

GRADUATE RESEARCH PROJECTS 2017

**THE UNIVERSITY OF MELBOURNE AT THE ROYAL MELBOURNE
HOSPITAL**

(RMH Departments: Medicine and Radiology, Surgery, Psychiatry, Obstetrics &
Gynaecology/RWH, and affiliated institutes)

Melbourne Medical School, The University of Melbourne

Affiliations: The Royal Women's Hospital, Western Hospital (Footscray & Sunshine), Northern Hospital, The Peter MacCallum Cancer Centre, The Burnet Institute, Melbourne Brain Centre, Florey Neuroscience Institute, Melbourne Neuropsychiatry Centre, Mental Health Research Institute, Baker IDI Heart & Diabetes Institute.

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*Listed below are brief outlines of some of the projects being offered in 2016-2017.
For further information, contact the supervisors on the numbers and email addresses as listed.*

AGEING

Project AG1: Lifestyle Factors for Healthy Ageing

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki ; E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Several studies have described the benefit of lifestyle change for healthy ageing and cognitive improvement. For example smoking, alcohol consumption and a lack of physical activity have been linked to an increased rate of cognitive impairment and cardiovascular diseases. Studies investigating lifestyle factors have been limited by cohort sampling bias, cross sectional designs, short follow-ups and small sample sizes. Furthermore the frequency and intensity of lifestyle alteration is still not defined. In this project we examine a 20 year longitudinal dataset to determine the influence of lifestyle (i.e. alcohol consumption, smoking, diet and physical activity) on morbidity and quality of life in health and ageing.

This project will involve direct hands-on participant evaluation. You will also have the opportunity to work with a rich database with lifestyle data that spans over 20 years. There will be the opportunity for publication.

Project AG2: Multimorbidity and ageing women

Supervisor/s: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki, E: cszoeki@unimelb.edu.au
T: 8344 1835

Project description: Multimorbidity is an under-researched area, despite 80% of elderly Australians having 2 or more chronic illnesses. The optimal measure for multimorbidity has not yet been established. This research project will investigate which of the currently available multimorbidity measures has the best predictive power, working with the Healthy Ageing Program in the Department of Medicine. This is a unique opportunity to work on an Australian dataset with midlife and late life data collected over 25 years.

This project will provide opportunity for publication within one year and suits a candidate with an interest in a number of disease areas.

Project AG3: Physical Activities for Healthy Ageing

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki, E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Several studies have described the benefit of lifestyle change for healthy ageing and cognitive improvement. A lack of physical activity have been linked to an increased rate of cognitive impairment and cardiovascular diseases. Studies investigating physical activity have been limited by cohort sampling bias, cross sectional designs, short follow-ups and small sample sizes. Furthermore the frequency and intensity of lifestyle alteration is still not defined. In this project we examine a 20 year longitudinal dataset to determine the influence of physical activity on cognitive performance and health. This project will involve direct hands-on participant evaluation and provide clinical skills experience. You will also have the opportunity to work with a rich database with lifestyle data that spans over 20 years, as well as an opportunity for publication.

Project AG4: Vitamin D levels and cardiovascular disease

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki, E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Low vitamin D levels are common amongst the Australian population, especially in ageing and elderly women. Vitamin D has been reported to be associated with increased cardiovascular risk. Cardiovascular disease is the primary cause of death in the first world and the top cause of death in the elderly. There is growing evidence that vitamin D is associated with a range of typical cardiovascular risk markers such as blood pressure and cholesterol, as well as a few studies demonstrating association with several other biomarkers that have been linked to cardiovascular risk such as C-reactive protein, homocysteine and fasting glucose. This study will investigate the relationship between vitamin D cardiovascular risk in healthy women.

The key benefits of this project are:

1. Opportunity for publication
2. Working with an internationally renowned cohort and research team
3. Working with a vast dataset with over 20 years of data already collected

This project is ideal for candidates with an interest in commercialisation, interaction with industry partners and media.

Project AG5: Diet and Healthy Ageing

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki; E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Several studies have described the benefit of lifestyle change for healthy ageing and cognitive improvement. For example smoking, alcohol consumption and a lack of physical activity have been linked to an increased rate of cognitive impairment and cardiovascular diseases. Studies investigating diet have been limited by cohort sampling bias, cross sectional designs, short follow-ups, small sample sizes, and most have examined the Mediterranean diet. Furthermore the frequency and intensity of lifestyle alteration is still not defined. In this project we examine a 20 year longitudinal dataset to determine the influence of diets on cognitive performance and health.

You will have the opportunity to work with a rich database with lifestyle data that spans over 20 years. This project will provide clinical skills experience as it involves direct hands-on participant evaluation, and will suit a student with an interest in nutrition who is interested in publishing findings.

Project AG6: Vitamin D levels and Mood

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki, E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Vitamin D is made in the skin, a process that requires sun exposure, ingestion in the diet or being taken as a nutritional supplement. Adequate levels of vitamin D are essential for healthy bones and muscle function, and research has only recently started to associate low levels of vitamin D to depression and other mood related disorders. The effects of mild to moderate deficiency are less clear-cut, but symptoms may include muscle pain, weak bones, low energy, fatigue, lowered immunity, and symptoms of depression; moods swings, and sleep irregularities. In Australia, mild to moderate vitamin D deficiency is relatively common in the adult population, but the health consequences of this deficiency in apparently healthy adults are poorly understood. It is also not clear below which level in the blood, vitamin D level mood disorders may arise. The purpose of this project is to investigate the consequences of mild to moderate vitamin D deficiency (blood already collected) on mood including depression, anxiety, and wellbeing (measures already collected) in healthy women from the Women's Healthy Ageing Project (WHAP).

Opportunities: You will have the opportunity to work with an internationally renowned cohort and research team, each with international recognition, and for publication. This project would suit a candidate with an interest in psychiatry.

Project AG7: Patterns of Violence in Australian Women – A twenty year follow up Study

Supervisors: A/Professor Cassandra Szoeki, Dr. Rae Kaspiw
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki , E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Women are more likely than men to experience various forms of violence. One in four Australian women experience physical or sexual assault from a current or former partner (Australian Bureau of Statistics, 2012), and since the age of 15 years, one in three women has experienced physical violence (Cox, 2015). Women are also over two times more likely than men to experience elder abuse (Boldy et al, 2002). This project will examine the cross-sectional relationship between women's experiences of violence and their health and quality of life outcomes, and the impact that experiences of violence have on women's health and quality of life over time.

The main opportunities in this project are:

- Working with a large dataset spanning over 20 years from an internationally renowned cohort
- Working with an internationally recognised research team
- You will also have the opportunity for publication
- This project would suit a student with an interest in women's health

Project AG8: Social engagement and ageing mental health

Supervisor/s: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki ; E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Mental health is a key aspect of health that is impacted by increasing population age.

Nearly half of the world's leading causes of life lost due to disability are mental illnesses such as mood and neurological disorders, accounting for 10% of the global burden of disease. Social engagement has been identified as a protective factor in ageing mental health, with a particular focus on the impact of loneliness. This project will investigate the relationship between social activities and mood, focusing particularly on loneliness from midlife into ageing. This study will access the Women's Healthy Ageing Project (WHAP); an epidemiologically sampled, longitudinal prospective ageing cohort.

This project will involve direct hands-on participant evaluation and provide clinical skills experience. You will also have the opportunity to work with a rich database with clinical and lifestyle data that spans over 25 years, as well as an opportunity for publication.

Project AG9: Inter- and intra-individual pattern of diseases

Supervisor: Professor Andrea Maier, A/Professor Cassandra Szoeki
Project Site: University of Melbourne, RMH, Department of Medicine and Aged Care
Contact: T: + 61 3 9342 2635, E: andrea.maier@mh.org.au

Project description: The accumulation of age related diseases is one of the most striking phenomenon during the (human) ageing process. Chronological age is the most important risk factor for the development of diseases due to the underlying ageing process, which has been partly unraveled during the last decennia. Little is known about the rate of ageing of different organ systems within individuals, which might eventually result in different pattern of diseases. This knowledge is essential to disentangle disease specific traits from ageing specific traits, which eventually defines the counteracting interventions to overcome multimorbidity at older age.

Prerequisite: epidemiological/statistical skills, capacity to work in a multidisciplinary team, fascination for the ageing process.

Project AG10: The intra-individual rate of ageing

Supervisor: Professor Andrea Maier
Project Site: University of Melbourne, RMH, Department of Medicine and Aged Care
Contact: T: + 61 3 9342 2635, E: andrea.maier@mh.org.au

Project description: The ageing process is the underlying cause of most age related diseases in humans. Antagonizing the ageing process prevents the development of age related diseases in model organisms. In humans, the accumulation of DNA damage and senescent cells has been shown to be positively associated with the chronological age as well as biological age, e.g. the rate of aging, of the donors of tissue. Currently, the rate of ageing of different organ / cell systems within individuals is unknown. The aim is to characterize different tissues of the same individual in terms of their senescent load to determine the rate of ageing intra-individually.

Prerequisite: biomedical background and preferable lab skills, basic epidemiological/statistical skills, capacity to work in a multidisciplinary team, passion to unravel the ageing process.

Project AG11: Towards a biological geriatric assessment

Supervisor: Professor Andrea Maier
Project Site: University of Melbourne, RMH, Department of Medicine and Aged Care
Contact: T: + 61 3 9342 2635, E: andrea.maier@mh.org.au

Project description: In current geriatric practice, patients are assessed by use of the comprehensive geriatric assessment (CGA) evaluating the functional, mental and social state of the aged patient using

predominantly subjective, not well defined and badly standardized tools. The consequence is that CGAs are not comparable and that the causal mechanisms of the geriatric condition often remain unidentified. The aim is to refine the CGA and define the biological basis of geriatric conditions to eventually introduce a standardized biological geriatric assessment being predictive for relevant outcomes and sensitive and specific for change over time.

Prerequisite: basic lab skills (preferable), basic epidemiological/statistical skills, capacity to work in a multidisciplinary team, passion to unravel the ageing process, enjoying to work with patients.

Project AG12: The underestimated power of human muscle

Supervisor: Professor Andrea Maier
Project Site: University of Melbourne, RMH, Department of Medicine and Aged Care
Contact: T: + 61 3 9342 2635, E: andrea.maier@mh.org.au

Project description: Muscle is one of the most powerful, but most neglected organs of our human body. Physical inactivity leads to immediate significant decrease in volume and therewith muscle function, whereas recovery of function is hard to accomplish without dedicated intervention. The EMPOWER II study aims to 1. Evaluate the course of muscle mass and function during acute hospitalization and geriatric rehabilitation and 2. Intervene by use of dedicated strength and nutritional interventions during geriatric rehabilitation to increase muscle mass and function. The EMPOWER II study is based on results of the EMPOWER I study conducted in the acute patient setting (papers in press), indicating the urgent need for individualized interventions to preserve physical function in the aged patient.

Prerequisite: conduct epidemiological studies / interventions, epidemiological/statistical skills, good communication skills, capacity to work in a multidisciplinary team.

Project AG13: Refining the comprehensive geriatric assessment

Supervisors: Professor Andrea Maier, A/Prof Kwang Lim
Project Site: University of Melbourne, RMH, Department of Medicine and Aged Care
Contact: T: + 61 3 9342 2635, E: andrea.maier@mh.org.au

Project description: The comprehensive geriatric assessment (CGA) is currently the most important assessment tool of geriatricians to define the functional, mental and social state of geriatric patients, but not well defined. There is an urgent need to refine the CGA to increase the power to predict detrimental outcome and to increase sensitivity and specificity for changes of geriatric conditions over time. From 2013-2015 all patients of a Dutch academic geriatric outpatient clinic were assessed using the same extensive CGA, the dataset is now available for data analysis to define 1. The functional, 2. Mental and 3. Social domain of the CGA. The defined CGA will then be validated in a dataset of Australian geriatric outpatients.

Prerequisite: epidemiological/statistical skills, write journal articles, good communication skills, capacity to work in a multidisciplinary team.

ALLIED HEALTH

Project ALL1: Social and physical activities in ageing women

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki, E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Social engagement is important for the maintenance of physical health and cognitive function, with these outcomes found to be particularly evident in women. However the role of social engagement in age-related cognitive function is not well understood. In this project we will examine the relationship between social and physical activities, and physical and cognitive health from a cross-sectional perspective. The relationship between these variables over time will also be examined.

