The Royal Melbourne Hospital

Bench to Bedside – Medical Research

THE UNIVERSITY OF MELBOURNE

PROJECTS 2017

THE ROYAL MELBOURNE HOSPITAL

(RMH Departments: Medicine, Radiology, Surgery, Psychiatry, Obstetrics & Gynaecology RWH and affiliated institutes)
Melbourne Medical School, Faculty of Medicine, Dentistry & Health Sciences,
The University of Melbourne

HONOURS

Bachelor of Biomedicine and Bachelor of Science
(Degree with Honours)

Honours enrolling department – Medicine RMH

Course Codes:

BH-BMED - Bachelor of Biomedicine (Honours)
For students who have successfully completed or are about to complete the Bachelor of Biomedicine at the University of Melbourne.

BH-SCI - Bachelor of Science (Honours)
For all other applicants who have successfully completed or are about to complete a Bachelor of Science or equivalent

MASTER OF BIOMEDICAL SCIENCE

Course Code: MC-BMEDSC

Affiliations: The Royal Women's Hospital, Northern Health, 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.

TABLE OF CONTENTS

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HONOURS/MBIOMEDSc
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Bachelor of Biomedicine (Honours) / Bachelor of Science (Honours) /
Master of Biomedical Science

THE UNIVERSITY OF MELBOURNE AT THE ROYAL MELBOURNE HOSPITAL

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

AGEING

1. Inter- and intra-individual pattern of disease – *also offered as MBiomedSc*

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 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.

2. The intra-individual rate of ageing – *also offered as MBiomedSc*

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.

3. Towards a biological geriatric assessment – *also offered as MBiomedSc*

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.

4. The underestimated power of human muscle – *also offered as MBiomedSc*

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. Three positions are available (one for the observational part and two for the intervention part).

Prerequisite: intention to learn how to conduct epidemiological studies / interventions, epidemiological/statistical skills, intention to write a journal article, good communication skills, capacity to work in a multidisciplinary team.

5. Refining the comprehensive geriatric assessment – *also offered as MBiomedSc*

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 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. Three positions are available (each domain is one project).

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

6. The blood pressure drop makes you fall……. – *also offered as MBiomedSc*

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: (Initial) orthostatic hypotension ((i)OH) is highly prevalent in older adults, especially in those with one or more chronic diseases. iOH is defined as a blood pressure decrease(BP) of 40 mmHg systolic blood pressure (SBP) and/or 20 mmHg diastolic blood pressure (DBP) within 15 seconds after standing up, whereas OH is classically defined as a drop in BP of at least 20 mmHg of SBP and/or 10 mmHg of DBP at 1 and 3 minutes after standing up. iOH has been shown to be most predictive for balance impairment, increased self-reported impaired standing balance and falls in geriatric outpatients. While OH diagnostics are occasionally performed in clinical practice using a sphygmomanometer, continuously measured blood pressure measurements using beat to beat analyses has not entered routine geriatric care yet. Two student positions are available:

Aim project 1: Define the determinates of iOH and OH and consequences of iOH and OH in geriatric outpatients using an existing database and a validation cohort.

Aim project 2: Analysis of effectiveness of non-pharmacological and pharmacological interventions to counteract iOH and OH in geriatric patients.

Prerequisite: intention to improve epidemiological/statistical skills, intention to write a journal article, good communication skills, capacity to work in a multidisciplinary team, pleasure to work with patients.

7. Lifestyle Factors for Healthy Ageing – *also offered as MBiomedSc*

Supervisor: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Dept of Medicine, Centre for Medical Research, Royal Melbourne Hospital, UoM, Parkville, Vic 3052.
Contact: A/Professor Cassandra Szoeke T: 61 3 8344 1835
E: cszoeke@unimelb.edu.au

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 cognitive performance and health.

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.

8. Multimorbidity and ageing women - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Dept of Medicine, Centre for Medical Research, Royal Melbourne Hospital, UoM, Parkville, Vic 3052.
Contact: A/Professor Cassandra Szoeke T:61 3 8387 2224 F : 61 3 9387 9384
E: cszoeke@unimelb.edu.au

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 and suits a candidate with an interest in a number of disease areas.

