy@baker.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Baker Heart and Diabetes Institute -Department of Cardiometabolic Health

Exploring how diabetes causes increased proliferation of haematopoietic stem cells carrying a mutation in DNMT3A

Project Description:
Clonal haematopoiesis of indeterminate potential (CHIP), caused by somatic mutations in haematopoietic stem cells (HSCs) causes a growth advantage in these cells causing them to outcompete non-mutated HSCs. CHIP was commonly thought to be a prerequisite to leukaemia, the disease ultimately responsible for death in these individuals. However, it was recently shown that people with CHIP more frequently die of cardiovascular disease. Interestingly, there is an association with CHIP and diabetes, but this has not been explored experimentally. We discovered that diabetes enhances the proliferation of HSCs carrying the most common mutation in CHIP (DNMT3A). This project will explore mechanism behind this using a variety of unique animal models and experimental techniques. This project will give the student a valuable insight into stem cell biology within a highly successful world class research laboratory.

Primary Supervisor: Prof Andrew Murphy

Diagnosis and therapy of inflammatory diseases using molecular ultrasound imaging

Project Description:
With steadily increasing health care expenses, a promising translational imaging application using ultrasound can fulfil the need for a cost-effective and non-invasive diagnostic tool. This project aims to investigate whether VCAM-1 targeted microbubbles will locate inflamed vessels using molecular ultrasound imaging, thereby providing a better diagnostic technology.

Primary Supervisor: Dr Xiaowei Wang
Exploring the therapeutic potential of protein phosphatases in cardiometabolic disease

Project Description:
Protein phosphorylation is a post-translational modification that switches proteins on and off to control cellular processes such as growth, survival and energy metabolism. Dysregulation of phosphorylation contributes to maladaptive cardiac remodelling and dysfunction in settings of cardiometabolic disease, including heart failure, and represents a potential target for therapeutic intervention. Research has identified numerous protein kinases that are activated in settings of cardiac stress and injury and which contribute to the development of heart failure. However, the development of therapies targeting protein kinase activity have so far failed to translate into the clinic. Targeting protein phosphatases, which counteract kinase activity by dephosphorylating proteins, represents an alternative approach for manipulating protein phosphorylation in settings of heart disease. However, there is a knowledge gap concerning the function of specific protein phosphatases in regulating cardiac physiology and pathophysiology in settings of disease.

Student projects are available which will explore the function of cardiac protein phosphatases using pharmacological and genetic interventions in cell culture models. There may also be scope for conducting proof-of-concept studies using novel therapeutic compounds in in vivo models of cardiometabolic disease.

Primary Supervisor: Dr Kate Weeks

Primary Supervisor Contact: kate.weeks@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Baker Heart and Diabetes Institute -Department of Cardiometabolic Health
Brain computer Interfaces offer hope of rehabilitation for people with paralysis. However, one major drawback of the state of the art BCIs are that they are slow. Recent work has shown the feasibility of semantic space decoding to visual stimuli. Using deep learning such as the natural language processing model, we can create a decoder that can generalize natural scenes within novel visual stimuli. Using data obtained from electrocorticography and the stentrode in a pre-clinical model we can develop a practical brain-machine interface with the ability to decode thought directly. In this project we aim to decode vector representations of scenes within the semantic space to assess data from a stentrode can be used to decode semantic representations of visual space.

**Primary Supervisor:** Dr Sam John

**Primary Supervisor Contact:** sam.john@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 0

**Department:** Biomedical Engineering and Howard Florey Building

### Brain stimulation for psychiatric disorders

**Project Description:**

In this project, you have the choice to focus on (i) enhancing our understanding of the neurobiology of mental health disorders through analysis of neuroimaging data or (ii) using neuroimaging to determine the optimal brain stimulation target site in the treatment of mental health disorders. Both approaches focus on analysis of brain connectivity from magnetic resonance data.

**Primary Supervisor:** Dr Robin Cash

**Primary Supervisor Contact:** robin.cash@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Department of Biomedical Engineering and Dept Psychiatry

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**Burnet Institute**

**Development of novel point-of-care diagnostics tests and surveillance tools for malaria**
Project Description:

There is an urgent need for diagnostic and surveillance tests that could be used in clinical settings and rural and remote communities. This project will work towards the development of novel semi-quantitative rapid tests for assessing malaria exposure and transmission in communities.

Primary Supervisor: Prof James Beeson

Primary Supervisor Contact: james.beeson@burnet.edu.au

Honours places available: 0

Master of BioMed places available: 1

Department: Burnet Institute

Development of novel vaccines against malaria

Project Description:

This project is suitable for a student with a keen interest in humoral and cellular immunology and vaccine development.

Primary Supervisor: Prof James Beeson

Primary Supervisor Contact: james.beeson@burnet.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Burnet Institute

Discovering the mechanisms and targets of immunity against malaria

Project Description:

Conduct immunologic assays to understand the mechanisms of protective immunity to malaria and identify key targets. This knowledge will be used to inform vaccine development.

Primary Supervisor: Prof James Beeson

Primary Supervisor Contact: james.beeson@burnet.edu.au

Honours places available: 1

Master of BioMed places available: 1
Healthy Mothers, Healthy Babies in Papua New Guinea – The impact of nutrition, malaria, and other infections on pregnant women and infants

Project Description:
In resource-poor regions globally, pregnant women experience high rates of malaria, undernutrition, and viral and bacterial infections, which can lead to maternal morbidity and mortality and low birth weight in infants, which results in a large number of infant deaths each year. The objective of this project is to determine the major preventable causes of poor maternal health and low birth weight to enable the development of future interventions to improve health and pregnancy outcomes. This project is offered as a laboratory or epidemiological project, or a combination of the two depending on student interests.

Primary Supervisor: Prof James Beeson
Primary Supervisor Contact: james.beeson@burnet.edu.au
Honours places available: 0
Master of BioMed places available: 1

Discovering the targets of drugs that stop malaria parasites invading red blood cells

Project Description:
This project will involve discovering the mechanism of action of several compounds that inhibit the invasion of human red blood cells by malaria parasites. The protein targets of the inhibitory compounds will be discovered in parasites along with the role the target proteins play during the invasion process.

Primary Supervisor: Dr Paul Gilson
Primary Supervisor Contact: paul.gilson@burnet.edu.au
Honours places available: 1
Master of BioMed places available: 1
Infectious diseases epidemiology, modelling and public health research: Ending AIDS, eliminating hepatitis B and hepatitis C, and controlling COVID-19 as public health threats in Australia and globally.

**Project Description:**

The Burnet Institute is a global leader in research contributing to efforts to end AIDS and eliminate hepatitis B and hepatitis C as public health threats by 2030. With a particular focus on key populations and health equity, the Burnet Institute is undertaking a series of projects that aim to reduce the transmission or improve the management of blood borne viruses in populations including gay and bisexual men, people who inject drugs, migrants and refugees, female sex workers and young people. In response to the COVID-19 pandemic, the Burnet is undertaking work to reduce the ongoing impact of COVID-19 on the community including long-COVID. Opportunities are available for people to undertake honours projects in population health and international development related to blood borne viruses and COVID-19. Fields of study include health promotion, epidemiology, quantitative and qualitative research methods, implementation science, mathematical modelling, social network modelling and phylogenetics. There are a number of specific projects available 1) examining the behaviours that put people at risk of a blood borne virus infection, 2) measuring the impact of community based point of care testing in HIV, hepatitis B and hepatitis C and 3) examining how to increase HIV, hepatitis B and hepatitis C treatment uptake in community settings, 4) measuring the impact “treatment as prevention” for HIV and HCV on reducing disease incidence, 5) examining community understanding and attitudes to COVID-19. Opportunities exist for research using quantitative and qualitative methods, or a mixed methods approach as well as mathematical and social network models, human centred design and health promotion. The includes both de-novo projects or working on a project that sits alongside an existing Burnet project to answer a research question of particular interest to the applicant.

**Primary Supervisor:** Prof Margaret Hellard

**Primary Supervisor Contact:** margaret.hellard@burnet.edu.au

**Honours places available:** 2

**Master of BioMed places available:** 2

**Department:** Burnet Institute

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**Sex, drugs and rock'n'roll: Young people and risk behaviours**

**Project Description:**

Every year, we conduct an online survey with young people, asking about social media use, sexual health and behaviour, alcohol and other drug use, mental health and other risks and behaviours. In
this project the student will use the data collected to investigate patterns of risk behaviours and health outcomes in young people.

**Primary Supervisor:** Dr Megan Lim  
**Primary Supervisor Contact:** megan.lim@burnet.edu.au  
**Honours places available:** 1  
**Master of BioMed places available:**

**Department:** Burnet Institute

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**Novel chemico-vaccine approaches to combat malaria**

**Project Description:**

Plasmodium falciparum parasites which cause the deadly disease malaria, are becoming resistant to current antimalarial drugs. This poses huge challenges for attempts to eradicate the disease. Further confounding the problem, is that the only licensed malaria vaccine is only 30-50% effective. We would therefore like to explore a novel concept where we use drugs to slow down the ability of malaria parasites to invade human red blood cells in which they grow, to allow more time for vaccine-generated antibodies to neutralise the parasites. This proof-of-concept project will involve culturing parasites treated with drugs and antibodies.

**Primary Supervisor:** Associate Professor Paul Gilson  
**Primary Supervisor Contact:** paul.gilson@burnet.edu.au  
**Honours places available:** 1  
**Master of BioMed places available:** 0  
**Department:** Burnet Institute

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**Department of Radiology – Royal Melbourne Hospital**

**Quantitative imaging in dementia**

**Project Description:**

The aim of this study is to explore the utility of advanced MR imaging approaches in detecting early dementia.

**Primary Supervisor:** Prof Patricia Desmond
Primary Supervisor Contact: Patricia.Desmond@mh.org.au
Honours places available: 1
Master of BioMed places available: 1
Department: Department of Radiology - Royal Melbourne Hospital

White matter imaging in the aging brain

Project Description:
The aim of this study is to study the influence of microstructure in the aging brain and its effects on dementia diagnosis.