The key benefits of this project are:

1. It will involve direct hands-on participant evaluation and provide clinical skills experience
2. The opportunity to work with a rich database with data that spans over 20 years already collected
3. The opportunity for publication

ANAESTHESIA AND PERIOPERATIVE MEDICINE

Project ANP1: Can real-time recovery assessment improve quality of recovery after surgery

Supervisors: Prof Colin Royse
Project Site: Melbourne Health
Contact: colin.royse@heartweb.com, 0408467548

Project description: Recovery after surgery is often delayed, incomplete, or of poor quality after surgery. The Postoperative Quality of recovery Scale (PostopQRS) is a tool to measure and score recovery in multiple domains after surgery (see postopqrs.com). Initial research shows that good early recovery is associated with good later recovery, whereas delayed recovery is associated with long term poor quality of recovery. A feature of the PostopQRS tool is the ability to score recovery in real time. This provided the health care providers with real time feedback on recovery, as well as the ability to drill down to identify where the problem is (for example, pain, cognition, emotive, function). This PhD will explore the relationship between early recovery and later outcomes, as well as to investigate whether early intervention to address the problems identified by the PostopQRS can improve longer term recovery.

ANTIMICROBIAL RESISTANCE (AMR) /ANTIMICROBIAL STEWARDSHIP (AMS)

Project AMR1: AMR/AMS in Aged Care Facilities

Supervisors: Dr David Kong, A/Prof Rhonda Stuart, A/Prof Caroline Marshall & Dr Deb Friedman
Project Site: Centre for Medicine Use and Safety, Monash University/NCAS Doherty Institute
Contact: Leslie Dowson leslie.dowson@monash.edu

Project description: This project plans to improve the care of older people with respiratory tract infections. in Australian residential aged care facilities with AMS.

Project AMR2: AMR/AMS in Veterinary Practices

Supervisors: Prof Glenn Browning
Project Site: Faculty of Veterinary and Agricultural Sciences/NCAS Doherty Institute
Contact: Laura Hardefeldt lhardefeldt@student.unimelb.edu.au

Project description: This project will focus on implementing the VetNAPS and investigating means of advancing antimicrobial stewardship in veterinary practices.

Project AMR3: Antimicrobial Stewardship in regional and rural hospitals

Supervisors: A/Prof Kirsty Buising, Dr David Kong, Prof Karin Thursky & Dr Tom Schulz
Project Site: NCAS Doherty Institute
Contact: Jaclyn Baker jaclynb@student.unimelb.edu.au

Project description: This focuses on effective models for Antimicrobial Stewardship in regional and rural hospitals. This aligns with her goals of improving the quality use of medicines and advocating for better health outcomes for people living in rural/regional areas.

Project AMR4: Antimicrobial Stewardship in acute hospitals

Supervisors: Prof Karin Thursky, Dr Trish Peel & Dr Darshini Ayton
Project Site: NCAS Doherty Institute
Contact: Courtney Ierano cierano@student.unimelb.edu.au

Project description: This project will focus on the acute tertiary stream of surgical antimicrobial prophylaxis (SAP), using a mixed methods approach to conceptualise factors contributing to inappropriate SAP rates. It is anticipated that by gaining further insight as to why SAP is inappropriately prescribed, then more specific AMS measures can be developed and implemented to improve this. This aligns with Courtney's goal of advocating for the evolving profession of AMS and improving the quality use of medicines, thus in turn improving patient health outcomes.

Project AMR5: Antimicrobial Stewardship in primary care

Supervisors: Prof Danielle Mazza, Prof Karin Thursky, A/Prof Kirsty Buising
Project Site: Monash University Faculty of General Practice/NCAS Doherty Institute
Contact: Lesley Hawes lesleyah@student.unimelb.edu.au

Project description: TBC

ARTHRITIS AND INFLAMMATION RESEARCH CENTRE

The Arthritis and Inflammation Centre is headed by Professor John Hamilton who leads a team of scientists that focuses on inflammation-associated diseases, including arthritis, host pathogen interaction and cancer. The pathology of most diseases involve some degree of inflammation with macrophages often being the major cell type; as a result the Centre focuses primarily on macrophage biology and the effects of macrophage-associated inflammation on other cell types such as stem cells.

We employ a variety of techniques and strategies including gene-based strategies (for example, micro-array technology) to understand disease causation, protein-based strategies (including proteomics, immunoprecipitation, cell transfection) to study the cellular signal transduction pathways associated with disease, and mouse models and clinical material to analyse disease in vivo.

Key components of the biology involve an analysis of how macrophage lineage cells are altered during inflammatory disease, how at a molecular level these cells survive, proliferate, differentiate or are activated, and how to down-regulate the cellular functions aberrant in disease. There is some emphasis on growth factor biology/biochemistry and on signal transduction pathways implicated strongly in human arthritis, cancer and stem cell biology.

Project AIRC1: Molecular signaling pathways controlling gene expression during chronic disease progression

Supervisors: Dr. Adrian Achuthan and Prof. John Hamilton
Project Site: Department of Medicine (RMH), University of Melbourne
Contact: Dr. Adrian Achuthan T: 8344 3298 E: aaa@unimelb.edu.au

Project description: Inflammation is now known to be associated with many chronic diseases such as cancer, Alzheimer's disease, obesity/type II diabetes and heart disease. 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 may lead to the development of novel therapies.

Techniques: You will acquire a wide-range of skills in cell biology (primary human monocytes/macrophage culture, ELISA assays, confocal microscopy and flow cytometry), and biochemistry and molecular biology (Western blotting, Real-Time PCR and siRNA-mediated gene knock-down).

Project title AIRC2: Elucidating molecular signaling pathways controlled by anti-inflammatory steroids

Supervisors: Dr. Adrian Achuthan and Prof. John Hamilton
Project Site: Department of Medicine (RMH), University of Melbourne
Contact: Dr. Adrian Achuthan T: 8344 3298 E: aaa@unimelb.edu.au

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. In this project you will use genome-wide approaches such as microarray to identify the genes that are regulated by glucocorticoids. More specifically, 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.

Techniques: You will acquire a wide-range of skills in cell biology (primary human monocyte/macrophage culture, ELISA assays, confocal microscopy and flow cytometry), and biochemistry and molecular biology (Western blotting, Real-Time PCR and siRNA-mediated gene knock-down).

Project AIRC3: Investigating the effects of GM-CSF and M-CSF derived human macrophages on phagocytosing *P. falciparum* infected erythrocytes and cytokine production

Supervisors: Dr. Adrian Achuthan and Professor Stephen Rogerson
Project site: Department of Medicine (RMH), University of Melbourne
Contact: Dr. Adrian Achuthan T: 8344-3298 E: aaa@unimelb.edu.au

Project Description: An important way in which the body clears malaria infection is through opsonisation of *P. falciparum*-infected erythrocytes (IE) and phagocytosis by monocytes/macrophages. This process leads to activation of signalling pathway and cytokine production. Current studies utilize human monocytes cultured *in vitro* in the presence of either granulocyte-macrophage colony stimulating factor (GM-CSF) or M-CSF to produce monocyte-derived macrophages (MDMs). Classical activation of monocytes by GM-CSF yields "M1-like" MDMs with a pro-inflammatory cytokine profile while M-CSF

promotes “M2-like” MDMs that produce an anti-inflammatory cytokine repertoire. In this project you will explore the effects of IE phagocytosis by M1-like and M2-like MDMs on cytokine production and trafficking. Furthermore, you will be investigating the expression and function of signalling proteins that govern phagocytosis and cytokine secretion in these two types of MDMs.

Techniques: The project involves a range of molecular and cell biology techniques including culture and purification of *P. falciparum*-infected erythrocytes, isolation and culture of human monocytes/macrophages, qPCR to assess cytokine mRNA, ELISA to measure cytokine secretion and Western blotting and confocal imaging to determine protein expression and localisation.

Project AIRC4: The role of granulocyte macrophage colony stimulating factor (GM-CSF) in arthritis and inflammation

Supervisors: Dr Andrew Cook and Dr. Ming-Chin Lee
Project Site: Arthritis Research and Inflammation Centre, Department of Medicine (RMH),
University of Melbourne
Contact: Dr Andrew Cook T: 8344 3290 E: adcook@unimelb.edu.au

Project Description: Rheumatoid arthritis (RA) is a chronic inflammatory disease affecting approximately 1% of the population. We have shown that GM-CSF is important for the development of several models of inflammation and arthritis. Furthermore, blockade of GM-CSF is effective at reducing arthritis severity. Phase 1 clinical trials are now underway in human rheumatoid arthritis. However, we still do not completely understand how GM-CSF is acting during inflammation and arthritis. In this project you will study the role of GM-CSF in inflammation and arthritis, and in particular, its role in monocyte/macrophage survival and activation.

Skill acquisition: experience with animal models of human disease, measurement of inflammatory mediator mRNAs by real time-PCR and their concentrations by ELISA, and the use of FACS and immunohistochemistry to study cell populations.

Project AIRC5: The role of Interferon Regulatory factors in Arthritis

Supervisors: Dr Andrew Cook, Prof John Hamilton and Dr. Ming-Chin Lee
Project Site: Arthritis Research and Inflammation Centre, Department of Medicine (RMH),
University of Melbourne
Contact: Dr Andrew Cook T: 8344 3290 E: adcook@unimelb.edu.au

Project Description: Macrophages are key cells involved in the destruction of joints during rheumatoid arthritis. In this project you will investigate how the transcription factors, called interferon regulatory factors (IRFs), control gene expression in macrophages during inflammatory models of arthritis. You will also determine if targeting IRFs would be a beneficial treatment for arthritis.

You will be cutting tissue sections and measuring the expression of these novel proteins. You will be inducing murine models of arthritis, measuring a number of clinical parameters, collecting and processing tissue, and measuring gene/protein expression by histology, real-time PCR, Western blotting and FACS analysis. You will also be using siRNA, and nanoparticles to deliver therapeutic drugs in the arthritis models.

Skill acquisition: a variety of molecular and cell biological, and biochemical techniques, such as PCR and cloning of recombinant DNA; tissue culture, and FACS analysis, SDS-PAGE and Western blotting.

Project AIRC6: The role of a novel macrophage inflammatory mediator in arthritis

Supervisors: Dr Andrew Cook, Prof John Hamilton and Dr. Ming-Chin Lee
Project Site: Arthritis Research and Inflammation Centre, Department of Medicine (RMH) ,
University of Melbourne
Contact: Dr Andrew Cook T: 8344 3290 E: adcook@unimelb.edu.au

Project Description: Through a microarray screen of inflammatory macrophages we have identified a novel potential therapeutic target for the treatment of arthritis. Macrophages are key cells involved in the destruction of joints during rheumatoid arthritis. In this project you will investigate the expression of this potential therapeutic target in patients' tissue samples and in an inflammatory model of arthritis, and determine if targeting this protein would be a beneficial treatment. In this project you will be cutting tissue sections and measuring the expression of this novel protein. You will be inducing a murine model of arthritis and measuring a number of clinical parameters, collecting and processing tissue, and measuring gene/protein expression by histology, real-time PCR, Western blotting and FACS analysis. You will also be using siRNA, and nanoparticles to deliver therapeutic drugs in the arthritis model.

Skill acquisition: a variety of molecular and cell biological, and biochemical techniques, such as PCR and cloning of recombinant DNA; tissue culture, and FACS analysis, SDS-PAGE and Western blotting.

AUTISM

Project AU1: Understanding gastrointestinal dysfunction in autism – how do synaptic mutations affect enteric neurons?

Supervisors: Dr Elisa Hill, Prof Joel Bornstein, Prof Terence O'Brien
Project Site: Department of Medicine & Department of Physiology, University of Melbourne
Contact: Dr Elisa Hill: elhill@unimelb.edu.au

Project description: Gastrointestinal disorders are common in patients with autism, but the biological mechanisms responsible are unknown. Many gene mutations identified in autism patients alter neuronal development and function, and studies in genetic mouse models show altered neural activity in the brain. Our recent studies show that mice carrying a mutation in a synaptic protein found in some autism patients have disordered gastrointestinal movements due to a change within the enteric nervous system.

In this project, you will use video-imaging of motility, immunohistochemistry, molecular and electrophysiological methods to determine how synaptic proteins in the enteric nervous system are modified in these mice and how this affects the neural circuits that control colonic motility.

BIOLOGY —WOMEN'S HEALTH

Project BWH1: Understanding parental support for daughters with significant menstrual health problems

Supervisors: Dr Jane Girling, Dr Yasmin Jaysinghe
Project Site: Department of Obstetrics and Gynaecology, Royal Women's Hospital
Contact: Dr Jane Girling (jgirling@unimelb.edu.au), Yasmin Jaysinghe
(Yasmin.Jayasinghe@thewomens.org.au)

Project description: Menstrual pain not only impacts on the individual girl/woman, but also on her family. Conversely, the attitudes of the family towards menstrual pain may have a significant impact on how the girl/women views, understands and manages her symptoms. Currently, there is no literature

available that considers the father's perspective of menstrual problems. Information on the father's perspective may help identify specific areas where education may help a father support and advocate for his daughter.