9. Physical Activities for Health Ageing- *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeke E: cszoeke@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.

10. Vitamin D levels and cardiovascular disease- *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeke E: cszoeke@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 commercialization, interaction with industry partners and media.

11. Vitamin D levels and Mood - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeke E: cszoeke@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.

12. Diet and Healthy Ageing - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeke E: cszoeke@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 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 diet on cognitive performance and health.

Opportunities: 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.

13. Patterns of Violence in Australian Women – A twenty year follow up Study - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke, Dr Rae Kaspiew (Australian Inst of Family Studies)
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeke E: cszoeke@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

14. Social and physical activities in ageing women - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeke E: cszoeke@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

15. Social engagement and ageing mental health - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeke E: cszoeke@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. However, there is a paucity of research that informs on specific social roles relevant to older adults. The currently study aimed to establish a multidimensional social profile of older Australian adults, and investigate the relationship between social engagement and ageing mental (cognitive and emotional) health. The study accessed participants from the epidemiologically sampled, longitudinal prospective Women's Healthy Ageing Project (WHAP). Social variables will include marital status, employment status, household composition, personal care, babysitting, grandparenting, volunteerism, and community organisation membership. Mental health was assessed using a battery of validated and establish neuropsychological and mood measures.

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.

16. Characterising the Degeneration of Brainstem Neural Circuits that Control Swallowing and Breathing - *also offered as MBiomedSc*

Supervisors: Dr Davor Stanic and A/Prof Mathias Dutschmann
Project Site: Florey Institute of Neuroscience and Mental Health (Howard Florey Laboratories)
Contact: Dr Davor Stanic T: 83440182 E: davor.stanic@florey.edu.au

Project description: Swallowing disorders that increase the risk of aspiration and subsequent pneumonia are prevalent in the elderly and patients suffering neurological diseases, such as Alzheimer's disease. Swallowing disorders are often attributed to weakening of the aging upper airway and digestive tract musculature. However, disturbed neural coordination of breathing and swallowing is increasingly evident in such diseases.
Recent research in our laboratory identified three key brainstem areas that are critically involved in the coordination of swallowing and breathing: 1) *Nucleus of the solitary tract (NTS)*, which generates a phasic or rhythmic 'command' to produce sequential swallowing in response to sensory stimuli; 2) *Nucleus ambiguus (NA)*, which contains the laryngeal motoneurons innervating the vocal folds; and 3) *Kölliker-Fuse nucleus (KF)*, which provides tonic drive for the laryngeal adductors and completely seals the trachea during, and between, swallows.

PROJECT 1

This project examines the underlying brainstem pathology linking dementia and swallowing dysfunction in an established mouse model of neurodegeneration. The onset and progression of tauopathy and neurofibrillary tangle-related morphology will be characterised in the brainstem of this mouse model, with particular focus on regions that control swallowing and breathing. This includes the NTS, NA and KF. The project will also identify neurotransmitter systems responsible for the emergence and manifestation of swallowing-breathing disorders.

PROJECT 2

Using adult born stem cells to replace neurons lost as a consequence of disease has the potential to be of great benefit to sufferers of neurodegenerative disorders. However, despite the extensive research efforts that have gone into examining the biology and therapeutic potential of adult stem cells, the precise cues that modulate the birth of neurons in the adult brain remain unknown.

In an established model of neurodegeneration, this project examines whether alterations occur in the:
1) Rate of stem cell division;
2) Migration of newly born cells; and
3) Positioning and phenotype of newly born cells in the olfactory bulb and dentate gyrus.
Techniques include: immunohistochemistry, and stereology.