Primary Supervisor: Dr Chris Steward
Primary Supervisor Contact: csteward@unimelb.edu.au
Honours places available: 0
Master of BioMed places available: 1
Department: Department of Radiology - Royal Melbourne Hospital

Improve the diagnostic prediction of imaging measures in dementia and epilepsy

Project Description:
The aim of this study is to study the impact of neuroimaging tools driven by machine learning on clinical diagnosis in dementia and epilepsy.

Primary Supervisor: Dr Vijay Venkatraman
Primary Supervisor Contact: vijay.venkatraman@unimelb.edu.au
Honours places available: 1
Master of BioMed places available: 1
Department: Department of Radiology - Royal Melbourne Hospital

Multimodal imaging measures to improve dementia diagnosis
Project Description:
The aim of this study is to study the influence morphological and longitudinal measures to improve dementia diagnosis.

Primary Supervisor: Dr Vijay Venkatraman

Primary Supervisor Contact: vijay.venkatraman@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Department of Radiology - Royal Melbourne Hospital

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Stroke assessment with multi-modal imaging

Project Description:
The aim of this project will be to explore the utility of multimodal imaging in stroke assessment.

Primary Supervisor: Dr Vijay Venkatraman

Primary Supervisor Contact: vijay.venkatraman@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Department of Radiology - Royal Melbourne Hospital

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Department of Endocrinology – Royal Childrens Hospital

Musculoskeletal health in children prescribed antiseizure medications: a longitudinal study

Project Description:
It is widely thought that anti-epileptic drugs (AEDs) impair bone health outcomes in childhood, but there is a lack of prospective, longitudinal data to underpin this assertion. We propose to build on our previous cross-sectional studies by establishing a longitudinal cohort of young people taking AEDs and sibling controls. A student will assist in setting up the cohort, recruiting subjects and controls, and overseeing study-based assessments. These will include bone density scanning (DXA and pQCT), muscle function testing and questionnaires re bone health, and biochemistry. The student will undertake analysis of baseline data, including more detailed analysis of pQCT scans
using finite element modeling. This project encompasses many of the key skills of clinical research, and will provide a solid grounding for future clinical projects.

**Primary Supervisor:** Dr Peter Simm

**Primary Supervisor Contact:** peter.simm@mcri.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Dept of Endocrinology, Royal Childrens Hospital

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**Department of Medicine – Royal Melbourne Hospital**

**Mobile Health App use by a diverse sample of Australians with lived experience of Multiple Sclerosis**

**Project Description:**

Conduct an on-line mixed-methods survey to understand how different social contexts of people living with MS might affect their engagement with mobile health applications. For example, caring responsibilities, family and support structures, flexible working arrangements etc. - To identify healthcare journey “pain points” amenable to digital health solutions. To assess the quality of available apps currently used by people with MS. The student will learn to work with REDCap (remote data capture) and data analysis, with an opportunity for publication. The findings will inform the future co-design of a mobile application to monitor disease activity and progression between neurologist visits.

**Primary Supervisor:** Dr Maya Panisset

**Primary Supervisor Contact:** maya.panisset@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Dept of Medicine, Royal Melbourne Hospital

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**Reliability and Variability of remote monitoring of walking in people with Multiple Sclerosis using mobile technology**

**Project Description:**
Aims: To assess the reliability of mobile-based measures of balance and walking quality. To compare the variability in balance and walking quality between healthy controls and pwMS. To explore patient-reported factors that may affect variability in balance and walking quality. This study will involve direct and indirect assessment of walking quality in people with Multiple Sclerosis, using novel measures calculated from inertial sensors. The student will learn to work with REDCap (remote data capture) and data analysis, with an opportunity for publication.

Primary Supervisor: Dr Maya Panisset

Primary Supervisor Contact: maya.panisset@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Medicine, Royal Melbourne Hospital

Elucidating molecular signalling pathways controlled by anti-inflammatory steroids

Project Description:
Steroids (glucocorticoids) are widely used to treat the chronic inflammation and pain associated with many diseases such as rheumatoid arthritis and osteoarthritis. Unfortunately, there are side effects associated with usage of glucocorticoids in such diseases. Our previous genomic experiments have provided a number of exciting candidate genes that may be involved in inflammatory functions. In this project you will investigate molecular signalling pathways that lead to activation of transcription factors that lead to differential expression of glucocorticoid-controlled genes in inflammatory conditions. Enhancing our understanding of molecular signalling pathways that are governed by glucocorticoids may lead to improved clinical therapies with minimal side effects.

Primary Supervisor: A/Prof Adrian Achuthan

Primary Supervisor Contact: aaa@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Medicine, Royal Melbourne Hospital

Molecular signalling pathways controlling gene expression during chronic disease progression

Project Description:
Inflammation is now known to be associated with many chronic diseases such as arthritis, cancer, Alzheimer’s disease, obesity, diabetes and heart diseases. This project aims to understand molecular signalling pathways controlling the expression of genes critical for the progression of such diseases. In this project you will explore in molecular terms how a particular inflammatory cell type (macrophage/dendritic cell) can adapt to provide a pro-inflammatory environment with consequences for persistence or otherwise of these significant diseases. More specifically you will investigate how transcription factors control the expression of pro-inflammatory and anti-inflammatory cytokines. Elucidation of these molecular pathways will lead to the development of novel therapies.

**Primary Supervisor:** A/Prof Adrian Achuthan

**Primary Supervisor Contact:** aaa@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Dept of Medicine, Royal Melbourne Hospital

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Global coagulation assays and molecular spectroscopy as novel biomarkers for coagulation risk prediction

**Project Description:**

Blood coagulation remains one the most enigmatic of essential physiological processes and is a major determinant of health and disease. Pathological thrombosis is a major cause of death and morbidity across a wide spectrum of diseases and patients. While a plethora of anti-thrombotic drugs are now available, a fine balance needs to be achieved between the prevention of thrombosis in individuals and the risk of bleeding complications. Indeed, one also needs to define, accurately, people who are most risk and who may best benefit from such interventions.

Current risk assessment models and blood tests do not accurately predict individual risk of thrombosis. Risk estimation of thrombosis and bleeding, at an individual level is performed only crudely, and implies that a proportion of patients with thrombosis, are either overâ€ or undertreated, leading to high lifetime risks of both recurrence and bleeding. It is therefore necessary to individually classify patients, accurately, with respect to thrombotic and bleeding risk, and subsequently determine who will benefit from anticoagulant treatment and who will be unnecessarily exposed to its risks.

We therefore require a model which assesses the various determinants of the coagulation cascade, including the structural basis of the clot formation, the coagulability of blood and the cellular (endothelial, platelet, immune) dysfunctional components, that contribute to this process.

â€œGlobalâ€ coagulation assays such as thrombin, fibrin and plasmin generation assays are blood tests with the unique capacity to assess the "whole blood clotting" capacity of an individual while
endothelial biomarkers such as tissue factor pathway inhibitor and inflammatory markers can help to identify endothelial dysfunction. We have previously demonstrated that the addition of global coagulation assays and endothelial biomarkers to clinical surrogate markers are superior to clinical markers alone in identifying diabetes complications and subsequent thrombotic events in patients with chronic kidney disease. This paradigm extends to a variety of other diseases as well.

**Molecular Spectroscopy** (Raman Scattering and Infra-Red Absorption) is a sophisticated method of assessing individual molecular structure, and is particularly useful in the identification of complex molecules in complex biological tissues such as blood. The advantage of Molecular Spectroscopy is that the technique does not need any molecular labelling, and can be performed on clinical samples without destroying them. Raman and Fourier Transform InfraRed Spectroscopy (FTIR) provide a “fingerprint” of the molecular structure, leading to the discovery and identification of complex structural molecules and their conformational variants.

In this project we propose to perform global coagulation assays and endothelial biomarkers on healthy control populations and populations at high risk of coagulation such as those with cardiovascular disease or risk factors, previous venous thromboembolism and malignancies. We will also test the patients plasma using Raman and FTIR spectroscopy to identify and build a library of spectral signatures within each of the high risk patient categories and compare that with healthy controls. A Machine Learning approach shall be used to determine the principal components that determine variance, in each of these categories so as to define the threshold for accurate classification within each class.

In combination, the combination of global coagulation assays and endothelial biomarkers with spectral biomarker signatures will provide a multi-modality approach which may strengthen our ability to predict individualised future thrombotic risks and allow for early intervention with reduction in the burden of disease.

**Primary Supervisor:** Assoc Prof Prahlad Ho

**Primary Supervisor Contact:** prahlad.ho@nh.org.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Department of Medicine - Northern Health

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**Roles of mammary adipose macrophages in breast cancer**

**Project Description:**

Mammary adipose forms the large fraction of breast tumour microenvironment (TME). Macrophages, in particular tumour associated macrophages, are known to promote immune suppression to promote cancer growth. In the last decade, immune checkpoint inhibitors have revolutionised cancer therapy. However, this approach has had only limited success in breast
cancers. While immune checkpoint inhibitors boost anti-tumour immune cells, immune suppression in TME could dampen this process. In this project, you will explore the role of mammary adipose macrophages and their response to immune checkpoint inhibitors.

**Primary Supervisor:** A/Prof Adrian Achuthan

**Primary Supervisor Contact:** aaa@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 0

**Department:** Dept of Medicine, Royal Melbourne Hospital

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**The role of Critical Signalling Pathways in Glioblastoma Mediated Immunosuppression**

**Project Description:**

The most severe form of brain cancer, Glioblastoma Multiforme is extremely lethal, with the average survival time of less than 12 months after diagnosis. Glioblastoma cells are generally highly proliferative, invasive. Recent evidence suggests that their micro-environment contains factors that suppress anti-tumour immune responses. However, the role of glioblastoma cell signalling in promoting an immunosuppressive environment is not well known. This project will evaluate the role of critical glioblastoma-promoting signalling pathways in promoting immunosuppression. Specifically, we will identify key immunosuppressive factors/cytokines secreted by glioblastoma cells and evaluate their role in blocking immune cell function (activation and killing activity).

**Primary Supervisor:** A/Prof Adrian Achuthan

**Primary Supervisor Contact:** aaa@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 0

**Department:** Dept of Medicine, Royal Melbourne Hospital

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**Brainwave and Electrophysiological Biomarkers of Cognition Enhancing Drugs**

**Project Description:**

Several drugs are able to improve cognitive performance quite considerably in animal models, and to some extent in humans. They are known as "nootropics". This project aims to study how brain wave patterns in mice change with these drugs, both to understand how they work, as well as to find biomarkers to identify such agents. It will involve training mice to perform simple memory and other
cognitive tasks, and to record their brain signals before and after drug administration. We will initially use simple double "depth" electrodes, but will progress to multielectrode arrays and miniscopes later in the project. This is a fantastic opportunity to get into modern cognitive neuroscience and discover some really neat things! Suitable for Honours, Masters and PhD.