We have recently conducted a study examining the understanding, involvement and attitudes of fathers towards their daughter's menstrual health concerns in a cohort of parents with daughters attending a tertiary hospital for menstrual complaints. These preliminary studies have highlighted the limited knowledge of fathers about potential problematic symptoms associated with menstruation and a concerning lack of understanding of both mothers and fathers about possible long-term consequences of menstrual problems and the medications associated with their treatment. These observations were concerning as they suggest parents lack sufficient information to provide informed consent for daughters dealing with significant menstrual health issues. Studies are being developed that will further explore the role and understanding of parents in regards to menstrual health issues with the aim of developing appropriate education tools suitable for mothers, fathers and their daughters.

Project BWH2: Investigation of genes associated with increased risk of endometriosis

Supervisors: Prof Peter Rogers, Dr Jane Girling, Dr Sarah Holdsworth-Carson, Dr Premila Paiva
Project Site: Department of Obstetrics and Gynaecology, Royal Women's Hospital
Contact: Prof Peter Rogers (parogers@unimelb.edu.au), Dr Jane Girling
E: jgirling@unimelb.edu.au

Project description: Endometriosis is a disease where endometrial tissue grows outside of the uterus, most commonly on the organs and tissues of the peritoneal cavity. It is a horrible disease that significantly reduces quality of life in up to 10% of women through chronic pelvic pain and infertility. There is no permanent cure and current treatment options are inadequate. There is a desperate need to understand the mechanisms responsible for this disease and for the development of diagnostic tools, prevention strategies and improved treatment options (precision medicine).

Endometriosis is a complex disease with a genetic basis. Recent genome wide association studies have identified several candidate genes linked to the risk of endometriosis. We are now working on a 4-year NHMRC-funded project that aims to examine the function of these genes in uterine tissues with the aim of determining how candidate genes and gene pathways may contribute to endometriosis pathophysiology. Potential projects will be based on information derived from our database and associated tissues from over 600 women that includes comprehensive clinical, quality of life, symptom, molecular and genetic information; our database is currently of the largest of its type in the world. Projects will largely be laboratory based with the potential to interact with expert clinicians and undertake questionnaire based studies.

BRAIN BIONICS

Project BB1: Brain Machine Interface – MRI Compatibility and Electrochemical Safety of a novel Brain Machine Interface.

Supervisors: Nicholas Opie, Sam John, Thomas Oxley
Project Site: Department of Medicine, Royal Melbourne Hospital
Contact: Nicholas Opie, T: 0438 089 306; E: Nicholas.opie@unimelb.edu.au

Project description: Our team has developed a stent-based brain machine interface that is capable of recording neural information without requiring invasive open brain surgery. We aim to implant in a first-in-human trial in 2018 and demonstrate the capability of our device to enable direct brain control of an

exoskeleton by a person with paralysis. This project will develop and conduct experiments to evaluate whether it is safe for patients implanted with our device to undergo MRI scans. Further, this project will evaluate electrochemical properties of the device, identifying and quantifying any degradation products caused through chronic implantation and material dissolution.

Project BB2: Brain Machine Interface – Biological Evaluation of a novel Brain Machine interface.

Supervisors: Nicholas Opie, Sam John, Thomas Oxley
Project Site: Department of Medicine, Royal Melbourne Hospital
Contact: Nicholas Opie, T: 0438 089 306; E: Nicholas.opie@unimelb.edu.au

Project description: Our team has developed a stent-based brain machine interface that is capable of recording neural information without requiring invasive open brain surgery. We aim to implant in a first-in-human trial in 2018 and demonstrate the capability of our device to enable direct brain control of an exoskeleton by a person with paralysis. The aim of this study is to histopathological evaluate the safety of chronically implanted neurovascular interface compared to subdural and epidural devices. Histopathological assessment will evaluate device encapsulation, foreign body response including inflammation as well as bacterial or fungal infections.

Project BB3: Brain Machine Interface – Evaluating feasibility of an Endovascular Brain Machine Interface for volitional control

Supervisors: Sam John, Nicholas Opie, Thomas Oxley
Project Site: Department of Medicine, Royal Melbourne Hospital
Contact: Sam John, T: 0433 030 540; E: sam.john@unimelb.edu.au

Project description: Our team has developed a stent-based brain machine interface that is capable of recording neural information without requiring invasive open brain surgery. We aim to implant in a first-in-human trial in 2018 and demonstrate the capability of our device to enable direct brain control of an exoskeleton by a person with paralysis. The aim of this study is to evaluate the feasibility of an endovascular brain machine interface by enabling volitional control in an animal model. The project will involve decoding neural signals obtained from an endovascular array to achieve volitional control.

CANCER

Project CAN1: Priorities and needs of women living with advanced cancer

Supervisors: Dr Jennifer Marino and Dr Michelle Peate
Project Site: The Royal Women's Hospital
Contact: jennifer.marino@unimelb.edu.au

Project description: Although the survival of patients with cancer has improved greatly over the past 30 years, between 2008 and 2012, a third of all patients with cancer survived less than five years. Generally, cancer research tends to focus on curative therapy, but many patients die of their cancer. These patients, not only have to cope with facing an incurable condition, but are often 'forgotten' or become 'invisible' in the context of this focus on survivorship outcomes. Many people who live with advanced cancer report a feeling of being seen negatively by society, and that they suffer from psychological, physical or financial problems for which they receive little support. Despite this, we know very little about the needs and priorities of people living with advanced cancer. This information is essential to inform clinical decision-making to maximise the quality of the life these patients have left – for some this is only a short time yet others will live with their cancer for many years. To aim of this project is to gather qualitative and quantitative data from advanced cancer patients, their families, and their providers to identify their needs, with the eventual goal of establishing clinical tools, including patient-reported outcome measures

and useful tools that can improve the end-of-life experience of these patients and their families.

Benefits to student: This is a multi-collaborative project, so student will gain experience working in a multidisciplinary team. They will also have the opportunity to learn develop qualitative and/or quantitative research skills, gain an understanding of ethical procedures, be trained in high quality data management, collection and analysis processes.

Requirements for students: Looking for a dedicated, passionate, sensitive and committed student with a good academic record and strong writing and communication skills.

Project CAN2: Integrated Genomics of metastatic, lethal Prostate Cancer

Supervisors: A/Prof Chris Hovens and Dr Niall Corcoran
Project Site: Department of Surgery (RMH), 5th Floor, Clinical Sciences Building and Prostate Cancer Epworth Hospital, Richmond
Contact: A/Prof Chris Hovens T: 9342 7703/4 E: cbhovens@gmail.com

Project description: With over 20,000 diagnoses per year, Australian men have the highest rate of prostate cancer in the world. Currently our research team are addressing some of the most important clinical questions today in prostate cancer management using genomics and proteomics experimental designs. We have access to human tissue samples taken from men undergoing surgery together with the clinical informatics that indicate their outcomes, therefore this project will have high clinical relevance and impact.

The aim of the project is to delve deeper into our analyses of the genomics of prostate cancers from patients who have either died or who have metastatic disease. We have identified a number of candidate regions and changes that may be key to driving prostate cancer metastasis and subsequent lethality. Projects will focus on validating these findings in independent cohorts of patients and starting to examine experimentally the biology behind the observed changes and how they impact on tumor behaviour. Research students will work within a team of experienced scientists and have access to scientific expertise and equipment through our department, associated institutions and existing collaborations with leading urologists. Our commitment to academic excellence and links with the Australasian Prostate Cancer Conference, one of the largest urology meetings in the region, ensure additional exposure to publication and presentation opportunities for the motivated researcher.

Benefits to student: Molecular and clinical research in the one, multi-collaborative project encompassing basic research and clinical interaction.

Requirements for students: Dedicated, passionate and committed.

Project CAN3: Double Jeopardy – dead prostate cancer cells can't recur

Supervisors: A/Prof Chris Hovens, Dr Michael Clarkson
Project Site: Department of Surgery (RMH), 5th Floor, Clinical Sciences Building
Contact: Dr Michael Clarkson E: mclarkson@unimelb.edu.au

Background/Rationale: The critical role of androgen (testosterone) signalling in Prostate cancer (CaP) is unequivocally supported by the fact that this cancer can be effectively treated by surgical castration or drugs that disrupt androgen action or production. While androgen deprivation therapy (ADT) provides significant respite from prostate cancer progression, treatment resistant tumors recur with high frequency and are generally associated with poor outcome. We hypothesise that cells are initially rendered "dormant" by ADT and in this state they accumulate mutations that allow them to escape from

growth suspension to recommence proliferation. Our recent results, and some published studies, indicate that this dormant state might render cells more sensitive to killing by other agents. If this is true then ADT in combination with a complementary drug has the potential to substantially improve patient treatment and outcome by killing prostate cancer cells rather than just rendering them dormant.

Project Description: We have established cell lines that contain a newly developed marker for programmed cell death (apoptosis) that turns fluorescent red when the cell death program is initiated. We will use this line to screen a library of drugs for their ability to induce cell death in combination with ADT. Our studies with patient derived samples has also provided some clues about what pathways would be best to target. We will prioritise these pathways. In addition to cell based studies we are using an ex vivo system that allows us to culture patient tissue samples, treat them with drugs and examine response.

Skills/Techniques: Advanced cell biology techniques, high throughput semi-automated drug screening, high throughput microscopy and analysis (Operetta system), ex vivo tissue culture, immunohistochemistry, qRTPCR, western blotting.

Benefits to student: Molecular and clinical research in the one, multi-collaborative project encompassing basic research and clinical interaction.

Requirements for students: Dedicated, passionate and committed.

Project CAN4: Regulation of invadopodium function and involvement in cancer cell invasion

Supervisor/s: Dr Stanley Stylli
Project Site: Dept of Surgery, Level 5, Clinical Sciences Building, The Royal Melbourne Hospital
Contact: Dr Stanley Stylli; T: 9035 5236, E: sstylli@unimelb.edu.au

Project description: The cause of death for up to 90% of cancer patients is the metastatic spread of cancer cells from the primary tumour and the subsequent development of a secondary tumour or tumours at a distant site. Many patients normally present with symptoms relating to the localized primary disease which can be managed with a number of therapies including surgery, radiation and chemotherapy. But numerous patients return post-therapy with a developed metastatic lesion at a secondary site. The dissemination of metastatic cells involving the migration and infiltration of these invasive cells is commonly thought to require two events. This includes increased cellular motility, accompanied with the proteolytic processing of the extracellular matrix (ECM) and subsequent penetration through the surrounding tissues.

A property shared by several types of tumour cells with high invasive or metastatic potential is an ability to form structures known as invadopodia. They are dynamic actin-rich protrusions which adhere to and proteolytically degrade ECM substrates via the activities of secreted extracellular proteases. Functional (matrix-degrading) invadopodia have been observed in tumour cell lines and primary tumour cells derived from ex vivo tumour specimens from a number of cancers, primarily head and neck squamous cell carcinoma and breast cancer specimens. This suggests that there is a possible role for invadopodia in tumour cell invasion of many cancers.

Invadopodia formation and function are dependent on multiple proteins and signaling pathways. Therefore understanding how invadopodia are regulated and controlled within a tumour cell is essential and strategies aimed at disrupting invadopodia could form the basis of novel anti-invasive therapies for treating cancer patients in the future. This honours project will involve studies that explore the role of a number of invadopodia proteins in cancer cells, how they contribute to their invasive/metastatic phenotype and ultimately influence response to treatment protocols.

Skills/Techniques acquired: Cell Biology techniques including cell culture and cell transfections (overexpression and siRNA gene silencing), western blotting, zymography, immunofluorescence and immunohistochemistry, confocal microscopy, migration/invasion assays, reporter assays.

CARDIOVASCULAR

Project CAR1: Lipoproteins and Cardiovascular Risk from Mid- to Late-life in Women

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki; E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Cardiovascular disease (CVD) remains as the number 1 cause of death worldwide and in Australia. Though elderly women have higher rates of cardiovascular disease compared to men, there is a lack of awareness and research of CVD amongst women. Whilst cholesterol is targeted lipid medication, we now know that statins do not have the benefit in women that was seen in men (Virani, 2013). In this study we explore the broader lipid profile and other lipid measurements and their relation to cardiovascular risk as measured by a risk score (non-lipid based Framingham 10-year CVD risk score). This study seeks to evaluate the relationship between all lipoproteins and cardiovascular risk as characterised by a risk score, in an Australian cohort of older women across 20 years.

This project will provide the opportunity to work with a rich database with data that spans over 20 years, as well as having participant contact and clinical skills experience. This project would suit a candidate who is interested in cardiovascular disease. There is also opportunity for publication.

Project CAR2: The Relationship of Physical Activity, Body Composition and Cardiovascular Risks in Older Women

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki, E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Physical inactivity and high BMI are major risk factors impacting cardiovascular diseases, particularly in women. There is a paucity in longitudinal research into the interactions between exercise and BMI that could lead to high cardiovascular risks (CVRs) in women. The aims of this study are to investigate the impact of exercise exposures on BMI and CVR, and to examine the causality between these factors in aged Australian women.