ALCOHOL

17. Why do some people with hepatitis C continue to drink? - *also offered as MBiomedSc*

Supervisor: Professor Margaret Hellard, Head, Centre for Population Health, Burnet Institute
Project Site: Burnet Institute
Contact: E: margaret.hellard@burnet.edu.au

Project Description: Acquiring hepatitis C (HCV) in the developed world, once infected with HCV, alcohol use is the strongest known modifiable determinant of HCV disease progression. Alcohol consumption has been found to raise the viral load and accelerate hepatic fibrosis in the context of HCV infection, and heavy alcohol consumption is a risk factor for premature death from HCV. Moreover, as well as impacting on liver disease progression, heavy alcohol use may influence the likelihood of successful HCV treatment.

The proposed project involves in-depth interviews with up to 25 consenting participants living with HCV from the Melbourne Injecting Cohort Study (MIX). Interviews will address alcohol use and other related exposures and outcomes, including participants' alcohol consumption prior to and after HCV diagnosis, any medical advice regarding alcohol consumption they may have received, advice from peers with HCV regarding alcohol consumption, perception of alcohol consumption practices amongst peers with HCV, participants' understanding of the relationship between alcohol-related and injecting drug use-related behaviours, clinical symptoms and other effects of HCV on relationships and self-perception, current self-management strategies for living with HCV.

ANAESTHESIA AND PERIOPERATIVE MEDICINE

18. The evaluation of anaesthetic drugs and techniques on the postoperative quality of recovery – *also offered as MBiomedSc*

Supervisors: Prof Colin Royse
Project Site: The Royal Melbourne and Epworth Hospital campuses
Contact: Prof Colin Royse colin.royse@unimelb.edu.au

Project description: Improving postoperative quality of recovery is a major initiative in anaesthesia and perioperative medicine. Different anaesthetic drugs and different techniques will be evaluated in clinical trails using the Postoperative Quality of Recovery Scale (PostopQRS) as the measurement tool. This tool measures recovery from the patient's perspective in physiological, emotive, nociceptive, functional and cognitive domains. Projects are already established, ethics in place and commenced.

ANATOMY & NEUROSCIENCE

19. Diet induced obesity: is it an addiction?

Supervisors: Dr Robyn Brown and Prof Andrew Lawrence
Location: Addiction Neuroscience Laboratory @ the Florey
Contact: Robyn Brown E: Robyn.Brown@florey.edu.au E: Andrew.Lawrence@florey.edu.au

Project description: Difficulty in managing food intake, especially highly palatable food, can result in obesity and substantial associated health liabilities. A cardinal feature of the pathological over-eating often underlying obesity is that although the individual can describe the negative consequences of their behaviour, they have great difficulty intervening and changing their behaviour. Thus, difficulty in reducing food intake has qualities of an addictive disorder. The disconnect between stated goals to reduce food consumption and actual behaviour suggests the presence of impairments in how information from the frontal cortex is integrating with basal ganglia circuitry to direct behaviour.

We have found that rats prone to diet-induced obesity display some features of 'addiction-like' behaviour towards palatable food. This provides important preliminary evidence to support our central hypothesis that the pathological over-eating commonly observed in diet-induced obesity shares common features with the compulsive drug-taking observed in drug addiction.

Therefore we aim to:
1: Investigate the presence of addiction-like behaviour in rats prone to diet-induced obesity.
2: Conduct a preclinical trial of the glutamate homeostasis restoring drug N-acetylcysteine to reverse synaptic impairments in obesity prone rats to ameliorate aberrant feeding behaviour.

20. Investigating Alcohol-Related Dementia

Supervisors: Dr Christina Perry and Prof Andrew Lawrence
Location: Addiction Neuroscience Laboratory @ the Florey
Contact: Christina Perry E: Christina.Perry@florey.edu.au E: Andrew.Lawrence@florey.edu.au

Project description: Alcohol-related dementia (ARD) is one of the leading causes of secondary (preventable) dementia, and younger onset dementia (onset of symptoms prior to 65 years) in Australia. Together with the high rates of alcohol consumption in Australia, this means that ARD is becoming an increasingly urgent public health issue. The only treatment currently available for ARD is alcohol rehabilitation and abstinence. However, emerging evidence from animal models indicates that exercise may act as a protective factor against the neurotoxic effects of alcohol, and is even able to reverse some of the brain injury that occurs following alcohol exposure.
The aim of this project is to use a validated rodent model to:
1) Characterise the cognitive and neuropathological symptoms of ARD.
2) Evaluate the restorative effects of abstinence combined with voluntary exercise on these symptoms.