**Primary Supervisor:** Dr Chris French

**Primary Supervisor Contact:** frenchc@unimelb.edu.au

**Honours places available:** 2

**Master of BioMed places available:** 2

**Department:** Dept of Medicine, Royal Melbourne Hospital

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**Can we Fix Dementia with Deep Brain Stimulation?**

**Project Description:**

"Lewy Body Dementia" is the second most common form of dementia after Alzheimer's disease, but we don't understand how it damages patients' ability to think and function. We suspect that part of the problem is that the brain goes "out of sync" like a misfiring engine, that is, has problems of signal timing. In an animal model, we want to see if we can detect signs of damaged brain signal synchronization, and see if we can improve or fix this either with drugs or a kind of "brain pacemaker". If we can show these treatments work in the animal model, it could lead to major improvements in therapies for these patients. Deep brain stimulation is incredibly effective for some neurodegenerative conditions such as Parkinson’s disease. Despite the success of this technique, little is actually known about how it works. The first half of this project involves implanting stimulation electrodes into the brains of mice, and looking for the changes in neuron firing as well as brain rhythms that result from stimulating particular areas of the brain. The second part is to see if the performance of animals with impaired cognition can be improved with brain stimulation. Check out https://ndl-lab.org/home.

**Primary Supervisor:** Dr Chris French

**Primary Supervisor Contact:** frenchc@unimelb.edu.au

**Honours places available:** 2

**Master of BioMed places available:** 2

**Department:** Dept of Medicine, Royal Melbourne Hospital

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**Effects of Drugs on Cognition-Related Brain Wave Signals in the Rat**
**Project Description:**

In this project, signals related to cognitive processing, including gamma frequency oscillations and place cells will be recorded with microelectrode arrays. The effects of antipsychotic drugs and some related compounds, including potassium and sodium channel modulators, will be examined.

**Primary Supervisor:** Dr Chris French

**Primary Supervisor Contact:** frenchc@unimelb.edu.au

**Honours places available:** 2

**Master of BioMed places available:** 2

**Department:** Dept of Medicine, Royal Melbourne Hospital

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**Effects of Drugs on Cognition-Related Brain Wave Signals in the Rodents**

**Project Description:**

It is increasingly recognised that the rhythmic signals recorded with the electroencephalogram (EEG), or “brain waves” are not just the “noise” of neural activity, but are probably frequency specific channels for cognition related signalling, including memory encoding. High frequency (“gamma”) brain wave activity has been associated with cognitive activity in humans and animals, and is disrupted in psychosis and schizophrenia. A largely neglected area of study in this area is the role of voltage-gated ion channels that have a significant role in the generation of neuronal and network rhythmicity. In this project, signals related to cognitive processing, including gamma frequency oscillations and place cells will be recorded with microelectrode arrays. The effects of antipsychotic drugs and some related compounds, including potassium and sodium channel modulators, will be examined. This project has considerable potential to reveal how psychoactive drugs work at the whole brain level, and provide clues for better therapies. Check out https://ndl-lab.org/home.

**Primary Supervisor:** Dr Chris French

**Primary Supervisor Contact:** frenchc@unimelb.edu.au

**Honours places available:** 2

**Master of BioMed places available:** 2

**Department:** Dept of Medicine, Royal Melbourne Hospital

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**Electrophysiological Properties of Human Brain Neuronal Tissue**
Project Description:

Almost all electrophysiological observations of neural normal function, drug responsiveness and abnormal states such as epilepsy in have been performed on rodent brain tissue. It is becoming clear, however, that human tissue has significant differences from rodent brain. This project presents an almost unique opportunity to study human brain tissue at the single neuron and network level by utilising tissue taken in the course of neurosurgical procedures. Individual neurons are prepared by enzymatic dissociation, and recorded with patch electrodes. Network properties are recorded using intact brain slice. For this project, the main aims are to identify the properties of voltage gated ion channels, in particular sodium and potassium currents. An area of special interest is the HERG channel subtype, which is likely to play an important role in brain function, but almost completely uncharacterised in any neural system. Check out https://ndl-lab.org/home.

Primary Supervisor: Dr Chris French

Primary Supervisor Contact: fren chc@unimelb.edu.au

Honours places available: 2

Master of BioMed places available: 2

Department: Dept of Medicine, Royal Melbourne Hospital

How to anti-epileptic drugs work?

Project Description:

Despite many years of use and research, it is still not clear how even some of the oldest forms of antiepileptic drugs (AED’s) work. What is known is generally based on the effects of these compounds on single neurons, rather than examining how activity of the whole inter-connected neural network of the mammalian CNS is modulated. This project involves studying the effects of AED’s at several levels of organization of the CNS – single channel (voltage-gated sodium, potassium and calcium channels), single neuron, principal neuron/interneuron dynamics, as well as glial cell effects. Patch clamp techniques are used for recording dissociated neuron and neurons in the intact brain slice, and these observations will be extended with high-speed calcium imaging with conventional microscopy as well as multiphoton techniques. This project affords excellent opportunities for skill development in electrophysiology, pharmacology advanced microscopy and computational neuroscience as well as conference presentation and publication opportunities. Check out https://ndl-lab.org/home.

Primary Supervisor: Dr Chris French

Primary Supervisor Contact: fren chc@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 2

Department: Dept of Medicine, Royal Melbourne Hospital
Massively Parallel Optical Imaging of Cognition Events in Neuronal Networks in Freely Behaving Mice

**Project Description:**

We have recently implemented for the first time in Australia the “miniscope” technique (see http://miniscope.org/index.php/Main_Page, and see our setup in https://ndl-lab.org/), in which we put small fluorescent microscopes into mouse brains and observe the activity of hundreds of neurons over many months while the animal is performing cognitive tasks such as memory encoding. We can also see the direct effects of cognition-affecting drugs such as antidepressants and antipsychotics in real time to correlate with neuronal network activity, allowing a whole new level of analysis and comprehension of brain phenomena. This is super neat. This project has several streams – it can be implemented for epilepsy, drug testing, dementia models, MS models etc. We would like to set up an epilepsy related project with miniscopes as an Honours/Masters/PhD project.

**Primary Supervisor:** Dr Chris French

**Primary Supervisor Contact:** frenchc@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 2

**Department:** Dept of Medicine, Royal Melbourne Hospital

Sodium Channels in Epilepsy

**Project Description:**

This project is to study voltage-gated sodium channels, membrane proteins that are the basis of almost all electrical signaling in the nervous system, and so of the greatest significance in normal function, as well as disease states including epilepsy.

**Primary Supervisor:** Dr Chris French

**Primary Supervisor Contact:** frenchc@unimelb.edu.au

**Honours places available:** 2

**Master of BioMed places available:** 2

**Department:** Dept of Medicine, Royal Melbourne Hospital
Stentrode: Tissue Response to Endovascular Stimulation

Project Description:
Tissue response influences the effectiveness of the bioelectric implants. The aim of this project is to evaluate the Acute and chronic histological, macroscopic changes due to endovascular electrical stimulation to the surrounding blood vessels.

Primary Supervisor: Dr Sam John
Primary Supervisor Contact: sam.john@unimelb.edu.au
Honours places available: 1
Master of BioMed places available: 0
Department: Dept of Medicine, Royal Melbourne Hospital

Linking brain activity to behaviour: neural oscillations and cognition

Project Description:
How do brain waves control cognitive processes? Using a combination of in vivo electrophysiology and sophisticated cognitive paradigms of working memory and attention, coupled with genetically modified mice, this project will record brain waves (local field potentials) and single unit activity during cognitive performance.

Primary Supervisor: A/Prof Nigel Jones
Primary Supervisor Contact: nigel.jones@monash.edu
Honours places available: 1
Master of BioMed places available: 1
Department: Dept of Medicine, Royal Melbourne Hospital

The role of microglial cells in epilepsy

Project Description:
Brain inflammation appears to play a critical role in the pathogenesis of epilepsy. A major cell type involved in inflammatory cascades are the microglial cells – brain-resident immune cells that become
activated after epileptogenic brain injuries. Despite years of research in this area, a clear role of microglia in epilepsy development has not been established. This is partly due to the dynamic nature in which these cells get activated. The function of these cells can oscillate between different phenotypes that are associated with the release of either pro- or anti-inflammatory mediators. Therefore, depending on the stage after initial epileptogenic brain injury, their activation may promote brain repair processes or conversely accelerate the epilepsy development. This project will utilise animal models to identify the role of microglia at different stages of epilepsy development. This will be achieved by pharmacologically eliminating microglia at different timepoints following induction of epilepsy, and evaluate the relevant epilepsy outcomes by electrophysiological, molecular, immunofluorescence imaging and techniques.

**Primary Supervisor:** A/Prof Nigel Jones

**Primary Supervisor Contact:** nigel.jones@monash.edu

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Dept of Medicine, Royal Melbourne Hospital

Using light to control brain activity

**Project Description:**

This project will use laser light to inhibit and activate a specific class of brain cell in mice, and observe how these impacts working memory.

**Primary Supervisor:** A/Prof Nigel Jones

**Primary Supervisor Contact:** nigel.jones@monash.edu

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Dept of Medicine, Royal Melbourne Hospital

Development of a low cost, point-of-care diagnostic platform

**Project Description:**

To develop a novel rapid, ultrasensitive real-time point of care platform targeting molecules in blood or saliva. This will be integrated on a single chip platform.
Primary Supervisor: Prof Patrick Kwan
Primary Supervisor Contact: patrick.kwan@unimelb.edu.au
Honours places available: 1
Master of BioMed places available:
Department: Dept of Medicine, Royal Melbourne Hospital

Inflammatory cytokines involved in obesity and osteoarthritis

Project Description:
Osteoarthritis (OA) is a most common form of arthritis and is associated with many risk factors, for example, obesity. Inflammatory cytokines have been implicated in facilitating OA progression. This project will use animal models of OA to identify a novel potential therapeutic target(s) for treating OA symptoms (i.e. pain).