Major benefits from this study are:
The study has data over 20 years already collected
You will work directly with participants
There is opportunity for a publication

COLORECTAL MEDICINE AND GENETICS

Project CMG1: Regulation of Stem Cell Dynamics by Phlda1 in the Normal Intestinal Epithelium and Cancer

Supervisors: A/Prof Oliver Sieber, Dr Anuratha Sakthianandeswaren
Project Site: Systems Biology and Personalised Medicine Division
Contact: A/Prof Oliver Sieber; sieber.o@wehi.edu.au

Project description: Intestinal stem cells (ISCs) produce all epithelial cell lineages of the human intestine and are the cells-of-origin of intestinal cancer. Major pathways required for ISC maintenance have been identified, but regulation of stem cell dynamics remains poorly understood. We have discovered Phlda1 as an ISC marker, and have shown that Phlda1 suppression inhibits intestinal tumour growth (Sakthianandeswaren et al, Cancer Research, 2010 71(10):3709). This project will utilize a newly developed model system to investigate the role of Phlda1 in normal and cancer stem cell dynamics. Cell biology studies will identify the pathways that mediate Phlda1 functions, and analyses of patient tumour specimens will elucidate clinical relevance. These studies will provide important insights into fundamental stem cell biology of the normal intestinal epithelium and human cancer.

Project CMG2: Serrated Polyposis Syndrome

Supervisors: Professor Finlay Macrae
Project Site: The Royal Melbourne Hospital
Contact: E: finlay.macrae@mh.org.au

Project description: Serrated polyposis syndrome is the last polyposis syndrome without a known genetic predisposition identified. Working with Dr Dan Buchanan in the Dept of Pathology, this project will be the clinical arm of phenotype data collection from the records of the Familial Cancer Clinic which will form the basis for the selection of cases for next gen whole genome sequencing in Dan's lab in the Dept of Pathology.

Project CMG3: Prospective studies on penetrance for cancer in Lynch Syndrome

Supervisors: Professor Finlay Macrae
Project Site: The Royal Melbourne Hospital
Contact: E: finlay.macrae@mh.org.au

Project description: Well-designed studies on prospectively collected data for studying penetrance, survival and treatment effects of cancers occurring in Lynch Syndrome are scarce. This project will collaborate with European investigators on a common design template to provide important data to guide clinical practice. Two consortia are already formed with whom the candidate will collaborate: the International Mismatch Repair Consortium (leads Robert Hale, Stanford, Mark Jenkins and Finlay Macrae (Melbourne) and Gabriela Moeslein (Dusseldorf, Germany); and the Majorca Group (lead Pal Moller, Norway)

Project CMG4: CAPP3: a randomized controlled trial of aspirin dosage in Lynch Syndrome

Supervisors: Professor Finlay Macrae
Project Site: The Royal Melbourne Hospital
Contact: E: finlay.macrae@mh.org.au

Project description: CAPP2 proved aspirin reduces the incidence of LS associated cancers by over 50%. CAPP3 is a dose finding RCT testing 100mg vs 300mg vs 600mg. This is an international study lead from Newcastle UK, with Australian leadership from RMH. Students will learn about multi centre, multinational RCTs, be immersed in aspirin science and cancer genetics, and participate in the clinical aspects of management of Lynch Syndrome.

Project CMG5: PillCam Colon and IBD

Supervisors: Professor Finlay Macrae
Project Site: The Royal Melbourne Hospital
Contact: E: finlay.macrae@mh.org.au

Project description: THE Royal Melbourne Hospital has the only substantial experience of PillCam colon use in Australia. This “camera in a pill” technology is now available for imaging the whole gastrointestinal tract. Research students have provided the most extensive experience with the technology in assessing mucosal healing in Crohn’s Disease. Further studies are available refining bowel preparation for the procedure, conducting interobserver studies, and comparing any changes in clinical management as a result of the information provided by the capsule.

Project CMG6: Locus Specific Databases in Hamartomatous polyposis syndromes

Supervisors: Professor Finlay Macrae
Project Site: Department of Colorectal Medicine & Genetics, Royal Melbourne Hospital
Contact: Professor Finlay Macrae E: Finlay.macrae@mh.org.au

Project description: Hamartomatous polyposis syndromes include : Peutz Jeghers Syndrome (gene locus STK11), Juvenile Polyposis (gene loci SMAD4 & BMPR1A, Cowden’s Syndrome (gene locus PTEN). Diagnostic laboratories around the world identify in the gene loci, sometimes clearly pathogenic, other times uncertain. International centralisation of gene variant information with clinical and familial information is one of the best ways to progress the interpretation of variants of uncertain significance. The Human Variome Project, at the University of Melbourne, aims to document variation in all genes across all countries in the world. The Hamartomatous Polyposis Syndrome project will relate to the HVP. The International Society for Gastrointestinal Hereditary Tumours (InSiGHT) hosts LSDB’s for genes responsible for inherited gastrointestinal cancers. The InSiGHT mismatch repair gene database is curated at the HVP and Department of Colorectal Medicine and Genetics at The Royal Melbourne Hospital. The Hamartomatous Polyposis LSDB Project will develop similar database, ascertaining variant and clinical data across the published literature, contacting the InSiGHT membership for unpublished information and assembling the data on a LOVD platform. The project will involve extensive international collaboration, understanding genetic variation and variants of uncertain significance, bioinformatics and clinical management of these syndromes.

Project CMG7: The Structure and Functions of an Inflammatory Bowel Disease Service

Supervisors: Professor Finlay Macrae
Project Site: Department of Colorectal Medicine & Genetics, Royal Melbourne Hospital
Contact: Profess Finlay Macrae E: Finlay.macrae@mh.org.au

Project description: This project will assist the IBD Service and the IBD Nurse Consultant to refine the structure required for the Inflammatory Bowel Disease Service through:

Development of clinical guidelines to manage well defined IBD Clinical management issues (eg. acute colitis)/ Integration with the new Pharmaco-genetics Service at The Royal Melbourne Hospital (ie. TPMT genotyping). Thiopurine metabolite testing. Transition arrangements of IBD patients from paediatric to adult care. Bone density monitoring and intervention. “Off label” use of anti TNF therapies eg. in ulcerative colitis. The Royal Melbourne Hospital IBD Database. The functions of one of several of these will be tested through “before and after” assessment, where appropriate and audits and /or surveys.

The project will provide an outstanding opportunity for clinical engagement in a busy IBD Service, collaboration with other Australian IBD services, understanding of the evolving role of IBD Nurse Practitioners in IBD care, endoscopy in IBD, and interaction of the clinical IBD service with a range of clinical research projects (microbiota pharma trials).

Project CMG8: C-reactive protein (CRP) and Crohn's disease – CRP as a potential phenotypic marker for disease

Supervisors: Dr Suresh Sivanesan, Prof. Finlay Macrae
Project site: Royal Melbourne Hospital, Parkville
Contact: Dr Suresh Sivanesan T: 03-84179900 or 03-93427584
E: suresh.sivanesan@mh.org.au

Project description: Crohn's disease is a chronic inflammatory condition which can affect any part of the gastro-intestinal tract to cause significant symptoms and morbidity. The condition can affect and segment of the gastrointestinal tract including the perianal region. It can develop into more complex disease resulting in abscesses, luminal strictures, fistulas and perforation. Clinicians have sought to classify Crohn's disease in terms of the disease distribution or complications that it has caused. The currently used classifications are helpful but they do not assist in reliably predicting appropriate treatment or outcomes.

CRP is a serum inflammatory protein that is commonly elevated in conditions such as rheumatoid arthritis, infection and Crohn's disease. It is produced by hepatocytes and is upregulated by cytokines IL-6, IL1 β and TNF α . It has been described that not all patients with Crohn's disease exhibit a rise in CRP. We hypothesize that if there are a subgroup of patients with active Crohn's disease and a express a normal serum CRP.

We intend to study our cohort of patients with active Crohn's disease to determine their levels of CRP, disease phenotype and assess their response to treatment. In particular if the hypothesis is true, we would hope to extend this work in the future to include cytokine and genotypic profiling of these patients.

This work could open the door toward a better understanding of Crohn's disease using widely available tools such as CRP. In future identifying subgroups of patients with Crohn's disease based on cytokine and genetic profiling will enable a more tailored approach to patient care.

ENDOCRINOLOGY

Project ENDO1: Sex Hormones and Cardiovascular Disease in Postmenopausal Women

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki, E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Cardiovascular disease is currently the leading cause of death in Australia, and around the world. Post-menopausal women are particularly at risk of developing cardiovascular disease, thought to be due to the change of circulating sex hormone levels such as estradiol. However results are conflicting with latest evidence indicating the time of exposure is most relevant. This study aims to test the association of these sex hormones with cardiovascular disease risk over 20 years from pre-menopause to post-menopause, to determine whether sex hormone levels over time play a significant part in cardiovascular health.

You will also have the opportunity to work with a large database from an internationally recognised cohort that spans over 20 years. This project will provide opportunity for publication and to work directly with participants. Candidates who are interested in endocrinology, as well as industry relationships, would be suited to this project.

EPILEPSY AND NEUROPHARMACOLOGY

Project EPN1: Investigating molecular and physiological determinants of Sudden Unexplained Death in Epilepsy in acquired and genetic animal models of epilepsy and in epileptic patients.

Supervisors: Dr. Kim Powell, Dr Pablo Casillas-Espinosa and Prof. Terry O'Brien
Project Site: Department of Medicine (RMH), MBC Neurosciences Building, Parkville
Contacts: Dr Kim Powell T: 9035 6394 E: kpowell@unimelb.edu.au

Project Description: People with epilepsy are at a higher risk of death than the general population. People with epilepsy may die suddenly without an obvious pathologic cause for death. Such deaths are termed Sudden Unexpected Death in Epilepsy (SUDEP), and this is the major clinical problem facing epilepsy patients, accounting for 17-38% of all epilepsy related deaths. Basic research investigating the causal mechanisms underlying SUDEP is lacking. Alterations in function or expression of ion channels expressed in both cerebral and cardiac tissue represent strong candidate mechanisms for SUDEP - defects in membrane excitability could predispose an individual to a dual phenotype of epilepsy and cardiac arrhythmia. In both a genetic and an acquired animal model of epilepsy we have identified altered cardiac electrophysiological function with an associated down-regulation of the cardiac pacemaker HCN2 channel. Based on this data We have hypothesised that the development of epilepsy itself can result in secondary changes in cardiac ion channel expression and function that could contribute to an increased risk of cardiac arrhythmias and therefore SUDEP.

Ion channels that coexist in the brain and heart would make ideal candidates for SUDEP because defects in intrinsic membrane excitability could predispose an individual to a dual phenotype of epilepsy and cardiac arrhythmias culminating in sudden death. Hyperpolarization-activated cyclic nucleotide-gated (HCN) channels and T-type calcium channels play an important role in the generation of pacemaker activity in the brain and heart. Furthermore, its functional role becomes more marked in the process of pathological cardiac hypertrophy and heart failure. Thus HCN and T-type calcium channels are attractive candidates for investigating molecular mechanisms of SUDEP. Our research has identified a cardiac transcriptional channelopathy of HCN2 and $Ca_v3.1$ and $Ca_v3.2$ T-type calcium channels, with associated detrimental cardiac electrophysiological changes, in rat models of both genetic generalised epilepsy (GAERS) and acquired temporal lobe epilepsy (kainic acid (KA) induced post-status epilepticus (SE)).

Aims

1. To investigate the molecular mechanisms contributing to the cardiac dysfunction on genetic and acquired animal models of epilepsy.
2. To investigate whether patients with chronic epilepsy have alterations in cardiac electrophysiology and ion channel expression compared to matched non-epileptic control subjects.
3. To investigate if decreased HCN2 expression translates to a decrease in HCN channel current (*I_f*) in cardiomyocytes in animal models of genetic and acquired epilepsy.
4. To investigate if by pharmacologically suppressing seizures we can alleviate the altered cardiac electrophysiological function and HCN2 and T-type calcium channel transcriptional repression
5. To investigate cardiac structure and function in genetic and acquired animal models of epilepsy.

Skills: The skills expected to be learnt from this project include: Small animal handling and surgery, Drug testing in animal models of epilepsy, electrophysiology recordings and analysis, biochemical and molecular analysis (real time PCR, western blotting).

GASTROENTEROLOGY

Project GAS1: Barrett's Oesophagus

Supervisors: Professor Finlay Macrae and Dr Andrew Metz
Project Site: The Royal Melbourne Hospital
Contact: E: Finlay.macrae@mh.org.au

Project description: Barrett's oesophagus is a premalignant condition which is challenging to manage. Detection of dysplasia is difficult but new advanced imaging modalities are assisting, and new treatments such as radio frequency ablation are allowing the condition to be treated without surgical resection. This project will evaluate new imaging and treatment modalities. It will involve close engagement with the Barrett's clinical service.