21. Context-induced relapse to alcohol-seeking after voluntary abstinence

Supervisors: Dr Erin Campbell and Prof Andrew Lawrence
Location: Addiction Neuroscience Laboratory @ the Florey
Contact: Erin Campbell E: Erin.Campbell@florey.edu.au E: Andrew.Lawrence@florey.edu.au

Project description: Substance abuse is a major health care problem. Accordingly, there is a real need to increase our fundamental understanding of the processes behind addiction, so that more targeted therapeutic strategies can follow. We have identified a potentially critical neural mechanism by which alcohol associated environments promote alcohol seeking during abstinence. We will further unravel the brain mechanisms of relapse to alcohol seeking, and will identify novel brain areas and circuits that future clinical studies can target in treatment-seeking alcoholics.

A limitation identified in animal models is that abstinence is achieved 'non-voluntarily' (experimenter-imposed). In humans, however, abstinence is typically voluntary (self-imposed), despite drug availability and often out of a desire to avoid the negative consequence associated with excessive alcohol use. A recently developed animal model addresses this limitation. In this model, the laboratory animal abstains voluntarily from alcohol use when alcohol-seeking is associated with a negative consequence. We will combine this novel animal model of relapse with an innovative procedure to manipulate neurons in defined neural circuits to determine which Nucleus Accumbens (NAc) shell output is critical for context-induced relapse to alcohol seeking.

22. Salt, opiates and addiction

Supervisors: Dr Craig Smith and Prof Andrew Lawrence
Location: Addiction Neuroscience Laboratory @ the Florey
Contact: Craig Smith E: Craig.Smith@florey.edu.au E: Andrew.Lawrence@florey.edu.au

Project description: We have recently used models of salt depletion / gratification in rodents to examine the central integration of this behaviour. By using gene set enrichment analysis, we found that genes regulated with sodium appetite were enriched for gene sets associated with cocaine and opiate addiction. Given the association of gene changes with salt appetite and opiate addiction, we hypothesize that the process of gratification of a salt appetite involves the release of endogenous opioids within the brain. This would be consistent with a rapid reinforcement that precedes physiological re-normalisation of plasma ionic balance. To test this hypothesis, we examined whether the opioid receptor antagonist, naltrexone (used clinically to treat heroin addicts and alcoholics), had any impact upon a salt appetite. Pretreatment of mice with naltrexone attenuated the gratification of a salt appetite. Furthermore, gratification of salt appetite is augmented in opiate-dependent mice, providing a link between instinctive behaviours and addiction.
Therefore, we aim to delineate the organisation and integration of salt (sodium) appetite in control, opiate-dependent and opiate-withdrawn mice. This will be achieved by a combination of behavioural, anatomical and electrophysiological studies.

23. Peptides and stress-induced relapse

Supervisors: Prof Andrew Lawrence
Location: Addiction Neuroscience Laboratory @ the Florey
Contact: Andrew Lawrence E: Andrew.Lawrence@florey.edu.au

Project description: Using a rat model of alcohol use and alcohol-seeking, we demonstrated that central administration of peptide antagonists for RXFP3 (relaxin family peptide 3 receptor), the cognate receptor for the neuropeptide, relaxin-3, decreased self-administration of alcohol in a dose-related manner and attenuated cue-induced reinstatement following extinction. Given the established role for relaxin 3 signalling in stress responses we also examined stress-induced reinstatement of alcohol-seeking using yohimbine as a chemical stressor. The selective RXFP3 antagonist, R3(B1-22)R, prevented yohimbine-induced reinstatement of alcohol-seeking, an effect greater than that for cue-driven alcohol-seeking. By comparison, RXFP3 antagonist treatment produced no significant change in self-administration of sucrose, suggesting a selective effect for alcohol. RXFP3 antagonist treatment had no effect on general ingestive behavior, activity