Primary Supervisor: Dr Kevin Lee
Primary Supervisor Contact: mingchinl@unimelb.edu.au
Honours places available: 1
Master of BioMed places available:
Department: Dept of Medicine, Royal Melbourne Hospital

Recipient immunity as a determinant of long term outcome in bone marrow transplantation

Project Description:
Allogeneic bone marrow transplantation (alloSCT) is a curative therapy for blood cancers. However, up to 50% of patients undergoing alloSCT continue to face the prospect of disease relapse, regimen-related toxicity, opportunistic infections and graft versus host disease. We have shown in mouse models that residual recipient immunity present at the time of alloSCT has a significant impact on outcome. We have launched multiple clinical trials to translate this finding to the clinic which incorporate significant correlative immunology analysis and will form the basis of this project.

Primary Supervisor: Prof David Ritchie
Primary Supervisor Contact: david.ritchie@mh.org.au
Honours places available: 1

Parkville Precinct Honours and Masters Project Handbook |
T cell function as a determinant of blinatumomab efficacy in B-ALL

Project Description:
The CD3/CD19 bispecific T cell engager blinatumomab (blin) is effective for the treatment of relapsed or refractory B cell acute lymphoblastic leukaemia (B-ALL). Total CD8 T cell numbers at the time of treatment have been associated with a higher likelihood of response. However, studies have not explored if patient T cell function has an impact on therapeutic efficacy. We hypothesise that response to blin will be dependent on pre-treatment T cell function.

Primary Supervisor: Prof David Ritchie

Primary Supervisor Contact: david.ritchie@mh.org.au

Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Medicine, Royal Melbourne Hospital

Understanding how immune cell function is impacted by novel therapies in patients with B cell malignancies

Project Description:
In recent years, new non-chemotherapy based small molecule inhibitors such as Venetoclax and Ibrutinib have been shown to offer improved outcomes in patients with B cell malignancies. Our existing data has demonstrated that these therapies have a significant impact on patient immune function when used long term which will be explored further in this project.

Primary Supervisor: Prof David Ritchie

Primary Supervisor Contact: david.ritchie@mh.org.au

Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Medicine, Royal Melbourne Hospital
Systematic Endoscopic Staging of Mediastinum to determine Impact on radiotherapy for locally advanced lung Cancer (SEISMIC): an international multi-centre cohort study

Project Description:
Lung Cancer remains the most common cause of cancer death in Australia & the western world. Non-small cell lung cancer (NSCLC) comprises 87% of all lung cancers, and of these over 25% are diagnosed with locally advanced disease – defined by involvement of mediastinal lymph nodes (LN). The SEISMIC study aims to identify the optimal method for mediastinal LN and planning of radiation therapy fields.

Primary Supervisor: A/Prof Daniel Steinfort
Primary Supervisor Contact: Daniel.Steinfot@mh.org.au
Honours places available: 1
Master of BioMed places available: 1
Department: Dept of Medicine, Royal Melbourne Hospital

Improving antimicrobial stewardship - still a priority in Australia

Project Description:
Older people are especially vulnerable to antimicrobial resistant infections. As recommended by the World Health Organization (WHO), it is critical that antimicrobial stewardship (AMS) programs are effectively implemented. The aim of this timely and important project is to investigate the quality of AMS policies and procedures in residential aged care. The successful student will be working with an internationally renowned team.

Primary Supervisor: Prof Dr Karin Joanne Thursky Tropea
Primary Supervisor Contact: joanne.tropea@mh.org.au
Honours places available: 1
Master of BioMed places available: 0
Department: Dept of Medicine, Royal Melbourne Hospital
Population frequencies of common genetic diseases

Project Description:
The population frequencies of many genetic diseases has been unknown but now using normal population frequency databases we are able more accurately identify how common these diseases are. This project will look at some of the common genetic diseases and analyse variants for pathogenicity using on line tools. We expect our students to be able to publish their results.

Primary Supervisor: Prof Judith Savige
Primary Supervisor Contact: j.savige@unimelb.edu.au
Honours places available: 0
Master of BioMed places available: 2
Department: Dept of Medicine, Royal Melbourne Hospital

Lets CHAT dementia project: optimising detection and management of cognitive impairment and dementia in Aboriginal and Torres Strait Islander People attending primary care

Project Description:
The risk of developing dementia is 3-4 times higher in First Nations Peoples of Australia. The Let’s CHAT dementia project is a Stepped wedge RCT that has collaborated with 12 Aboriginal health services nationwide, to address ways to optimise brain health and improve management of those with dementia. As part of the 4 year project, information has been collected through 6 monthly audits (approx. 1100) and comprehensive assessment in approximately 80-100 participants. This project involves exploring the data base for the quantitative and qualitative factors that contribute to a model of care that optimises detection and management of cognitive impairment and dementia in Aboriginal Primary Health Care Services. We encourage Aboriginal and Torres Strait Islander students to apply.

Primary Supervisor: A/Prof Dina LoGiudice
Primary Supervisor Contact: dina.logiudice@mh.org.au
Honours places available: 1
Master of BioMed places available: 0
Department: Dept of Medicine, Royal Melbourne Hospital
An online insomnia intervention for brain tumour patients (SHUTi) - a feasibility study to test its acceptability and usefulness in a brain tumour cohort. (Prof Kate Drummond; Dr Verena Schadewaldt)

Project Description:
SHUTi is a validated online behavioural 6 week program to manage and improve insomnia. It will be offered through our newly developed online platform for people affected by brain tumours, called Brain Tumours Online. SHUTi will be offered to those who suffer from insomnia. The AIM of this study is to identify the feasibility of SHUTi for a cohort of brain tumour patients who suffer from insomnia. A pre- and post standardised survey will establish changes in the participant's sleep pattern. In addition feedback from interviews with participants will support the survey data to establish feasibility of SHUTi in preparation for an RCT.

Primary Supervisor: Prof Kate Drummond
Primary Supervisor Contact: kjd@unimelb.edu.au
Honours places available: 1
Master of BioMed places available: 0
Department: Dept of Medicine, Royal Melbourne Hospital

A supportive online community for brain tumour patients, carers and health care professionals - creation and analysis of social media content (Prof Kate Drummond; Dr Mahima Kalla; Dr Kara Burns)

Project Description:
Brain tumour patients and their families are socially and physically isolated and in particular those living in rural areas lack access to peer support. Our team of patients, carers, health care professionals, digital health experts and digital product developers have developed an online platform for people affected by brain tumours, called Brain Tumours Online. This platform offers those affected by brain tumours a safe and closed space to connect with their peers and share stories and experiences. They can connect through chats, reading or posting stories, contacting peers or health professionals and joining online Q &A sessions. The AIM of this study is to assist with the co-creation of the content posted within the online community and conduct an analysis of the social media content. This will facilitate the evaluation of how participants engage and use the online community and will provide the basis for improving the online community.

Primary Supervisor: Prof Kate Drummond
Primary Supervisor Contact: kjd@unimelb.edu.au
Investigate the implementation process including barriers and enablers of a digital health platform - a process evaluation (Prof Kate Drummond; Dr Verena Schadewaldt; Dr Mahima Kalla; Prof Meinir Krishnasamy)

Project Description:
Our team of patients, carers, health care professionals, digital health experts and digital product developers have co-designed an online platform for people affected by brain tumours, called Brain Tumours Online. The platform offers trusted information, connection with peers and health professionals and access to self-help tools (online interventions). The platform will be evaluated in a cohort of 300 patients, carers and health professionals across four Victorian health services and brain cancer organisations. The AIM of this study is to specifically investigate the implementation process and identify barriers and enablers in preparation for implementing the platform across more health services and make it available to all Australians affected by brain tumours. The methodology will be guided by process evaluation theory and comprises qualitative and quantitative data analysis methods.

Primary Supervisor: Prof Kate Drummond

Primary Supervisor Contact: kjd@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 0

Department: Dept of Medicine, Royal Melbourne Hospital

Interventions to reduce medication errors in hospitalised older patients: a systematic review

Project Description:
In this project, we will compare the effectiveness of different interventions in reducing prescribing, dispensing and administration medication errors in hospitalised older patients. The systematic review will examine and analyse the types of interventions to determine effectiveness in reducing medication errors and patient harm, which clinicians and policymakers could use for implementation in hospital settings. New directions for future research will be identified for interdisciplinary collaborative approaches involving doctors, pharmacists, nurses, and nurse practitioners. Students will gain skills in searching of library databases, extraction of relevant data from research papers, etc.
conduct of meta-analysis and display of data using forest plots, synthesis of findings, writing results for journal publication, and identifying implications for practice and policy. Results will also be disseminated to key policymakers and health professionals to enable implementation in practice and set initiatives for further research.

Primary Supervisor: Professor Elizabeth Manias

Primary Supervisor Contact: emanias@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Medicine, Royal Melbourne Hospital

Department of Obstetrics and Gynaecology - RWH/Mercy

Uncovering the mechanisms of abnormal uterine bleeding

Project Description:

Menstruation remains a taboo subject in the 21st century, despite abnormal uterine bleeding impacting ~50% of people who menstruate. Abnormal uterine bleeding is chronically underdiagnosed and undertreated, with no advancement in novel treatments for the condition in more than 20 years. Menstrual health is a global area of clinical unmet need, with impacts on quality of life beginning in adolescence and extending into adulthood. The economic burden associated with heavy or painful periods is significant and includes loss of income, work absenteeism and loss of productivity while at work. Novel tools to detect and diagnose menstrual abnormalities are imperative for improving overall menstrual and reproductive health. Our group has an established biobank of patient samples that includes various benign gynaecological pathologies that contribute to abnormal uterine bleeding, including adenomyosis, uterine fibroids, heavy menstrual bleeding, and endometriosis. This project will investigate genes and pathways that contribute to the pathogenesis of abnormal uterine bleeding. The findings from this work will pave the way for new therapeutic targets and diagnostic possibilities for abnormal uterine bleeding.