GENETICS AND GENOMICS

Project GEN1: New therapies for inherited renal disease – chaperones, stem cells and other agents

Supervisors: Prof Judy Savige, Dr Dongmao Wang
Project Site: University Department of Medicine, Royal Melbourne Hospital
Contact: Prof Savige on + 613 8344 3260 or jasavige@unimelb.edu.au

Project description: Alport syndrome is an inherited renal disease that results in end-stage renal failure, hearing loss, and ocular abnormalities. Forty % of cases are due to missense and 40% to nonsense mutations. The aim of this study is to investigate treatments that can be used for these types of different mutations, using cell lines derived from patients. The aim is to derive the optimum dose, and to understand the mechanisms by which these agents have their effect. They will then be used in a pilot study in patient to determine the effect on the rate of deterioration in renal function.

Project GEN2: Understanding the genetic changes that contribute to neurological disorders.

Supervisors: Slavé Petrovski and David Balding
Project Site: Department of Medicine RMH, Kenneth Myer Bldg
Contact: Slave Petrovski E: slavep@unimelb.edu.au

Project description: The human genetics community has made important advances in identifying genes that contribute to disease risk. However, it remains the case that interpreting the roles of individual variant(s) within genes can be difficult. The major goal of this project is to develop and refine tools to accurately classify risk alleles in established disease genes. We will make use of many sources of information in order to achieve a holistic evaluation of the risk of novel variants in established epilepsy genes. These include population genetic analyses of normal genetic variation, predictions of function based on physical and chemical properties of the variant in its context, assessments of phylogenetic conservation across species, and for some genes we will also use experimental read-outs of patient and background variation generated by colleagues working in the wet-lab environment.

Skill Development: This project is suitable for candidates interested in furthering their bioinformatics / biostatistics experience. Candidates undertaking this project will also gain experience in study design, data managements, data analysis, data interpretation and scientific reporting.

Project GEN3: Using bioinformatics approaches to unravel the SCN2A neuro-spectrum.

Supervisors: Slavé Petrovski and Steven Petrou
Project Site: Department of Medicine RMH, Kenneth Myer Bldg
Contact: Slave Petrovski E: slavep@unimelb.edu.au

Project description: Mutations in *SCN2A* have emerged as relatively common causes for epilepsy, autism, intellectual disability and even schizophrenia. These represent clinically distinct conditions that often share a very high comorbidity. There are few examples of genes where a given mutation may cause one or a combination of these disorders and it represents a fascinating opportunity to better characterize what properties of *SCN2A* might result in various clinical presentations. This project will take the bioinformatics lead on the search for patterns of genetic variation linking mutations to the various clinical conditions and will work closely with the Petrou lab that are actively pursuing functional characterization of *SCN2A* patient and population variants.

Skill Development: This project is suitable for candidates interested in furthering their bioinformatics / biostatistics experience. Candidates undertaking this project will also gain experience in study design, data managements, data analysis, data interpretation and scientific reporting.

Project GEN4: Comparing the importance of genes across species.

Supervisors: Slavé Petrovski and David Balding
Project Site: Department of Medicine RMH, Kenneth Myer Bldg
Contact: Slave Petrovski E: slavep@unimelb.edu.au

Project description: This is a population genetics project that will leverage two collections of information. Much excitement has emerged from our recent ability to quantify with good resolution the human-specific constraint (also called “intolerance”) of human genes. We will use a collection of human gene intolerance metrics and compare them to traditional metrics of phylogenetic conservation. The goal of this study is to use standing human genetic variation from large population studies to identify genes in which the selective pressures among modern humans differs from that estimated from cross-species comparisons (considering vertebrate, mammalian and primate species). That would indicate a recent change in the role of selection that could highlight genes of functional importance in human development and disease. This project has the potential to gain insight into human adaptations, but also may facilitate predictions of which human disease genes are more likely to be amenable to animal modelling of human disease.

Skill Development: This project is suitable for candidates interested in furthering their bioinformatics / biostatistics experience. Candidates undertaking this project will also gain experience in study design, data managements, data analysis, data interpretation and scientific reporting.

GLOBAL HEALTH

Project GLOB1: Global gastroenterology

Supervisors: Professor Finlay Macrae; Assoc Pro Jioji Malani
Project Site: The Royal Melbourne Hospital and Fiji National University
Contact: E: finlay.macrae@mh.org.au

Project description: In 2016, the Australian and New Zealand Gastroenterology International Training Association is supporting an honours student from Melbourne University to document the burden of pancreatico-biliary disease in Fiji Islands, with a view to justifying training in biliary endoscopy and later,

introduction of a biliary endoscopy service in Fiji (ERCP). Opportunities to study biliary disease in other South Pacific countries are emerging and there is a need to document the work of ANZGITA in capacity building in gastroenterology in Fiji and elsewhere in the Pacific. This project will attract Honours students interested in Global Health.

IMAGING

Project IMG1: Development of novel neuroimaging biomarkers in Neurological diseases

Supervisors: Professor Patricia Desmond, Dr.Chris Steward,Dr.Tie-Qiang Li, Dr.Vijay Venkatraman
Project Site: The Brain Imaging Laboratory, Department of Medicine and Radiology, Level 2, 1B building, Royal Melbourne Hospital.
Contact: Prof. Patricia Desmond E: Patricia.Desmond@mh.org.au

Project description: There is presently a paradigm shift in the way in which patients with neurological diseases (such as Brain Tumours, Stroke and Epilepsy and Dementia) are treated. Old methods are being replaced by individualised patient management protocols using spatially, molecularly and genetically targeted therapies. Similarly, there is also currently a paradigm shift occurring in the field of Neuroimaging. Imaging Biomarkers are being developed to image biological, molecular and functional targets of interest to neuroscientists and clinicians. With this in mind The Brain Imaging Laboratory is currently works closely with clinicians to better understand and predict patient disease and response to treatment. Imaging techniques being studied are : Structural imaging, Functional Diffusion Mapping, Diffusion Tensor Imaging, Magnetic Resonance Spectroscopy and Perfusion MRI, functional MRI.

Project IMG2: Early detection of age associated diseases using imaging

Supervisors: Professor Patricia Desmond & A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki; E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Australia's population is ageing at a dramatic rate with about two million people aged over 70 years at present. Studies have identified cardiovascular diseases to be the most prevalent chronic disease in the elderly, followed by cognitive impairment. Identifying the at-risk population for these illnesses is an important step towards developing treatment and prevention strategies. An aim of this study is to examine emerging measures for identifying early at risk populations in an epidemiologically sampled cohort of women. These measures include the use of Magnetic Resonance Imaging (MRI) neuroimaging quantifying the accrual of white matter hyperintensities (WMH) as a measure of cerebrovascular disease (CVD). It has been found that white matter hyperintensity volume could predict 1-year cognitive decline, and therefore should be considered as a variable of interest in AD trials. This study will examine the two to ten year predictive capacity of baseline MRI.

Major benefits from this study are:

The study has data over 20 years already collected

There is opportunity for a publication

This project will suit a candidate with an interest in neuroimaging

INFECTIOUS DISEASES AND IMMIGRANT HEALTH

Project INF1: Monitoring the efficacy of a training program in gastroenterology in the Pacific

Supervisors: Professor Finlay Macrae
Project Site: Department of Colorectal Medicine and Genetics, The Royal Melbourne Hospital
Contact: Professor Finlay Macrae T: +61 3 9347 0788 E: finlay.macrae@mh.org.au

Project Description: Diseases in the GI tract are common in the South Pacific. GI Endoscopy access is limited, and training even less available. In association with the World Gastroenterology Organization, we have recently introduced a training program in gastroenterology to support postgraduate training in gastroenterology at the Fiji School of Medicine, with expertise provided from Australia. The project is designed to monitor the effects of this across the South Pacific, through documentation of higher levels of service delivery in the region, epidemiology of disease detection (eg helicobacter pylori) and skills' acquisition by graduates of the program that can be applied in remote communities in the South Pacific with high GI disease burdens.

The applicant would be required to visit South Pacific regions to assess qualitatively and quantitatively, disease burdens and the provision of services to address these needs, with a view to reports for Faculty, the Gastroenterological Society of Australia, the World Gastroenterology Organization and the Australian Government (AusAid).

INNATE PHAGOCYTOSIS & NEURODEGENERATION

Project INN1: The Role of Innate Phagocytosis in the Pathogenesis and Treatment of Alzheimer's Disease

Supervisors: Dr. Ben J. Gu, Prof. James S. Wiley
Project Site: Florey Institute, Kenneth-Myer Building
Contact: ben.gu@florey.edu.au Ph: 03 9035 6317

Project description: Emerging genetic evidence suggests that impaired removal of aggregated or fibrillar A β -peptides due to defects in innate phagocytosis is a major contributor to the risk of sporadic Alzheimer's disease (AD). We found that both proinflammation and innate phagocytosis can be mediated by the P2X7 receptor in the presence or absence of its ligand extracellular ATP. In a blind pilot study we measured the phagocytic ability of fresh peripheral monocyte subsets from over 90 patients and controls recruited via the Australian Imaging Biomarker and Lifestyle Study of Aging (AIBL). Cells treated with ATP showed decreased phagocytic ability while Copaxone (CPX, also known as glatiramer acetate, a peptide polymer drug for multiple sclerosis) promoted innate phagocytosis. Significant differences of ATP and CPX altered phagocytosis were found between cognitively normal older controls and patients with mild cognitive impairment (MCI) or AD, and both were correlated with amyloid burden as assayed by A β amyloid-PET imaging (Gu et al, *Acta Neuropathologica* 2016). In this project, the candidate will further investigate the underlining biological mechanisms of these correlations through cell ageing, membrane fluidity, innate phagocytosis and inflammation. A combination treatment targeting both innate phagocytosis and inflammation will be developed in an animal model of AD and a small-scale Phase IIa pilot clinic trial for prodromal or mild/moderate AD patients, based on our novel findings. The safety and tolerance for the treatment combination (CPX which promotes innate phagocytosis and AZD9056 which inhibits P2X7 mediated proinflammation) and its therapeutic effect will be assessed during this trial. Outcome measures for Proof of Concept and Proof of Mechanism include reversal of the peripheral monocyte phagocytic deficits and changes in brain microglial activation as assessed by PET-TSPO imaging. This study will lead to better understanding of the pathogenesis of AD and a novel treatment strategy for AD.

Techniques involved include flow cytometry, microsurgery, cell culture, animal handling, fluorescent microscopy and biochemistry.

MALARIA

Project MAL1: Development of an ultra-sensitive non-invasive point-of-care immunosensor for malaria elimination

Supervisors: Prof. Stephen Rogerson, Prof. Patrick Kwan, Prof. Stan Skafidas
Projects site: Doherty Institute, Department of Medicine (RMH), Centre for Neural Engineering, University of Melbourne
Contact: Professor Stephen Rogerson, E: sroger@unimelb.edu.au;
Patrick Kwan, E: patrick.kwan@unimelb.edu.au

Project description: Detection of very low-density malaria infection is essential for malaria elimination, but current diagnostics are insensitive and/or costly. Supported by the Bill & Melinda Gates Foundation, this project aims to develop a low-cost, point-of-care diagnostic device based on our novel electrical immunosensor platform with ultra-sensitive detection capacity. The platform will be applicable to blood (for detection of very low density infection) and saliva (for non-invasive testing) to fulfill diagnostic gaps required for malaria elimination. Our pilot data suggest superior sensitivity that can detect protein at levels three logs lower than conventional malaria rapid diagnostic tests (RDTs), and two logs lower than next generation IDTs (Infection Detection Tests).

Project MAL2: Hiding out in the Placenta. Investigating how glycosaminoglycans can modulate the immune system during malaria and pregnancy.

Supervisors: Dr Louise Randall and Professor Stephen Rogerson
Project Site: Department of Medicine, University of Melbourne. The laboratory is located at the Peter Doherty Institute for Infection and Immunity
Contact: Dr Louise Randall E: louise.randall@unimelb.edu.au T: 8344 2181

Project description: Malaria during pregnancy can impact both the mother and the developing fetus, resulting in increased morbidity and mortality. Placental malaria is characterised by the accumulation of *P. falciparum*-infected red blood cells in the placenta. Parasite-derived proteins on the infected red blood cell membrane bind to chondroitin sulfate A, a glycosaminoglycan associated with the syncytiotrophoblasts and the intervillous spaces of the placenta. Studies performed in our laboratory suggest that this glycosaminoglycan can modulate the immune system response to the malaria parasite. This new project aims to examine this modulation more closely and to understand the interaction between the parasite, the placenta and the mother's immune system.

MATERNAL AND PERINATAL MENTAL HEALTH

Project MAT1: Building Early Attachment and Resilience (BEAR) Study – evaluation of group intervention programs for parents with risk factors for attachment disorders.