or cognition in the paradigms assessed. These data suggest relaxin-3/RXFP3 signalling regulates alcohol intake and relapse-like behavior, adding to current knowledge of the brain chemistry of reward-seeking.
We have extended these findings by using targeted microinjections into brain nuclei that are (i) known components of alcohol-seeking circuitry and (ii) localise dense expression of RXFP3. In this regard, we have shown that local microinjections of R3(B1-22)R into the bed nucleus of the stria terminalis (BNST) reduce alcohol self-administration, and also markedly attenuate stress-induced reinstatement of alcohol-seeking. We hypothesise that stress activates ascending networks containing relaxin-3 to regulate alcohol-seeking via actions at RXFP3 within the BNST and possibly other component areas of the 'extended amygdala'.
Therefore, our aims are to determine the -

- Mechanism by which acute stress activates RLN3 neurons to precipitate relapse to alcohol-seeking.
- Nature of RXFP3-mediated modulation of neural signalling within BNST and the neurochemical phenotype of RXFP3-expressing neurons in forebrain areas implicated in regulation of stress-induced relapse to alcohol-seeking.
- Ability of stress and/or alcohol to regulate RLN3, CRF and orexin systems.

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.

24. The role of urokinase plasminogen activator (u-PA) and its receptor (u-PAR) in arthritis and inflammation

Supervisor: A/Prof 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. Fibrin deposition, cell migration, and tissue destruction and remodeling are key components in the pathology of RA joints. The plasminogen activators (PAs), urokinase (u-PA) and tissue-type (t-PA), which converts plasminogen to plasmin, are implicated in these processes; however their precise roles in such processes, particularly for u-PA and its receptor (u-PAR), have yet to be defined. In this project you will study the role of u-PA and the u-PAR, in inflammation and arthritis using mice genetically altered mice such that u-PA or u-PAR have been rendered inactive. In particular, the effect of u-PA on cell migration to an inflammatory site, on tissue destruction and remodeling, and in activating/suppressing other key cytokines/proteases (eg metalloproteinases (MMPs)) involved in these processes will be studied.

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.

25. The role of granulocyte macrophage colony stimulating factor (GM-CSF) in arthritis and inflammation

Supervisor: A/Prof 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.

26. The role of a novel macrophage inflammatory mediator in arthritis

Supervisors: A/Prof Andrew Cook, Dr Ming-Chin Lee and Prof John Hamilton
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

27. 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).

28. 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 indentify 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 glucocoritcoid-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).

AUTISM

29. Characterising changes in neuronal activity in brain regions regulating aggression in a mouse model of Autism - *also offered as MBiomedSc*

Supervisors: Dr Elisa Hill, Professor Anthony Hannan & Professor Terence O'Brien
Project Site: Department of Medicine (RMH), University of Melbourne
Contact: Elisa Hill E: elhill@unimelb.edu.au;

Project description: Autism Spectrum Disorder (ASD) is a prevalent neurological disorder characterised by impairments in social interactions, communication, and repetitive behaviour. Challenging behaviours including aggression are also commonly associated with ASD. NL3 mice express a mutation in the Neuroligin-3 gene identified in autism patients and show a robust aggressive phenotype. We have shown changes in neural activity in the basal amygdala, a brain region involved in regulating aggressive behaviour, in these mice. This project will extend these studies to examine neuronal activity in two other specific brain regions involved in the neurobiology of aggression: the ventromedial hypothalamus (VMH), and the periaquaductal gray (PAG).

Skills: Characterisation of neuronal subtypes and network activity using patch clamp electrophysiology in brain slices, fluorescence immunohistochemistry in fixed slices for cellular morphology.

30. Understanding gastrointestinal dysfunction in autism – how do synaptic mutations affect enteric neurons? - *also offered as MBiomedSc*

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: E: 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.

Skills: 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.