Primary Supervisor: Dr Jacqueline Donoghue

Primary Supervisor Contact: jacqueline.donoghue@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Obstetrics and Gynaecology - RWH/Mercy

Functional role of VEZT over expression in endometrium
**Project Description:**

VEZT is the first protein coding gene that can be directly linked to increased susceptibility for endometriosis. At a population level, SNPs associated with an increased risk for endometriosis are also associated with increased VEZT expression in the endometrium. To date, it is unclear what functional role VEZT has in the development or progression of endometriosis. To generate new knowledge about VEZT and endometriosis, we have developed a novel mouse model that conditionally over-expresses VEZT ubiquitously including the reproductive system. Our primary aim is to characterise the impact increased expression VEZT has on fertility as well as endometrial lesion formation. This project will include working with an animal model of endometriosis, protein and molecular studies.

**Primary Supervisor:** Dr Jacqueline Donoghue

**Primary Supervisor Contact:** jacqueline.donoghue@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Dept of Obstetrics and Gynaecology - RWH/Mercy

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**Guiding the creation of national guidelines in CAYA Oncofertility**

**Project Description:**

The Fertility Preservation Taskforce is working with the Australia and New Zealand Consortium on Paediatric Oncofertility (ANZCO) on creating national guidelines for use in ANZCHOG paediatric oncology centres around Australia and New Zealand.

**Primary Supervisor:** A/Prof Yasmin Jayasinghe

**Primary Supervisor Contact:** yasmin.jayasinghe@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Dept of Obstetrics and Gynaecology - RWH/Mercy

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**Novel animal model to discover CRISPR treatments for preeclampsia**

**Project Description:**

Parkville Precinct Honours and Masters Project Handbook |
Preeclampsia is a serious complication of pregnancy affecting 3-5% of pregnant women. Currently, there are no medical treatments. We are developing an animal model of preeclampsia utilising human placenta. In this project you will perform xenograft transplant surgery in mice with human placenta. You will characterise the model and use CRISPR to target one of the key pathogenic molecules secreted. We hope this will lead to a PhD project.

**Primary Supervisor:** Dr Elif Kadife

**Primary Supervisor Contact:** elif.kadife@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Dept of Obstetrics and Gynaecology - RWH/Mercy

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**New treatments for fetal growth restriction**

**Project Description:**

Fetal growth restriction is a serious complication of pregnancy and leading cause of stillbirth. Currently, there are no medical treatments. We are developing an animal model of fetal growth restriction. In this project you will perform surgery in mice to cause fetal growth restriction and treat with our novel compounds to rescue the disease.

**Primary Supervisor:** Dr Elif Kadife

**Primary Supervisor Contact:** elif.kadife@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Dept of Obstetrics and Gynaecology - RWH/Mercy

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**Understanding the membrane proteome of amniotic fluid extracellular vesicles**

**Project Description:**

In this project, we will use proteomics to characterize membrane proteins of extracellular vesicles(EVs). Amniotic fluid is rich in EVs from virtually all fetal cells and EVs carry a protein barcode of its cell type of origin. Researchers are interested in separating EVs according to their origin, especially for biomarker discovery purposes. However, no robust methods exist so far. Understanding and characterizing the membrane proteome will enable sorting EVs according to the
expression of cell-specific membrane proteins. Therefore this project will be an essential first step towards the translational goal of identifying novel fetal diagnostic markers.

**Primary Supervisor:** Dr Ishara Atukorala  
**Primary Supervisor Contact:** ishara.atukorala@unimelb.edu.au  
**Honours places available:** 1  
**Master of BioMed places available:** 1  
**Department:** Dept of Obstetrics and Gynaecology - RWH/Mercy

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**Vitrification of animal prepubertal testicular tissue**

**Project Description:**

This project will compare the slow freezing procedure currently used for human prepubertal testicular tissue with rapid freezing, referred to as vitrification. The aim is to assess temperature, media composition, rate of cooling and warming on animal prepubertal testicular tissue. Multiple cells are required for spermatogonial stem cells to progress through to formation of mature sperm, the impact of these variables in the freezing of each cell type will be assessed.

**Primary Supervisor:** A/Prof Yasmin Jayasinghe  
**Primary Supervisor Contact:** yasmin.jayasinghe@unimelb.edu.au  
**Honours places available:** 1  
**Master of BioMed places available:** 1  
**Department:** Dept of Obstetrics and Gynaecology - RWH/Mercy

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**Elimination of leukemic cells from ovarian tissue**

**Project Description:**

Ovarian tissue frozen to preserve fertility from women and girls with leukaemia has the potential to harbour leukemic cells, and if grafted back could re-initiate disease. The overall project aim is to produce an artificial ovary reconstructed from ovarian follicles and stromal cells free from leukemic contamination. The aim of this part of the project is to isolate ovarian follicles, seed these within a 3-dimensional matrix and determine factors which are required for these to grow these in vitro.

**Primary Supervisor:** A/Prof Yasmin Jayasinghe  
**Primary Supervisor Contact:** yasmin.jayasinghe@unimelb.edu.au
Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Obstetrics and Gynaecology - RWH/Mercy

Fertility preservation in children with cancer

Project Description:

One in 900 children is a cancer survivor. Cancer treatment can significantly affect future fertility. Determining an accurate risk assessment helps in counseling families considering fertility preservation procedures. We have one of the largest registries of paediatric cancer patients, from which we can research risk factors, counseling and effectiveness of procedures.

Primary Supervisor: A/Prof Yasmin Jayasinghe

Primary Supervisor Contact: yasmin.jayasinghe@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Obstetrics and Gynaecology - RWH/Mercy

Use of a respiratory function monitor to improve training efficiency in neonatal face mask ventilation: A feasibility trial

Project Description:

At birth, newborn infants undergo a complex physiological transition. Respiratory changes include lung aeration, airway liquid clearance, and the initiation of pulmonary gas exchange. Approximately 5% of term newborns need respiratory support to successfully complete this transition, therefore providing rapid and effective positive pressure ventilation (PPV) via a face mask is considered to be the most important component of neonatal resuscitation. Face-mask ventilation is an essential skill taught in neonatal resuscitation training, but competence is difficult to achieve and maintain. Respiratory Function Monitors (RFMs) are used to determine the effectiveness of newborn ventilation. RFMs may help clinicians improve resuscitation performance by providing feedback on face-mask leak and delivered tidal volume. We hypothesise that using a respiratory function monitor during self-directed face-mask ventilation training, compared with training without using the RFM, will improve effectiveness of resuscitation by reducing mask leak. The aim of this study is to compare the leak and tidal volume during face-mask ventilation training, performed by first responders after monthly RFM-assisted self-directed face-mask ventilation training, to first responders training without a RFM, and to assess the feasibility of such a training program.
Use of a respiratory function monitor to improve training efficiency in neonatal face mask ventilation

Project Description:

Face-mask ventilation is a frequent and important intervention during newborn resuscitation. This skill is difficult to master. Large leaks around the mask are common even in expert hands and can lead to ineffective resuscitation. Respiratory Function Monitors (RFM) provide feedback on face-mask leak and tidal volume, but they are not widely available for use either for training or for actual newborn resuscitations. This randomised control trial will determine whether using a newly designed portable Respiratory Function Monitor (RFM), improves training in face-mask ventilation.

Primary Supervisor: Dr Marta Thio

Primary Supervisor Contact: mthio@unimelb.edu.au

Honours places available: 1
Master of BioMed places available: 1

Department: Dept of Obstetrics and Gynaecology - RWH/Mercy

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Department of Psychiatry – Royal Melbourne Hospital

Sleep and neurodevelopment in adolescence

Project Description:

Healthy sleep is critical for good health, including mental health and cognitive function. Accumulating research has demonstrated a link between sleep and brain structure or function although the nature of the relationship remains unclear. Using population based studies, this project will investigate whether and how changes in sleep influence brain development in early adolescence. It may also examine factors that moderate such relationships, and whether/how links between sleep and neurodevelopment confer risk for a range of psychopathology.
Synthesising, dismantling and optimising cognitive interventions

Project Description:

Our group is a world leader in research synthesis of cognitive interventions across the lifespan and brain disorders. Using large datasets from hundreds of clinical trials, we use cutting-edge meta-analysis techniques to identify the active ingredients and core components of interventions, and define the most effective intervention and treatment strategies for different populations of individuals. We produce robust evidence and high-impact publications that that have influenced changes in both policy and clinical practice. Our group offers a range of projects (Honours to PhD), with a particular interest in ageing (older adult populations), neurodegenerative disorders (e.g., multiple sclerosis), psychiatric disorders (e.g., depression) and cancer.

Primary Supervisor: Dr Amit Lampit

Primary Supervisor Contact: amit.lampit@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Psychiatry - Royal Melbourne Hospital

Animal models of Brain Development assessed using MRI

Project Description:

A newly commenced Program Grant aims to map brain-structure-function relationships and molecular signatures across developmental stages in the mouse, as measured through novel neuroimaging techniques and microscopy. The aim of the current project is to model hippocampal structure in the mouse brain using a combination of structural and spectroscopy neuroimaging techniques, and to determine whether differences are present between age groups.

Primary Supervisor: Prof Christos Pantelis
Cognition and brain connectivity in psychosis

**Project Description:**

The aim of this project is to determine whether impairments in episodic memory, attentional set-shifting, and spatial working memory are related to disrupted brain connectivity (as measured by MRI-derived structural covariance; see Wannan et al, 2019) in key regions associated with performance on these tasks in individuals with first-episode psychosis.

**Primary Supervisor:** Prof Christos Pantelis

**Primary Supervisor Contact:** cpant@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Psychiatry - Royal Melbourne Hospital

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Ferroptosis in Schizophrenia

**Project Description:**

Schizophrenia is a debilitating mental illness that disrupts the functioning of the mind, with onset typically occurring in young adulthood. Impairments in certain cognitive functions, such as working memory, are core features of Sz, which are not addressed for existing drug targets. Our general hypothesis is that schizophrenia is a complex disease resulting from a loss-of-function of key pathways that govern neurodevelopment, neurotransmission, intracellular redox state and synaptic connectivity. Our data indicate that iron is elevated in the orbitofrontal cortex in post mortem brain samples from individuals with schizophrenia relative to age- and sex-matched controls. We propose that a rise of cytosolic iron is upstream of key lesions associated with negative and cognitive symptoms of schizophrenia, including neuronal development (e.g., parvalbumin-interneurons and synaptic pruning), neurotransmission (e.g., GABAergic and glutamatergic pathways), as well as iron homeostasis, antioxidant defence (e.g., haem oxygenases), and ferroptosis (e.g., an iron-dependent pathway for lipid peroxidation recently associated with loss of parvalbumin-interneurons). The
project aims to investigate the status of proteins involved in iron metabolism as well as levels of markers of oxidative stress.