Supervisors: Prof. Louise Newman
Project Site: RWH and RMH
Contact: Prof. Louise Newman; T: 83452070; E: louise.newman@thewomens.org or
Dr Angela Komiti; T:90357122; E: angelaak@unimelb.edu

Project description: The primary aim of the BEAR study is to evaluate the efficacy of two psychologically-based interventions for infants of 'at risk' mothers (experiencing mental health problems) in order to

promote the development of mother/infant attachment and therefore foster the development of resilient children. The interventions are: [1] the Mindbabybody program – a mindfulness-based program delivered in the antenatal period, focused upon decreasing maternal stress and anxiety by increasing self-awareness and acceptance through meditation-based practices, and [2] the Parenting with Feeling program- an attachment-based group parenting program delivered in the postnatal period, focused upon improving parental self-representation, emotional understanding and attachment relationship with their child. These two programs have been designed to help parents with mental health issues, improve their emotional responsiveness to their infants to foster secure attachment relationships between parents and child which in turn promote resilience for both groups. Recruitment for the study commenced mid-2015 and is ongoing.

Project MAT2: Safe Mothers-Safe Babies – developing a screening tool and intervention program for pregnant women at risk of domestic violence.

Supervisors: Prof. Louise Newman
Project Site: RWH and RMH
Contact: Prof. Louise Newman; T: 83452070; E: louise.newman@thewomens.org or
Dr Angela Komiti; T: 90357122; E: angelaak@unimelb.edu

Project description: The Safe Mothers, Safe Babies project has been developed with the overall aim of improving identification and intervention approaches for women during pregnancy and the perinatal period who are at risk of, or experiencing interpersonal violence. It is recognised that this is a significant problem and a major contributor to stress and anxiety during pregnancy with significant implications for both the mother and for foetal development and infant outcome. The program components include both an antenatal (MindBabyBody) and postnatal group (Parenting with Feeling) intervention programs. The research component will include a trial of the intervention program in this particular cohort and incorporate the NBO (Newborn Behavioural Observation) as part of the group program with the aim of enhancing parent-infant interaction and relational outcome. The study is projected to commence mid-2017.

MULTIPLE SCLEROSIS/NEUROLOGY

Project MS1: Measuring long-term disability outcomes in multiple sclerosis

Supervisors: Dr Tomas Kalincik; Dr Viliija Jokubaitis; Prof Helmut Butzkueven
Project Site: Department of Medicine / Royal Melbourne Hospital / The University of Melbourne
Contact: Tomas Kalincik; E: tomas.kalincik@unimelb.edu.au

Project description: Prevention of irreversible disability is the most important goal of multiple sclerosis disease modifying therapy. However, assessment of disability outcomes in multiple sclerosis therapeutic trials is complicated by the great individual and time-dependent variability of disability and measurement error. In particular, the design of modern clinical trials with 1–3 year follow-up infers long-term irreversible disability outcomes from short-term disability measures. We have previously shown that the currently used definitions of disability accrual are suboptimal, as they are not associated with long-term disability outcomes in up to 25% of the recorded events.

This project develops a new metric of short-term change in disability that is highly predictive of long-term irreversible disability accrual, suitable for use in clinical trials of therapies. It builds on the definition of confirmed disability progression (Kalincik et al., Brain 2015, 138:3287) and utilizes MSBase, a large global observational multiple sclerosis cohort of more than 39,000 patients.

This project will suit students with interest in statistics and health outcomes research. During the project, you will improve your statistical skills, learning some of the more complex statistical techniques. Knowledge of elementary statistics is a requisite. You will contribute to the evidence-based clinical management of multiple sclerosis.

Project MS2: Therapy of progressive forms of multiple sclerosis

Supervisors: Dr Tomas Kalincik; Prof Helmut Butzkueven
Project Site: Department of Medicine / Royal Melbourne Hospital / The University of Melbourne
Contact: Tomas Kalincik; E: tomas.kalincik@unimelb.edu.au

Project description: Treatment options for relapsing and progressive forms of multiple sclerosis differ greatly. While more than 10 disease modifying therapies are available for treatment of relapsing multiple sclerosis, effective management of progressive multiple sclerosis is lacking. It is possible that the immunomodulatory therapies effective in relapsing multiple sclerosis are also suitable for treatment of progressive multiple sclerosis; however, conclusive evaluation of this hypothesis is needed. Due to the very slow disability accrual in progressive multiple sclerosis, evaluation of treatment efficacy in prospective randomised trials is impractical. On the other hand, large observational cohorts provide the opportunity to generate these much needed answers.

This project compares effectiveness of different available disease modifying therapies in progressive multiple sclerosis forms. We hypothesise that the highly potent immunosuppressive therapies modify disability trajectories in progressive multiple sclerosis. The project utilizes MSBase, a large global observational multiple sclerosis cohort of more than 39,000 patients, which we have recently used to develop an objective definition of secondary progressive multiple sclerosis (Lorscheider et al., Brain, in press). It uses advanced statistical modelling, including propensity score-based comparisons and marginal structural models, in order to control multiple biases inherent in observational data.

This project will suit students with interest in statistics and health outcome research. During the project, you will improve your statistical skills, learning some of the more complex statistical techniques. Sound knowledge of elementary statistics is a requisite. The generated evidence will influence clinical management of multiple sclerosis globally.

NEUROLOGY – DEMENTIA

Project ND1: Can statins protect against cognitive decline associated with dementia?

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki, E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Cognitive impairment is becoming an increasingly researched field in ageing, particularly with dementia being in the top five leading causes of burden in Australia. Despite these already high and increasing prevalence rates, there is no curative treatment for AD. Therefore the identification of individuals who are at increased risk of AD and the implementation of preventive interventions is necessary until a treatment is found. Cardiovascular risk factors, including cholesterol, are typically thought to be associated with an increased risk of dementia. However the use of statins (cholesterol lowering medication) and its effect on cognitive performance has not been thoroughly investigated, particularly assessing duration of use. This research examines the short term and long term effects of cholesterol-lowering medication on cognition to determine the importance of timing and duration of statins as prevention against dementia.

The project will provide a unique opportunity to work on an Australian dataset with midlife and late-life data collected (data over 20 years), and will suit a candidate with interest in commercialisation and ageing. There is also opportunity for publication.

Project ND2: Nutrient intake and cognitive decline

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki, E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: There is increasing evidence to suggest that diet may play an important role in preventing or delaying the on-set of Alzheimer's disease (AD). Research has reported that a Mediterranean-type diet is associated with a lower risk of prevalent AD. One important pathological hallmark of AD is beta-amyloid (A β) peptide deposition in the brain, resulting in formation of plaques. However little is known about the possible association between nutrient intake and A β plasma. In this study, we will examine whether dietary intake of nutrients (data already collected from a food frequency questionnaire) is associated with plasma A β levels in a cross-sectional analysis of women aged 65 years and over. A β levels will be examined using Positron Emission Tomography (PET) scans (data already collected) in collaboration with imaging experts.

A major benefit of this project is that the nutritional data set has already been collected. The project will suit a candidate with interest in dietary factors and health, as well as media or commercialisation and industry interaction. This project also provides opportunity for publication.

Project ND3: Lifestyle Factors and Cognitive Health

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki; E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Several studies have described the benefit of lifestyle change for healthy ageing and cognitive improvement. Studies investigating lifestyle factors have been limited by cohort sampling bias, cross sectional designs, short follow-ups and small sample sizes. Furthermore the frequency and intensity of lifestyle alteration is still not defined. In this project we examine a 20 year longitudinal dataset to determine the influence of lifestyle factors on cognitive performance and health.

The main opportunities for this project are:

1. An opportunity for publication
2. Hands-on involvement in participant evaluation
3. Work with a large database with over 20 years of lifestyle data
4. This project would suit a candidate with an interest in neuropsychology

Project ND4: Examining neuropsychological trajectories using data collected from a longitudinal study

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki; E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: In this study we will examine neuropsychological trajectories over the 16 years for which we have cognitive data and the many associated factors such as menopausal status, psychological status, health status, cognitive performance, APOE e4 status, and so on, to determine risk and protective

factors for cognitive decline. The WHAP also has neuroimaging data (structural and functional) for about half of its cohort, which we may be able to explore in connection with cognition in this project.

The project will suit a candidate with interest in neuropsychology. Benefits of this project include the opportunity for publication and that the data set has already been collected.

Project ND5: Subjective memory complaints, frailty and dementia

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki; E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: The early detection of those likely to develop dementia is essential. Subjective memory complaints have been associated with low mood and subjective cognitive decline. However better selection of those with subjective memory complaints to distinguish the worried well from those with disease is required. Some imaging studies have shown that increased amyloid in those subjective memory complaints despite no objective memory change. In this study we will examine 15 years of cognitive decline with subjective memory complaints and frailty measures, adjusting for mood.

Major benefits from this study are:-

- There is opportunity for publication
- You will work with a well-known longitudinal database with over 20 years of data already collected

NEUROPSYCHIATRY, CANCER AND IMAGING

Project NCI1: The neuropsychiatric consequences of androgen deprivation

Supervisors: Richard Kanaan
Project Site: Austin Hospital
Contact: Professor Richard Kanaan, Richard.kanaan@unimelb.edu.au

Project description: Patients with prostate cancer are often treated with androgen-deprivation therapy (ADT), which dramatically reduces their testosterone but is also responsible for some significant side effects, including on mood and cognition. Recent evidence suggests that, in men, some important biological actions attributed to testosterone are mediated via its metabolite, estradiol. We will conduct a randomized, placebo-controlled trial in 130 men receiving ADT to investigate whether selective restoration of estradiol is sufficient to prevent the side effects. This project in particular will examine the mood and cognition of the patients undergoing ADT and see whether they respond to estradiol replacement, using a combination of clinical and neuropsychological assessment, and functional and structural neuroimaging.

NEUROPSYCHIATRY AND STRESS BIOLOGY

Project NSB1: Neuroimaging in schizophrenia-spectrum disorders

Supervisors: Dr Vanessa Cropley, Dr Tamsyn Van Rheenen, Dr Chad Bousman, Professor Christos Pantelis
Project Site: Melbourne Neuropsychiatry Centre, The Alan Gilbert Building, 161 Barry Street, Carlton South, The University of Melbourne.
Contact: Dr Vanessa Cropley; T: (03) 8344 1876; E: vcropley@unimelb.edu.au or Dr Tamsyn Van Rheenen E: Tamsyn.van@unimelb.edu.au

Project description: The Melbourne Neuropsychiatry Centre (MNC) is a joint centre of Melbourne Health (North Western Mental Health) and The University of Melbourne (Department of Psychiatry). Research at MNC focuses on improving our understanding of the neurobiological processes involved in disorders of the brain and mind.

Our group has structural Magnetic Resonance Image (MRI) scans previously collected from the Australian Schizophrenia Research Bank (ASRB). The ASRB is an Australian register and storage facility of medical research data that links clinical and neuropsychological information, blood samples and structural MRI scans from people with schizophrenia and healthy non-psychiatric controls. This data is collected across five research sites within Australia, including the MNC. The data is accessible to researchers wanting to undertake research using the resources of the ASRB.

The Psychosis and Developmental Neuropsychiatry Stream of MNC has several projects available that will investigate gene x environment interactions on structural neuroimaging parameters and behaviour in schizophrenia or risk for psychosis. These projects will utilise MRI scans and associated clinical, cognitive and genetic data collected as part of the ASRB. Projects for 2016 include:

- Investigating the influence of prefrontal and striatal dopaminergic genes, cannabis exposure and their interaction on cognition and prefrontal-striatal volumes in high and low schizotypy
- Examining the interaction between the brain derived neurotrophic factor (BDNF) gene and childhood adversity on hippocampal subfield volume in schizophrenia and healthy controls
- Investigating the impact of neurodevelopmental genes (e.g. neuregulin) on neurological soft signs and its association with cortical gyrification, cognition and age of illness onset in schizophrenia

The student will be responsible for pre-processing, tracing (if applicable) and statistical analysis of MRI scans and associated clinical and genetic data. The student will also be trained in the application of imaging analysis in neuropsychiatry.

Project NSB2: Towards a brain-based measure of human anxiety sensitivity

Supervisors: Assoc Prof Ben Harrison and Dr Chris Davey
Project Site: Melbourne Neuropsychiatry Centre, and Department of Psychiatry,
The University of Melbourne
Contact: Assoc Prof Ben Harrison; T: 03 8344 1876 E: habj@unimelb.edu.au

Project Description: Anxiety disorders are the most prevalent and costly of all mental disorders for Australians aged between 18 and 45 years. Despite this, we lack a clear understanding of the biological mechanisms that give rise to their symptoms and how to effectively treat them.