BONE AND MINERAL RESEARCH

31. Bone health in children and young people with epilepsy treated with anti-epileptic drugs (AEDs) – *also offered as MBiomedSc*

Supervisors: Profesor John Wark, Dr Peter Simm, Professor George Werther, Dr Sandra Petty
Project Site: Department of Medicine (RMH)
Contact: Professor John Wark T: 9342 7109 E: jdwark@unimelb.edu.au

Project Description: Epilepsy and the use of anti-epileptic drugs (AEDs) are known to be associated with low bone mass and the risk of bone disease. In most patients, AED therapy once initiated is taken for many years if not for life. Moreover, it is well-established that AED therapy is a major cause of bone fractures in our community. However, there are still limited data concerning bone problems in children and adolescents taking these medications. We propose a novel study to explore their bone health looking at a number of measures, including analysing bone geometry and bone strength, which have not been described previously in this cohort. We will also follow these patients' growth and development as well as their bone mass accrual and the number of fractures and other injuries that they sustain. These data will give great insight into the effects of epilepsy and its treatment on bone health and lead to improved management of bone health issues in young patients taking AEDs. The findings also will help us to establish a clinical model for the management of bone health in these patients.

Students undertaking this project will gain substantial experience in clinical study design, data collection and management, data analysis and interpretation, as well as translational aspects of biomedical research.

32. Real world assessment of falls risk using novel mobile technology – *also offered as MBiomedSc*

Supervisor: Prof John Wark, Dr Tharshan Vaithianathan, Dr Frances Batchelor
Project Site: Department of Medicine (RMH), National Ageing Research Institute, Parkville.
Contact: Professor John Wark E: jdwark@unimelb.edu.au

Project description: Comprehensive testing regimens for balance and falls risk require sophisticated, expensive laboratory resources and highly-trained staff. The test procedures also do not truly simulate daily living conditions where most falls occur. This project will comprise clinical testing of a novel approach to falls risk assessment using simulated daily living conditions and mobile sway detection technology incorporating low cost inertial sensors (accelerometers, gyroscopes and magnetometers) developed by National ICT Australia (NICTA). The ability to detect age-related differences in performance and impairments, particularly in postural sway, associated with a history of falls will be evaluated and compared with conventional testing procedures. Students will gain first-hand experience in a wide range of functional motor testing, the use of novel motion-sensing technology including signal processing, and in the quantitative analysis of movement data.

BIOINFORMATICS

33. Comparing the importance of genes across species – *also offered as MBiomedSc*

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.

34. Using bioinformatics approaches to unravel the SCN2A neuro-spectrum – *also offered as MBiomedSc*

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.

35. Understanding the genetic changes that contribute to neurological disorders – *also offered as MBiomedSc*

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.

BIOLOGY —WOMEN'S HEALTH

36. Understanding parental support for daughters with significant menstrual health problems – *also offered as MBiomedSc*

Supervisors: Dr Jane Girling, Dr Yasmin Jaysinghe
Project Site: Department of Obstetrics and Gynaecology, Royal Women's Hospital
Contact: Jane Girling E: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.

37. Investigation of genes associated with increased risk of endometriosis – *also offered as MBiomedSc*

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 E: 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.

38. A critical analysis of Sunsmart behaviour in young Australian women - *also offered as MBiomedSc*

Supervisors: Prof John Wark, Dr George Varigos, Dr Asvini K Subasinghe, Prof Suzanne Garland.
Project Site: Department of Medicine, (RMH) Parkville Campus
Contact: E: jdwark@unimelb.edu.au

Project description: Recommendations re sun-smart behaviour can be complex and confusing. What do young women understand about sun-smart behaviour and how do they perceive their own sun-smart behaviour? Young women's understanding of recommended sun-smart behaviours and their perception of their own sun-smart behaviours will be the focus of this research project. Self-reported data will be compared to objectively measured sun exposure using personal UV dosimeters.

39. Air pollution may impair vitamin D status in young Victorian women - *also offered as MBiomedSc*

Supervisors: Prof John Wark, Ms Alexandra Gorelik, Dr Asvini K Subasinghe,
Project Site: Department of Medicine, (RMH) Parkville Campus
Contact: E: jdwark@unimelb.edu.au

Project description: Recent European research has identified a potentially worrying relationship between vitamin D status and local measures of air quality. Is there an association between air quality and vitamin D levels in young women living in Victoria? This project will explore a possible association between air quality in postcode of residence and serum vitamin D levels in young women. Validated models of air quality based on monitored levels of air pollution will be applied to study these relationships.