**Primary Supervisor:** Prof Christos Pantelis  
**Primary Supervisor Contact:** cpant@unimelb.edu.au  
**Honours places available:** 1  
**Master of BioMed places available:** 1  
**Department:** Dept of Psychiatry - Royal Melbourne Hospital

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**Multinuclear MRI biomarkers in schizophrenia**

**Project Description:**

Schizophrenia is a debilitating neuropsychiatric disorder characterised by positive symptoms (delusions, hallucinations), negative symptoms (lack of motivation, poverty of speech), cognitive deficits and impaired social and occupational functioning. The aetiology of schizophrenia remains unknown and the mechanisms underlying the pathogenesis of schizophrenia are poorly understood. Previous studies have identified altered brain metabolism as one of the putative mechanisms contributing to schizophrenia, partly due to neuroinflammation and pathological oxidative processes. However, there is a paucity of research investigating oxidative and neuroinflammatory processes in the brain in vivo. Sodium (23Na) MRI is an emerging metabolic imaging technique that employs ultra-high field MRI (7T and above) to characterise tissue sodium content, and together with iron (1H) MRI provides an invaluable tool to investigate brain structure and chemical composition in the living brain. By employing advanced multivariate statistical techniques, this program of work aims to combine complementary information from clinical, cognitive and biological data in order to identify unique patterns of cognition and structural changes associated with schizophrenia.

**Primary Supervisor:** Prof Christos Pantelis  
**Primary Supervisor Contact:** cpant@unimelb.edu.au  
**Honours places available:** 1  
**Master of BioMed places available:** 1  
**Department:** Dept of Psychiatry - Royal Melbourne Hospital

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**Neurodevelopmental trajectories and biopsychosocial risk factors in autism and schizophrenia**

**Project Description:**

Parkville Precinct Honours and Masters Project Handbook |
Children with neurodevelopmental disorders often have worse outcomes than typically developing children on a range of measures, including education, mental health, social dysfunction, vocational achievement, and conduct problems. Furthermore, overlap between the symptoms of many neurodevelopmental disorders, along with intra-illness heterogeneity, results in frequent misdiagnosis, ineffective treatment, and increased disability in affected children. There is therefore an urgent need to identify biopsychosocial markers that characterise specific neurodevelopmental disorders and impact on illness severity and outcomes. The key aims of our research are therefore to (1) map the developmental trajectories of cognition, behaviour, and brain structure and function in autism-spectrum disorder (ASD) and schizotypal disorder of childhood (SDC) over critical periods of brain development, and (2) identify the candidate biopsychosocial risk/resilience markers that might impact these trajectories and illness outcomes. Our work will consider a range of biopsychosocial markers, including genetics, inflammation, clinical profiles, early life stress and physiological stress reactivity, and psychosocial indices such as socioeconomic status and parenting styles.

**Primary Supervisor:** Prof Christos Pantelis

**Primary Supervisor Contact:** cpant@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Dept of Psychiatry - Royal Melbourne Hospital

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**Ubiquitin Proteasome System in Schizophrenia**

**Project Description:**

The ubiquitin-proteasome system (UPS) is a master regulator of neural development and the maintenance of brain structure and function. It influences neurogenesis, synaptogenesis and neurotransmission by determining the localization, interaction and turnover of scaffolding, presynaptic and postsynaptic proteins. Moreover, UPS signalling transduces epigenetic changes in neurons independent of protein degradation and as such dysfunction of components and/or substrates of this system have been linked to a broad range of brain conditions. Although links between UPS dysfunction and neurodegenerative disorders have been known for some time, only recently have similar links emerged for neurodevelopmental disorders, such as schizophrenia. We and others have found that different components of the UPS are dysregulated in schizophrenia. The project aims to investigate whether specific poly-ubiquitin changes are altered in brain samples from individuals with schizophrenia.

**Primary Supervisor:** Prof Christos Pantelis

**Primary Supervisor Contact:** cpant@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1
Characterizing brain-body relationship with respect to biological aging in elderly population

Project Description:

This project aims to comprehensively characterize patterns of aging in various human biological systems including the brain and other organ systems such as the cardiovascular, respiratory and skeleton systems, and to understand the relationship between the brain and the body with respect to the aging trajectory and health outcomes.

Primary Supervisor: Dr Ye Tian

Primary Supervisor Contact: ye.tian2@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Psychiatry - Royal Melbourne Hospital

Decoding neural mechanisms underpinning human cognition in health and disease using machine learning

Project Description:

This project aims to understand the neural mechanisms underpinning higher-order cognitive function in humans. This student will be guided in using state-of-the-art neuroimaging techniques and machine learning to decipher the complex network of brain circuits that give rise to individual variation in cognition in healthy adults as well as abnormal brain changes associated with cognitive decline in neurodegenerative diseases such as Alzheimer’s disease and mild cognitive impairment.

Primary Supervisor: Dr Ye Tian

Primary Supervisor Contact: ye.tian2@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Psychiatry - Royal Melbourne Hospital
How trauma shapes empathy and resilience in bipolar disorder

Project Description:

We are seeking an enthusiastic and academically high-performing student to be involved in an honours project investigating how subjective ratings of trauma relate to ones empathy and resilience in bipolar disorder.

Primary Supervisor: Dr Tamsyn Van Rheenen

Primary Supervisor Contact: tamsyn.van@unimelb.edu.au

Honours places available: 0

Master of BioMed places available: 1

Department: Dept of Psychiatry - Royal Melbourne Hospital

Is medication use related to cognitive variability? An examination of cross-diagnostic cognitive subgroups on the bipolar-schizophrenia spectrum

Project Description:

We are seeking an enthusiastic and academically high-performing student to be involved in an honours project investigating the medication use profiles of individuals in cross-diagnostic cognitive subgroups on the bipolar-schizophrenia spectrum.

Primary Supervisor: Dr Tamsyn Van Rheenen

Primary Supervisor Contact: tamsyn.van@unimelb.edu.au

Honours places available: 0

Master of BioMed places available: 1

Department: Dept of Psychiatry - Royal Melbourne Hospital

Markers in Neuropsychiatric Disorders (MiND) study

Project Description:

The Markers in Neuropsychiatric Disorders (MiND) aims to study whether neurofilament light and other biomarkers, clinical, cognitive, imaging and other markers can improve diagnosis, prognostication, care and treatment, and health economic outcomes, for people with cognitive,
neuropsychiatric and neurological symptoms. By studying a broad range of symptoms and conditions, from neurodegenerative dementias such as Alzheimer disease and behavioural variant frontotemporal dementia, to many other neurological and neurodegenerative disorders, to schizophrenia and other severe psychiatric illnesses, the MiND study ultimately aims for clinical translation such as a screening blood test and precision care use of biomarkers and other markers, to improve outcomes for patients, their families, clinical trials and healthcare systems.

Primary Supervisor: Prof Dennis Velakoulis

Primary Supervisor Contact: dennisv@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Psychiatry - Royal Melbourne Hospital

Validating a new self-report depression scale

Project Description:
In this project, we will validate a new self-report depression scale called the Melbourne Depression - 5 item (MELD-5) scale. The MELD-5 has been designed to enable both clinical and non-clinical populations to quickly and easily rate themselves on five common depressive symptoms. The questionnaire can be administered frequently (i.e., daily) to enable effective monitoring of changes in mood over time. This project will validate and refine the MELD-5 by comparing it to existing, commonly used but outdated self-report depression scales across two clinical samples and one non-clinical sample. The two clinical samples will be drawn from the Advanced Interventions in Mood Disorders (AIM) Clinic ketamine treatment service at the Royal Melbourne Hospital and the University of Melbourne Psychology Clinic.

Primary Supervisor: Dr Orli Schwartz

Primary Supervisor Contact: orli@unimelb.edu.au

Honours places available: 0

Master of BioMed places available: 1

Department: Dept of Psychiatry - Royal Melbourne Hospital

Ultra-high field neuroimaging of transdiagnostic mental health symptoms

Project Description:
Recent studies have illustrated poor reliability between correlations of psychopathology and neuroimaging parameters, including resting-state and structural measures, commonly used in the field. Fortunately, ‘ultra-high field’ (UHF) magnetic resonance imaging shows much greater capacity in characterising structural and functional alterations common across mood and anxiety disorders, due to its vastly improved anatomical resolution and signal mapping capabilities. By identifying which neurobiological features are specific to and common between mental health disorders, this work will aid to improve our conceptualisations of these conditions. This project aims to investigate transdiagnostic mental health symptoms, including maladaptive rumination, distress, and emotional arousal, using UHF imaging to better characterise the neurobiological basis of these symptoms across diagnoses.

**Primary Supervisor:** Prof Ben Harrison

**Primary Supervisor Contact:** habj@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 0

**Department:** Dept of Psychiatry - Royal Melbourne Hospital

The impact of early life stress on neurodevelopmental trajectories across different mental health diagnoses in children

**Project Description:**

Over the past several decades there has been a growing understanding that exposure to early life stress is also associated with adverse mental health outcomes. However, while it is clear that psychosocial stress is a risk factor for many mental health disorders, it is less clear whether particular types of stressors are more strongly associated with particular diagnoses, or whether these stressors represent a general, non-specific, risk factor for poorer health outcomes. Furthermore, the impact of early life stress on brain and cognitive development across mental health diagnoses is currently unclear. The broad aims of this research are therefore to (1) identify early life stressors that ‘hang together’ in a large longitudinal sample of children and adolescents, (2) determine the prevalence of these stressors across neurodevelopmental and psychiatric disorder diagnoses, (3) examine the impact of different stressors on brain development trajectories across diagnoses, and (4) examine the impact of different stressors on cognitive trajectories across diagnoses. Students will focus on select aims depending on their degree (honours, Masters, PhD). This study will utilise data from the ABCD Study, a large multi-site longitudinal study of more than 11,000 children.