This PhD project will test the hypothesis that human anterior insular cortex activity underlies individual differences in trait “anxiety sensitivity”: an established psychological risk factor for clinical anxiety disorders. The project will recruit a large cohort of adolescent and young adult participants and assess them with functional magnetic resonance imaging (fMRI) combined with psychophysiological monitoring. As well as characterising the brain basis of human anxiety sensitivity, it is expected that this project will identify a novel biological risk marker of clinical anxiety, in particular, panic disorder. We have close collaborations with Orygen Youth Health and headspace Western Melbourne, and there is scope for the project to be extended to patient groups from these clinics.

Candidates (*Masters only*) with an interest in psychology, biological psychiatry and imaging neuroscience are encouraged to apply. Further detail about this project is available upon request.

Project NSB3: Predicting treatment response in young people with major depression using functional neuroimaging

Supervisors: Dr Chris Davey and Assoc Prof Ben Harrison
Project Site: Melbourne Neuropsychiatry Centre, and Department of Psychiatry, The University of Melbourne
Contact: Dr Chris Davey, T: 03 9342 2800 E: c.davey@unimelb.edu.au

Project Description: Mental illnesses are the "chronic diseases of the young", and the mental illness that causes most disability in young people is depression. While antidepressant medications are an effective treatment for adolescent depression, only about two-thirds of patients will demonstrate a clinical response, and less than a third will reach remission. The identification of valid biomarkers to assist in the prediction of treatment response is therefore of great clinical relevance.

This Masters project will use functional magnetic resonance imaging (fMRI) combined with novel emotional provocation tasks. We will test the hypothesis that individual differences in pretreatment activity of the medial frontal cortex will predict treatment response in young patients experiencing their first episode of depression. Patients will be recruited from Orygen Youth Health and headspace Western Melbourne, where Dr Davey works as a psychiatrist.

Candidates (*Masters only*) with an interest in psychology, biological psychiatry and imaging neuroscience are encouraged to apply. Further detail about this project is available upon request.

Project NSB4: The worldwide ENIGMA MDD consortium: detecting robust imaging markers of depression

Supervisors: Dr. Lianne Schmaal and Dr. Chris Davey
Project Site: Orygen the National Centre of Excellence in Youth Mental Health, University of Melbourne
Contact: Dr. Lianne Schmaal, T: 0393422886, E: lschmaal@unimelb.edu.au

Project description: Major depressive disorder (MDD) is a highly debilitating disorder that has an enormous detrimental impact on patient's life and a high social and economic burden. Many studies have identified structural and functional brain alterations in MDD. However, to date, volumetric and functional brain differences have not always been consistent, which may in part be explained by small sample sizes and differences in methodological and clinical characteristics between studies. To address the limited statistical power of prior studies, the MDD working group within the "Enhancing NeuroImaging Genetics through Meta-Analysis", or ENIGMA, was initiated a few years ago, see <http://enigma.ini.usc.edu/ongoing/enigma-mdd-working-group/>

The overall aims of the ENIGMA MDD consortium are to 1) identify robust imaging markers of MDD, 2) establish the neurobiological correlates underlying variation in disease profile and disease course, and 3) identify the genetic factors affecting neurobiological alterations in MDD using available genome-wide data, and relate the genetic risk profile to the implicated brain circuits. Currently, 31 research sites from around the world are participating in ENIGMA MDD and sharing neuroimaging data.

The PhD student will support ongoing ENIGMA MDD work, which includes development and execution of data processing, quality assurance and statistical analyses protocols for neuroimaging (structural MRI, resting state fMRI and DTI) and genetic data, organising and harmonising databases, communicating with members of the consortium, writing scientific papers on the above topics, and incorporating the research into a PhD thesis. Candidates with an interest in psychology, biological psychiatry and imaging neuroscience are encouraged to apply. Having prior experience with neuroimaging analyses and having strong statistical and computer programming skills is desirable. Further detail about this project is available upon request.

PHARMACOGENETICS AND PRECISION MEDICINE

Project PHM1: Express ambulatory point-of-care molecular diagnosis

Supervisors: Professor Patrick Kwan, Dr Marian Todaro
Project Site: Department of Medicine (RMH), Melbourne Brain Centre (Parkville), Centre for Neural Engineering
Contact: Patrick Kwan, Department of Medicine (RMH)
E: patrick.kwan@unimelb.edu.au;
Dr Marian Todaro, Department of Neurology E: Marian.Todaro@mh.org.au

Project Description: This is an inter-disciplinary, technology driven program with multiple projects that aim to develop point-of-care molecular diagnostics for a range of important diseases, including epilepsy, HIV infection, coeliac disease, and malaria. Conventional laboratory tests have been indispensable for disease diagnosis. However, their high costs and need for skilled personnel to operate complicated equipment have limited their abilities to cope with escalating demand from the growing population, and the need for application in resource poor and remote areas. Therefore, development of portable, on-site, point-of-care (POC) testing devices has become increasingly important in medical research. POC testing performed at the time of consultation will allow the results to be used for making immediate, informed clinical decisions on patient care. In short, it will transform medical practice.

This innovative project will combine novel biochemical and engineering technologies that will perform molecular diagnosis rapidly using compact 'smart' devices at the point of care. The platform technology can be customised for any molecule of interest, including DNA, RNA and protein. There is very strong potential for technological innovation and eventual application and commercialisation of the devices to meet the rapidly expanding need of molecular diagnosis. The global molecular diagnostic market is estimated to be US\$21.7 billion in 2014 with projected 5-year compound annual growth rate (CAGR) of 12.5% to reach \$45.2 billion in 2020. In this market, POC testing using lab-on-chip systems is the fastest growing segment, valued at >\$2 billion in 2014 with CAGR of 16.5% (BCC Research, 2015).

This project is open for different students with different skills and background, including:

- Molecular biology
- Electrical engineering
- Electronic engineering
- Software engineering

Potential students are strongly encouraged to contact the supervisors to discuss their suitability for the project based on their interests and skills.

Project PHM2: Genomics of adverse response to antiepileptic drugs

Supervisors: Prof. Patrick Kwan
Projects site: Department of Medicine (RMH), University of Melbourne
Contact: Professor Patrick Kwan, E: patrick.kwan@unimelb.edu.au

Project description: Although highly efficacious, antiepileptic drugs (AEDs) are associated with a range of side effects. This project will focus on two types of side effects: skin reactions and psychosis, which are severe and largely unpredictable by clinical risk factors but likely to have a strong genetic basis. Identifying the genetic markers will help patient selection and inform future drug development.

Severe cutaneous adverse drug reactions (cADRs), such as Stevens Johnson syndrome (SJS) and toxic

epidermal necrolysis (TEN), are among the most feared adverse effects of antiepileptic drugs (AEDs) not only because of their high mortality and morbidity, but also because of their unpredictability. Dissecting the genetic basis for these ADRs will have major impact on “personalised” drug selection, and the insights gained on the chemico-biological pathways will help future design of safer medications.

This project represents an exceptional opportunity to effectively and efficiently discover these variants in a unique subject cohort (drug-exposed cases and controls) using the latest genotyping and sequencing platforms. More than one student will be needed for various aspects, including patient recruitment and phenotyping. In addition, there will be opportunity for the student to be part of the data analysis team, thus basic knowledge in bioinformatics and genetic statistics is essential.

Project PHM3: Wearable devices for non-invasive, ambulatory seizure monitoring and prediction

Supervisors: Prof. Patrick Kwan, Prof. Terence O’Brien
Projects site: Department of Medicine (RMH), University of Melbourne
Contact: Professor Patrick Kwan, E: patrick.kwan@unimelb.edu.au

Project description: The development of reliable, accurate, non-invasive methodologies for continuous, long-term seizure monitoring is a critical part of the precision medicine approach in epilepsy management. While the gold standard for diagnosing and detecting seizures remains inpatient simultaneous EEG and video recording, it is costly and impractical for extended use outside the hospital setting. Conventional outpatient seizure monitoring relies on self-completing seizure diary which is inexpensive but highly inaccurate. There is a need for novel technologies that combine low cost, non-invasiveness with reliability for extended seizure monitoring. This project aims to develop an integrated wearable sensor system for the clinical management of seizures in patients with epilepsy. The device will be tested in patients admitted for video-EEG monitoring at the Royal Melbourne Hospital.

Project PHM4: Stroke and epilepsy a bi-directional relationship?

Supervisors: Prof. Patrick Kwan, Prof. Bernard Yan
Projects site: Melbourne Brain Centre, The Royal Melbourne Hospital
Contact: Prof. Patrick Kwan, E: patrick.kwan@unimelb.edu.au;
A/Prof. Bernard Yan, E: Bernard.Yan@mh.org.au

Project description: Stroke is one of the leading causes of acquired epilepsy in industrialised countries. Seizures are a major complication in stroke survivors and are associated with increased mortality and poorer functional recovery. Patients with post-stroke seizures have increased risk of in-hospital complications, leading to prolonged hospitalisation. Conversely, patients with epilepsy also have an increased risk of de novo stroke, the reasons for which are unclear. Utilising our access to local and international databases, this project aims to identify the biomarkers, including clinical, genomic, and radiological factors predictive of post-stroke epilepsy and post-epilepsy stroke. The findings will shed new lights in understanding the patho-mechanisms of these disorders. The project will be based on the expanding RMH stroke database with several thousands of patients recruited, as well as the epilepsy database of new onset patients.

Project PHM5: Clinical utility of clinical whole exome sequencing for epilepsy

Supervisor: Prof. Patrick Kwan
Projects site: Department of Medicine (RMH), University of Melbourne
Contact: Professor Patrick Kwan, E: patrick.kwan@unimelb.edu.au

Project description: Genetic variants have been found to cause epilepsy as well as affect how people respond to treatment. Whole exome sequencing is a new method of genetic testing that has the

advantage of being able to screen all the genes in a person. Currently it is mainly being used for research purposes. The purpose of this prospective study is to find out whether whole exome sequencing offers value for money when used in the clinical setting to help diagnose people with epilepsy.

Project PHM6: Pharmacogenomics in IBD

Supervisors: Professor Finlay Macrae and Prof Les Sheffield
Project Site: Colorectal Medicine and Genetics, The Royal Melbourne Hospital
Contact: Prof Finlay Macrae E: finlay.macrae@mh.org.au

Project description: The Royal Melbourne Hospital, with GenesDX, is pioneering the implementation of a pharmacogenomics clinical support program. In the case of inflammatory bowel disease, this relates to the use of thiopurines. The project will assist in the implementation of the program and its evaluation. It will gauge the clinical utility of TPMT genotyping and the clinical decision support tools that will be built into the program, and thiopurine metabolite testing, in the management of inflammatory bowel disease.

POPULATION HEALTH

Project POP1: Life-long exposures for Healthy Ageing

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki ; E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Several studies have described the benefit of lifestyle change for healthy ageing and cognitive improvement. For example smoking, alcohol consumption and a lack of physical activity have been linked to an increased rate of cognitive impairment and cardiovascular diseases. Studies investigating lifestyle factors have been limited by cohort sampling bias, cross sectional designs, short follow-ups and small sample sizes. Furthermore the frequency and intensity of lifestyle alteration is still not defined. In this project we examine a 20 year longitudinal dataset to determine the influence of lifestyle (i.e. alcohol consumption, smoking, diet and physical activity) on health.

This project will involve direct hands-on participant evaluation. This project will involve direct hands-on participant evaluation. You will also have the opportunity to work with a rich database with lifestyle data that spans over 20 years and opportunity for publication.

Project POP2: Iron and Fatigue

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki ; E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Iron deficiency is prevalent in ageing women. Studies have shown that iron deficiency results in fatigue, reduced physical performance and impaired cognition. These symptoms are commonly reported in ageing populations. The Women's Health Ageing Project is an epidemiological sampled longitudinal prospective study that contains 20 years' worth of data on a number of measures including blood, cognition, diet and lifestyle, mood and wellbeing, hormones, illnesses, bone, and genes among others. This unique resource will therefore have the potential to identify new preventive health interventions and address issues relating to social determinants of health and health inequalities through social epidemiology across two decades. Over a hundred papers on this study have been published in peer reviewed journals. The results of this study have been internationally recognised and contributed

significantly to the understanding of healthy ageing.

The benefits of this project are:

- Opportunity to publish
- The study has data over 20 years already collected
- Will suit a candidate with an interest in industry partnerships

Project POP3: Vitamin D deficiency and balance

Supervisors: A/Professor Cassandra Szoeki & Professor Meg Morris
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki; E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Low levels of vitamin D are relatively common in older women Australian, which is concerning given that vitamin D is essential for the maintenance of healthy bone and muscle. There is evidence to suggest that vitamin D may also be important for the maintenance of balance in women. This project will examine the relationships between vitamin D and balance in non-elderly postmenopausal women from the internationally renowned Women's Healthy Ageing Project (WHAP).

Opportunities: You will have the opportunity to work with an internationally renowned cohort and research team each with international recognition.

The study has already collected data over 20 years and there is opportunity for publication. This project will suit a candidate with an interest in balance, sports physiology and physiotherapy. There will be interaction with industry partners.

Project POP4: Iron interventions in young children in rural Bangladesh: effects on child development, infection and haematology

Supervisors: Dr Sant-Rayn Pasricha, Prof Beverley-Ann Biggs
Project Site: Department of Medicine, RMH
Contact: Prof Beverley-Ann Biggs, babiggs@unimelb.edu.au

Project description: Anaemia affects over 400 million children worldwide, but the best strategy to control this problem remains unclear. The risks and benefits of iron interventions in young children are unclear and have not been confirmed in a suitably powered randomized controlled trial. We are undertaking a large Phase III RCT in rural Bangladesh. Children will be randomized to placebo, iron supplementation and multiple micronutrients. Key outcomes include child development, infectious disease morbidity, growth and haematologic endpoints. There are several opportunities to identify substudies which engage with the particular interests of the student, as well as gaining experience with the design, management and analysis of a large international trial. This project would suit a student interested in global health, field epidemiology, nutrition, haematology and infectious diseases. The project may involve some travel to Bangladesh. The student will be expected to be familiar with all aspects of the study, and take leadership on an element of the project central to their research topic. The student will have opportunities to join existing international collaborations and present at international meetings.

Major Benefits of this project include:

1. Opportunity to work on and develop skills in managing a major international randomized controlled trial.

2. Opportunity to participate in and develop multiple high impact publications.
3. Opportunities to travel and gain field experience in epidemiology in low income countries.
4. Opportunity to work with an experienced multidisciplinary team.

PREGNANCY RESEARCH

Project PR1 Testing novel therapeutics in a novel mouse model of preeclampsia

Supervisors: Dr Natalie Hannan and Prof Stephen Tong
Project Site: Mercy Hospital for Women, Heidelberg (Dept. Obstetrics and Gynaecology)
Contact: Dr Natalie Hannan E: nhannan@unimelb.edu.au

Project description: Preeclampsia affects around 2-8% of all pregnancies, and claims the lives of over 60,000 women annually with far greater rates of perinatal loss. There is no medical therapeutic available, besides the delivery of the placenta and baby. A treatment is urgently needed. This project will use an innovative mouse model of preeclampsia to test novel therapeutic strategies to prevent, delay or treat preeclampsia. This model is unique in that it overexpresses the toxins of preeclampsia specifically in the placenta (via lentiviral transduction of mouse blastocysts) similar to the disease in women.

Project PR2: Understanding the pathophysiology of preeclampsia

Supervisors: Dr Natalie Hannan and Prof Stephen Tong
Project Site: Mercy Hospital for Women, Heidelberg (Dept. Obstetrics and Gynaecology)
Contact: Dr Natalie Hannan E: nhannan@unimelb.edu.au

Project description: Preeclampsia affects around 2-8% of all pregnancies, and claims the lives of over 60,000 women annually with far greater rates of perinatal loss. There are no efficacious treatments available or predictive tests for early diagnosis. This project aims to understand the pathophysiology behind this disease by examining key pathways thought to be central to disease progression and severity in clinical samples and animal models of disease.

Project PR3: Can dietary phytochemicals prevent the development of diabetes in pregnancy?

Supervisors: Associate Professor Martha Lappas
Project site: Department of Obstetrics & Gynaecology, University of Melbourne located at the Mercy Hospital for Women
Contact: T: 8458 4370 E: mlappas@unimelb.edu.au

Project description: Gestational diabetes mellitus (GDM) affects up to 20% of all pregnancies. It has an impact that extends well beyond pregnancy and childbirth, with the potential for lifelong morbidity or mortality for both mother and baby. Despite the enormous health-impact of this condition, little progress has been made with interventions aimed at prevention; rates of GDM are increasing in parallel with the obesity epidemic. A safe and effective intervention that can reduce the burden of GDM would be a major public health initiative. Of promise, however, is the increasing volume and quality of evidence that high fruit and vegetable intake in pregnancy is associated with a decreased risk of adverse pregnancy outcomes. Many of the beneficial effects are due to phytochemicals which are natural products found in fruits and vegetables and beverages derived from plants. Thus, in this study, we will use a mouse model to determine if phytochemicals can prevent the development of GDM.

Techniques: Animal work, PCR-based analysis, Western blotting and ELISA

Project PR4: Can dietary phytophenols stop preterm birth?

Supervisors: Associate Professor Martha Lappas
Project site: Department of Obstetrics & Gynaecology, University of Melbourne located at the Mercy Hospital for Women
Contact: T: 8458 4370 E: mlappas@unimelb.edu.au

Project description: The single most important complication contributing to poor pregnancy and neonatal outcome is preterm birth. Of the 130 million babies born each year, 8 million die before their first birthday. Up to 2.7 million of these deaths are attributable to being born too early. Bacterial infection is the most common trigger for preterm birth. It activates inflammation in placenta which can trigger the processes that lead to preterm birth. In our in vitro studies, we have shown that natural plants chemicals (i.e. phytophenols), such as luteolin which is found in celery, can reduce inflammation in the placenta. Although this data is very promising, in vivo studies are needed to determine if these plant chemicals will be useful as therapeutics to prevent preterm birth. In this project, we will induce preterm birth in mice (using bacterial infection). We will then determine if phytochemicals can prevent infection induced preterm birth. The possibility of phytophenols as therapeutic agents offers an exciting step forward into the management of a condition responsible for unequalled morbidity and mortality in infants.

Techniques: Animal work, PCR-based analysis, Western blotting and ELISA

PSYCHIATRY

Project PSYC1: Causes of Depressive Symptoms in Early Ageing

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki, E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: It is predicted that by 2051, 26.1% of Australians will be older than 65 years and 9.4% will be 80 years or older (Australian Bureau of Statistics, 2001). With prevalence rates of depression in the elderly set to rise in accordance with the population surge identifying preventative measures and means of early detection in this population is especially important. The focus of this project will be to examine factors which affect the rating of depressive symptoms on three different standardised and widely used measures in a cross-section of women entering late-life. The Hospital Anxiety and Depression Scale (HADS), the Centre for Epidemiological Studies – Depression Scale (CES-D) and the Geriatric Depression Scale (GDS) will be administered to the cohort of the Women’s Healthy Ageing Project. Analysis will be conducted examining the consistency of item rating between measures in order to identify correlations between scales. Psychological and social data will also be obtained from the cohort and will allow for the identification of any factors influencing the rating of measures.

Major benefits of this study are:

1. There is opportunity for publication
2. You will have access to a unique database with two decades of psychological and social data
3. This study would be particularly suited to an individual wishing to gain experience in the areas of geriatric psychology and/or depression.

Project PSYC2: Project title: Alcohol use and effects on mood in elderly women

Supervisors: A/Professor Cassandra Szoeki
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeki ; E: cszoeki@unimelb.edu.au; T: 8344 1835

Project description: Alcohol consumption in women is becoming an increasing public health concern. Depression, the most prevalent and persistent mental disorder in women, has been shown to be related to alcohol consumption. This study examines the association between alcohol intake and depression in community-dwelling older women.

The Women's Healthy Ageing Project (WHAP) has prospective longitudinal, epidemiological data on alcohol consumption and mood of Australian women from age 45 over 25 years. This project will provide the opportunity for publication, as well as participant contact and clinical skills experience.

PSYCHOSIS, EARLY

Project PSE1: Multimodal machine learning approaches to predicting outcome in early psychosis

Supervisors: Prof Stephen Wood, plus others to be added
Project Site: Orygen
Contact: Prof Stephen Wood; E: S.J.Wood@bham.ac.uk; sjwood@unimelb.edu.au

Project description: PRONIA is an EU FP7 and NHMRC funded study that is looking to use machine learning techniques to improve the prediction of various clinical outcomes in people presenting with first episode psychosis. Initial efforts have focused on single modalities of data; for example, structural neuroimaging, or neurocognitive performance. However, it is believed that greatly improved accuracies will be possible if multimodal analyses can be conducted that combine the relevant information from the unimodal data. This PhD project will work closely with the local investigators, Prof Stephen Wood & Prof Christos Pantelis, as well as the co-ordinating centre in Munich led by Dr Nikos Koutsouleris.

PSYCHOSOCIAL RESEARCH/FERTILITY PRESERVATION /WOMEN'S HEALTH

Project PSR1: The evaluation of a decision aid for women considering non-medical egg freezing

Supervisors: Dr Michelle Peate, Prof Martha Hickey
Project Site: Royal Women's Hospital, Parkville
Contact: Dr Michelle Peate, mpeate@unimelb.edu.au

Project description: There is a growing trend in developed countries for women to delay starting a family until their early 30's or later. This delay can mean that some women miss the opportunity to have children due to age-related infertility. Egg freezing can offer women the option of delaying pregnancy and lower the risk of age-related infertility. However, making choices around egg freezing and family planning is complicated, as health, financial and psychological implications for a procedure with no guarantee of success. Although increasing numbers of women are freezing their eggs, very little is known about their understanding of egg freezing and its potential impact. Nor is it known what information women need in order to make an informed decision. The aim of this study is to investigate the decisional conflict, knowledge of egg freezing, and information needs amongst women considering egg freezing for non-medical reasons. Declining fertility is an urgent social and economic problem in Australia and most other developed countries. The most common and potentially avoidable factor contributing to declining fertility is advanced female age. Advances in technology mean that women now have access to egg freezing to try and overcome the effects of age-related infertility. This procedure is being widely

promoted by commercial providers, but is also costly and carries potential physical and emotional risks. Currently, women are relying on information from commercial providers and internet sources such as unmoderated forums and blogs. There is a need for objective and evidence-based information to support decision-making.

An interactive, online decision aid for women considering egg freezing for non-medical reasons has been developed. This will be the first study to develop and evaluate a decision aid in the context of non-medical egg freezing. It is anticipated that the decision aid will lead to better understanding of fertility-related issues and educated involvement in decision-making.

Benefits to student: This is a multi-collaborative project, so the student will gain experience working in a multidisciplinary team. They will also have the opportunity to learn, develop qualitative and/or quantitative research skills, gain an understanding of ethical procedures, be trained in high quality data management, collection and analysis processes.

Requirements for students: Looking for a dedicated, passionate, sensitive and committed PhD student with strong writing and communication skills. Students who have their own PhD scholarships or are willing to apply for scholarships are preferred.

GRADUATE RESEARCH PROGRAMS - GENERAL INFORMATION

HOW TO APPLY LINKS

<http://mdhs-study.unimelb.edu.au/future-graduate-researchers>

<http://futurestudents.unimelb.edu.au/admissions/applications/research>

Available GR programs

There are a range of research degrees offered at Masters and Doctorate level, whereby students undertake a specific research project under the supervision of research staff at The Royal Melbourne Hospital/RWH. The programs include PhD and other doctorates, MPhil and other masters by research. Please refer to: <http://mdhs-study.unimelb.edu.au/degrees>

Overview and Entry Requirements

PhD: <http://mdhs-study.unimelb.edu.au/degrees/doctor-of-philosophy/entry-requirements#entry-requirements>

Doctor of Medical Science: <http://mdhs-study.unimelb.edu.au/degrees/doctor-of-medical-science/entry-requirements#entry-requirements>

Master of Philosophy: <http://mdhs-study.unimelb.edu.au/degrees/master-of-philosophy/entry-requirements#entry-requirements>

Master of Surgery: <http://mdhs-study.unimelb.edu.au/degrees/master-of-surgery/overview>

Find a Supervisor

You can either contact the supervisors listed in this handbook or refer to the Find an Expert link at: <http://www.findanexpert.unimelb.edu.au/>

For details of the research groups at the Parkville precinct, please refer to:
<http://medicine.unimelb.edu.au/research/department-research-summaries>
<http://medicine.unimelb.edu.au/research/research-groups>

SCHOLARSHIPS

GR Scholarships link:

<http://mdhs.unimelb.edu.au/study/scholarships/graduate-research-scholarships>

Scholarship eligibility

<http://mdhs.unimelb.edu.au/study/scholarships/graduate-research-scholarships/which-scholarships-are-you-eligible-for>

SCHOLARSHIP KEY DATES

Application Timelines - 4 major rounds

<http://mdhs.unimelb.edu.au/study/scholarships/graduate-research-scholarships/timelines>

ENQUIRIES

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Parkville, VIC 3050

PARKVILLE PRECINCT DEPARTMENT LINKS:

Department of Medicine (RMH): <http://www.medrmhwh.unimelb.edu.au/>
Department of Surgery (RMH): <http://www.surgeryrmh.unimelb.edu.au/>
Department of Psychiatry (RMH): <http://www.psychiatry.unimelb.edu.au/>
Department of Radiology (RMH): <http://www.melbourne-radiology.org/>
Department of Obstetrics and Gynaecology: <http://www.obsgyn.unimelb.edu.au/>