**Primary Supervisor:** Dr Cassandra Wannan

**Primary Supervisor Contact:** wannanc@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1
Investigating the link between phenotype change and treatment resistance in prostate cancer

Project Description:

The development of resistance to androgen (male sex hormone) deprivation therapy (ADT), the primary treatment for aggressive prostate cancer, is not clearly understood. Our phylogenetic analyses of resistant tumours demonstrate no significant tumour evolution or clonal/subclonal selection with therapy, supporting the concept that resistant tumours are "hardwired" to survive in the castrate environment. We have previously found no mutation or structural variant consistently shared between resistant tumours at any of the gene/pathway/ontology levels, and no evidence of previously characterised genomic drivers of resistance. We have performed whole genome and RNA sequencing on paired pre- and post-treatment tumour samples obtained from high-risk patients undergoing profound androgen suppression for 6 months before prostatectomy, in whom clinical responses ranged from complete involution to no effect. Transcriptional profiling indicated that resistant cells undergo a phenotypic reprogramming in response to therapy that may be important for cellular survival, and suggests that these changes are regulated by alterations in post-translational histone modifications. This raises the possibility that hardwired resistance is epigenetically, and not genomically mediated. Our data from patient-derived tumours grown in androgen-deprived conditions support the concept that cancer cells adapt to castration though histone mediated transcriptional reprogramming and development of a stem cell–like phenotype. This project will involve establishing an organoid model of prostate cancer and investigating the effect of perturbing key nodes in this adaptive process.

Primary Supervisor: A/Prof Niall Corcoran

Primary Supervisor Contact: con@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

The role of invadopodia in brain cancer invasion and response to therapeutics

Project Description:
This project will involve studies that investigate the role of invadopodia in glioblastoma cells, how they contribute to the invasive phenotype of this deadly brain cancer and also exploring the use of repurposed FDA approved drugs to inhibit their ability in facilitating glioblastoma cell invasion throughout the surrounding normal brain.

**Primary Supervisor:** Dr Stanley Stylii

**Primary Supervisor Contact:** sstylli@unimelb.edu.au

**Honours places available:** 0

**Master of BioMed places available:** 1

**Department:** Dept of Surgery - Royal Melbourne Hospital

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**Examining Pro-tumorigenic Cross-talk between Brain Tumour Cells, Astrocytes and Immune cells.**

**Project Description:**

Glioblastoma is the most severe form of brain tumour and is currently incurable with an average survival rate of only 12-15 months post diagnosis. This poor survival rate is largely due to the highly invasive and highly immunosuppressive nature of these tumours. However, the complete mechanisms used for tumour cell invasion and immune escape and the key interactions and cross-talk (via growth factor, cytokine and chemokine secretion) between glioblastoma cells, local astrocytes and the immune cell population is not fully understood. Our lab has a major focus to gain a better understanding of these glioblastoma-induced mechanisms and how we can overcome these mechanisms to reduce glioblastoma progression. This Honours project seeks to specifically explore the key proteins secreted by glioblastoma cells, astrocytes and immune cells that are responsible for glioblastoma invasion and reduced immune cell activity using healthy donor and glioblastoma patient samples and patient derived cell lines. Furthermore, this project has the scope to evolve into a PhD project pending the ability of the incumbent student and grow into a larger research project involving key members of the Melbourne cancer research community.

**Primary Supervisor:** Dr Rod Luwor

**Primary Supervisor Contact:** rluwor@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Dept of Surgery - Royal Melbourne Hospital

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**Florey Institute of Neuroscience and Mental Health**

**Biophysics of leaky HCN ion channels**
Project Description:
The hyperpolarisation-activated, cyclic nucleotide-gated (HCN) channel, opens and conducts positively charged ions when the transmembrane voltage is negative on the inside. Several variants in the HCN1 subtype channel have been reported in patients with severe epilepsy. Functional analyses of these variants revealed a converging functional impact of ‘leaky’ channels, which remain open and conduct ions at membrane voltages in which the channels are meant to be closed. Our goal is to elucidate HCN1 channel function at the molecular scale using naturally occurring variants as novel functional tools. Successful applicants will have the opportunity to learn and operate two-electrode voltage clamp, voltage clamp fluorometry (which measures channel movement in real-time), electrophysiological analysis, Xenopus oocyte handling/injections, molecular biology, and be involved in manuscript preparation.

Primary Supervisor: Prof Christopher Reid

Primary Supervisor Contact: christopher.reid@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Florey Institute of Neuroscience and Mental Health

Modelling severe childhood epilepsy

Project Description:
Epilepsy is a common neurological disorder with a third of patients not responding to currently available treatments. To better understand the underlying mechanisms, our lab is developing and analysing disease models for genetic forms of epilepsy.

Primary Supervisor: Dr Snezana Maljevic

Primary Supervisor Contact: snezana.maljevic@florey.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Florey Institute of Neuroscience and Mental Health

Can we achieve precise medication use in people living with Alzheimer's disease?
Project Description:

Alzheimer’s disease (AD) is the most common form of dementia, affecting 1 in 9 people >65 years. AD is featured by progressive neuron loss in the brain and decline in cognitive function. However, recent evidence suggests that AD may also affect peripheral organs. In line with this, we have for the first time demonstrated that the expression and function of drug transporters and metabolising enzymes in the peripheral organs are altered in AD mouse models, leading to altered drug disposition. Some of these changes have been validated in AD human tissues, however, if drug disposition is affected in people with AD is yet to be determined.

Polypharmacy, or the use of multiple medications, is prevalent in older populations and people with AD are prescribed 5-10 more medications than their peers. This heightened polypharmacy places people with AD at a greater risk of adverse drug reactions (ADRs), particularly if the disease alters the drug disposition. For nearly all medications, medical practice is based on single disease guidelines derived from clinical trials that do not include people with AD. If drug disposition is altered in AD, a standard dose may produce unexpected therapeutic outcomes (e.g. increased risk of ADRs) in people with AD. People with cognitive impairment are also less likely to report ADRs, which presents an additional challenge in caring for people with AD and is likely to lead to suboptimal healthcare outcomes.

In this project, we will use high-throughput proteomics to profile drug transporter and drug metabolising enzyme expression in AD and non-AD human tissues, leading to the development of a physiologically based pharmacokinetic models for dose adjustment in people with AD. These models will be validated using plasma samples collected via Australian Imaging, Biomarker & Lifestyle (AIBL) study of aging. The ultimate goal of this research program is to achieve precise medication use in people with AD.

Primary Supervisor: Dr Nicholas Pan

Primary Supervisor Contact: yijun.pan@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Florey Institute of Neuroscience and Mental Health

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Exploring the genetics links between Alzheimer’s disease and type 2 diabetes

Project Description:

There is a considerable body of literature on associations between type 2 diabetes (T2D) and Alzheimer’s disease (AD). It has been calculated in a meta-analysis that individuals with T2D were 39% more likely to develop AD than non-diabetics. Pathophysiologically this relationship between T2D and AD has not been completely elucidated. Insulin resistance in T2D has been shown to exacerbate directly amyloid and tau pathologies, and their shared pathophysiological traits of synaptic dysfunction, inflammation, and autophagic impairments. In this study, we aim to determine if a genetic link exist between AD and T2D to improve our understanding of the shared pathways.
The students will have access to the genetics data collected via The Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL), and will be provided training on genetic analysis.

**Primary Supervisor:** Dr Nicholas Pan

**Primary Supervisor Contact:** yijun.pan@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Florey Institute of Neuroscience and Mental Health

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**Exploring the role of fatty acid-binding proteins in microglia immunometabolism**

**Project Description:**

Microglia are the resident immune cells in the central nervous system (CNS). They interact with the CNS microenvironment through different molecules such as chemokines, cytokines, and trophic factors which, in turn, modulate microglia activities converting the homeostatic microglia into activated microglia (broadly defined as proinflammatory and anti-inflammatory) and vice versa. By transforming between a spectrum of phenotypes, microglia can clear cell debris through phagocytosis, stimulate repair and regeneration of neurons, and maintain the homeostasis in the CNS. The microglia immune phenotype transformation is supported by cellular metabolism reprogramming. Given the tight relationship between immune function and metabolism in microglia, they are often collectively referred to as immunometabolism. Fatty acid-binding proteins (FABPs) are a family of intracellular proteins involved in cell metabolism. We have confirmed the presence of FABP3, 4, and 5 isoforms in microglia, however, their roles in the microglia are not clearly defined. In this project, we will use CRISPR-Cas9 genome editing, in vivo cross linking, proteomics, single-cell RNA sequencing, automated high throughput metabolism profiling, magnetic activated cell sorting, transgenic mouse models and human microglia to explore the roles of FABPs in microglia immunometabolism, and potential involvement in neurodegenerative diseases.

**Primary Supervisor:** Dr Nicholas Pan

**Primary Supervisor Contact:** yijun.pan@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Florey Institute of Neuroscience and Mental Health

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Using novel animal and stem cell models to investigate the role of genetic cardiac arrhythmia in sudden unexpected death in epilepsy (SUDEP).

**Project Description:**

We recently provided evidence that epilepsy patients carrying loss-of-function variants in a cardiac arrhythmia gene are at greater risk of sudden death, known as SUDEP. This project aims to understand how genetic cardiac arrhythmia contribute to SUDEP risk by using EEG-ECG to monitor the changes in brain and heart function during seizures and sudden deaths in novel SUDEP mouse models. Furthermore, the project aims to develop and measure electrophysiology of stem cell-derived cardiomyocytes, including 3D “mini heart” cardiac organoids, that express the cardiac arrhythmia variant identified in SUDEP patients. These models provide an opportunity to test cardio-protective strategies on SUDEP risk. Successful applicants will have the opportunity to learn to operate multi-electrode array system, optogenetics, patch-clamp electrophysiology, perform EEG-ECG surgery/monitoring/analysis, mouse handling/injections, stem cell culture, molecular biology, and be involved in manuscript preparation.

**Primary Supervisor:** Prof Christopher Reid

**Primary Supervisor Contact:** christopher.reid@unimelb.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Florey Institute of Neuroscience and Mental Health

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Investigating cardiac mechanisms underlying stimulant-mediated sudden death

**Project Description:**

This is an exciting pilot study that will record brain and heart electrophysiology using an optimised video-electrocorticography-electrocardiogram (vECoG-ECG) in a cardiac arrhythmia mouse model to study the additive impact of stimulants and genetic cardiac arrhythmia on sudden death risk. The mouse model also provides an opportunity to test cardio-protective strategies on sudden death risk. Successful applicants will have the opportunity to join a friendly team and perform ECoG-ECG surgery/recording/analysis, mouse handling/injections, behavioural studies and be involved in manuscript preparation.

**Primary Supervisor:** Dr Ming Soh

**Primary Supervisor Contact:** mingshiuan.soh@florey.edu.au

**Honours places available:** 1

**Master of BioMed places available:** 0

**Department:** Florey Institute of Neuroscience and Mental Health
Department of Infectious Diseases

Development of malaria transmission blocking drugs.

Project Description:
Our laboratory investigates the cellular mechanisms underpinning malaria parasite transmission and disease. We investigate the novel banana shaped sexual stages of Plasmodium falciparum, focused on understanding their unique biology and how this contributes to transmission. We are interested in developing and testing drugs and vaccines that may block transmission of the parasite from infected humans to Anopheles mosquitoes.

Primary Supervisor: Dr Matthew Dixon
Primary Supervisor Contact: matthew.dixon@unimelb.edu.au
Honours places available: 1
Master of BioMed places available: 1
Department: Infectious Diseases

Malaria: going bananas for sex

Project Description:
The malaria parasite Plasmodium falciparum undergoes a remarkable transformation that allows asexual stage multiplication in a human host and sexual reproduction in a mosquito vector. Gametocyte maturation represents a ‘bottle neck’ in the parasite’s development; inhibition of this process would ablate disease transmission. This transformation sees an amoeboid shaped asexual stage parasite morph into a banana shaped sexual stage parasite, which is essential to disease transmission.

Despite the importance of this stage of the parasite we understand very little about its unique biology. This unique shape is driven by the assembly of a membrane complex termed the inner membrane complex and the elaboration of a dense microtubule cytoskeleton that drives the unique gametocyte shape. In this project we are interested in determining the cellular and molecular players driving this shape change and how this influences survival within the host and mosquito transmission.

Primary Supervisor: Dr Matthew Dixon
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Department of Nephrology, Austin Health

Targeting Metabolic Dysregulation in Autosomal Dominant Polycystic Kidney Disease (A/Prof Peter Mount; Dr Mardiana Lee; Dr Marina Katerelos)

Project Description:

Background: Autosomal dominant polycystic kidney disease (ADPKD) is the most common genetically determined cause of kidney failure. Abnormal kidney energy metabolism has been observed in ADPKD and this has been proposed to be a therapeutic target.

Hypothesis: Kidney cells in ADPKD metabolise glucose and fatty acids differently compared to normal kidney cells due to low activity of the metabolic fuel gauge AMP-activated protein kinase (AMPK) and that this can be corrected by AMPK activating drugs.

Project aims:

1) To determine the differences in energy metabolism (e.g. glycolysis and fatty acid oxidation) between human ADPKD cells and normal kidney cells

2) To study the role of the LKB1/AMP-activated Protein Kinase (AMPK) pathway in human ADPKD cells

3) To determine whether activation of AMPK, using the novel direct AMPK activator O304 or the diabetes drug metformin, corrects changes in glycolysis and fatty acid oxidation seen in ADPKD cells.

Significance of project: Demonstration that activation of AMPK with O304 corrects abnormal kidney cell metabolism in ADPKD will form the basis for pursuing this therapeutic approach in animal models and clinical trials. A successful outcome with this strategy could improve the lives of people with ADPKD and would represent a significant research advance. Better understanding of the changes to metabolic pathways in ADPKD is a promising therapeutic strategy to control cyst growth in ADPKD, thereby slowing progression to kidney failure.

Primary Supervisor: A/Prof Peter Mount

Primary Supervisor Contact: Peter.Mount@austin.org.au

Honours places available: 1

Master of BioMed places available:
Exploring the effects of dimensions of early life adversity on cognition and mental health in young adults

Project Description:

Dimensional models of early-life adversity (ELA) propose that there are core features of early-life environmental experiences that vary along a continuum of severity and in forms of adversity. Recent work has outlined three primary dimensions along which specific types of ELA may fall: threat/harshness, neglect/deprivation, and unpredictability. Although emerging evidence suggests that partially distinct mechanisms may underlie the association between these different dimensions of ELA with psychopathology and cognitive functioning in children and adolescents, the persistence of these associations into adulthood remain unclear. Further, few studies have studied the unique effects of threat/harshness, deprivation, and unpredictability simultaneously in relation to mental health and cognition.

The current project will examine the associations between experiences of threat, deprivation and unpredictability with cognition and mental health functioning in a sample of young adults. The student will use preliminary data from an on-going study that includes measures of early life experiences of adversity, cognitive functioning and self-report measures of psychopathology. The student will develop the project, conduct a literature review and perform statistical analyses.

Primary Supervisor: A/Prof Vanessa Cropley

Primary Supervisor Contact: vcropley@unimelb.edu.au

Honours places available: 1

Master of BioMed places available: 1

Department: Dept of Psychiatry - Royal Melbourne Hospital
to identify people who are at clinical high risk can help clinicians treat people early before their symptoms worsen. It can also help researchers understand who is likely to develop schizophrenia, who is likely to develop other mental health conditions, and who is unlikely to experience longer-term issues. At Orygen, we are leading the largest study in the world to look for measurable indicators of illness, known as biomarkers, that can help to predict the likelihood that a person will progress to psychosis and other health outcomes. Once we have identified these biomarkers, they will be translated clinically and used in drug development pipelines. We are currently focussed on clinical, brain EEG, brain MRI, speech, and digital biomarkers. Our methods include machine learning approaches in addition to methods from dynamic systems theory. We work with global collaborators to achieve these aims within international teams. Students on the projects will learn how to identify biomarkers using advanced methods and how these results may integrate into large-scale international studies. There will be opportunities to continue in the projects after the end of the masters or honours project.

**Primary Supervisor:** Dr. Domonic Dwyer

**Primary Supervisor Contact:** dominic.dwyer@orygen.org.au

**Honours places available:** 2

**Master of BioMed places available:** 4

**Department:** Orygen Centre for Youth Mental Health

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**Epigenetics as a predictor of mental illnesses: discovering methylomic subgroups for future treatments**

**Project Description:**

Mental illnesses are known to be the result of complex interactions between genes and the environment. Such interactions are thought to be partially mediated by epigenetic changes that switch genes "on" or "off". These switches can be detected in methylomic profiles, which have been detected to be abnormal in some individuals with mental illness and may be treatable in the future through targeted therapies. The aim of this project is to look into whether subgroups of individuals can be found with particularly high epigenetic burden for future targeted therapies. The students will use existing datasets to achieve this and will collaborate with international colleagues in Germany (ZI Mannheim; Prof. Schwarz). The detection of epigenetic risk subgroups will lead the field towards greater understanding and more precise treatments for mental illness.

**Primary Supervisor:** Dr. Domonic Dwyer

**Primary Supervisor Contact:** dominic.dwyer@orygen.org.au

**Honours places available:** 1

**Master of BioMed places available:** 1

**Department:** Orygen Centre for Youth Mental Health
Implementing precision medicine approaches for youth mental health

Project Description:
Schizophrenia is a serious mental illness associated with significant health, social, and economic concerns, and it is one of the top 15 leading causes of disability worldwide. Young people may start to show signs of risk for psychosis months or even years before they receive a diagnosis. At Orygen, we have developed treatments to potentially prevent the onset of psychosis and schizophrenia. However, they are only effective approximately 50% of the time. Precision medicine techniques are needed to match young people at risk of psychosis to the therapies that they will specifically respond to. In this project, the student will build on existing methodological work to identify subgroups of young people at-risk of psychosis who respond to different treatments. The subgroups will be identified using clinical, cognitive, and brain imaging data. This work will contribute to the establishment of precision psychiatry.

Primary Supervisor: Dr. Domonic Dwyer
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Honours places available: 1
Master of BioMed places available: 1
Department: Orygen Centre for Youth Mental Health

Individualised neurocognitive and neuroimaging trajectories in individuals at high risk for psychosis: predictors of trajectories and implications for outcomes

Project Description:
There is a large degree of heterogeneity in terms of cognitive and neuroimaging profiles and trajectories observed in individuals with psychosis. However, it is unclear whether these profiles are driven by specific risk and protective factors. Furthermore, the relevance for these different profiles for later outcomes, including transition to first-episode psychosis, persistence or remission of ultra high risk status, diagnosis of other non-psychotic psychiatric disorders, and social and occupational functioning. This study will identify individualised neuroimaging and cognitive trajectories, determine the risk and protective factors that drive them, and investigate the implications of these trajectories for later outcomes.

Primary Supervisor: Dr Cassandra Wannan
Primary Supervisor Contact: wannanc@unimelb.edu.au
Honours places available: 1
Master of BioMed places available: 1

Department: Orygen Centre for Youth Mental Health

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Using machine learning tools in psychiatric primary care to prevent psychosis

Project Description:

Schizophrenia is a serious mental illness associated with significant health, social, and economic concerns, and it is one of the top 15 leading causes of disability worldwide. Young people may start to show signs of risk for psychosis months or even years before they receive a diagnosis. At Orygen, we founded the largest primary care network in the world for youth mental illness and risk states called 'headspace'. Over 130 sites around Australia assess thousands of young people with a range of mental health challenges. We also devised a way to determine if young people were at-risk of psychotic illnesses, like schizophrenia, that can lead to lifelong disability, but our tools are not precise enough and new approaches are needed. In this project, we will use machine learning methods to predict psychosis onset in individuals who are at-risk of psychosis using clinical data from headspace sites with the aim to translate the tools clinically through our national infrastructure. Achieving this translational goal will change care for thousands of young people and may lead to the prevention or delay of illness. The projects will involve learning and applying translational machine learning methods and implementation science approaches using pre-existing data. There will also be the opportunity to develop predictive models using clinical, brain, social, or digital biomarker data from some of the largest studies in this field globally we are currently leading (e.g., see https://www.ampscz.org/).

Primary Supervisor: Dr Domonic Dwyer

Primary Supervisor Contact: dominic.dwyer@orygen.org.au

Honours places available: 2

Master of BioMed places available: 1

Department: Orygen Centre for Youth Mental Health