40. Fear of needles: evaluation of BrightHearts: A biofeedback mediated relaxation/ distraction app

Supervisors: Professor John D Wark, Professor Suzanne M Garland, A/Professor Rachel Skinner, Dr Asvini K Subasinghe
Project Site: Department of Medicine, RMH, Parkville Campus
Contact: suzanne.garland@thewomens.org.au; 8345 3670; jdwark@unimelb.edu.au; 9342 7109 rachel.skinner@health.nsw.gov.au; asvini.subasinghe@mcri.edu.au

Project description: Some young people experience considerable anxiety associated with receiving injections and needles[1], such as in blood collection and immunisation. BrightHearts (BHs) is a novel biofeedback[2] mediated interactive digital artwork app, developed to reduce anxiety and perception of pain during painful medical procedures. BHs uses an iPad to display a colourful geometric artwork and musical sounds, which respond to changes in heart rate transmitted by a wireless wristband heart rate monitor. Users learn to reduce their heart rate through slower breathing and are rewarded with more interesting and intense visual display and sounds.

Aim: to reduce self-reported anxiety and perception of pain, prior to and during venepuncture.

Setting: Participants will be young women aged 16-25 years attending a health assessment visit for the research project SAFE-D.

Design: A randomized controlled trial. 120 women will be recruited to the study and 60 randomly assigned to use BHs before and during venepuncture and 60 to standard practice during venepuncture. Post intervention, all participants will complete an 8-10 minute questionnaire via iPad, assessing pain, fear and anxiety. The primary outcome is self-reported anxiety. We compare anxiety scores between groups. If BHs is found to be successful, it has the potential to be used to reduce anxiety in young people having medical procedures such as venepuncture and immunisation. Given fear of needles has the potential to result in young people avoiding these important procedures, BHs could make a difference in uptake of procedures and improve the procedural experience for young people.

41. Risky behaviours in females aged 16-29 years - *also offered as MBiomedSc*

Supervisors: Prof John Wark, Prof Suzanne Garland, Ms Alexandra Gorelik, Dr Asvini Subasinghe.
Project Site: Department of Medicine, (RMH) Parkville Campus
Contact: Prof John Wark E: jdwark@unimelb.edu.au

There is strong evidence to show that young adults exhibit a number of poor health behaviours such as alcohol use, smoking, lack of physical activity, and risky sexual behaviours. Researchers who have examined risky behaviour patterns have speculated that poor health behaviours established during emerging adulthood may persist into later stages of adulthood.

The Young Female Health Initiative (YFHI) and Safe-D studies are comprehensive female health studies conducted with 16-25 year old females. Students will have the opportunity to investigate the prevalence and determinants of risky behaviours in a representative sample of young Australian females as well as determining variations in these behaviours longitudinally using data collected from two year follow up visits. Findings from this study will be able to consolidate whether established risky behaviours may persist throughout adulthood and may suggest factors that influence these behaviours. This project would suit a student interested in women's health. Suitable for Honours, Masters, PhD or MPH studies.

42. Dietary habits and mental health in females aged 16-29 years - *also offered as MBiomedSc*

Supervisors: Dr Asvini Subasinghe, Prof John Wark, Prof Suzanne Garland, Ms Alexandra Gorelik.
Project Site: Bio21 Institute, Parkville
Contact: Dr Asvini Subasinghe E: asvini.subasinghe@mcri.edu.au

There is a large body of evidence linking a poor intake of nutrients and unhealthy dietary patterns with the development and management of mental health conditions such as depression. Using self-reported and clinical data on mental health and dietary intake data collected from a validated food frequency questionnaire (FFQ), in the Young Female Health Initiative (YFHI) and Safe-D studies, students will have the opportunity to investigate the association between diet and

several indices of mental health and other behavioural and lifestyle factors. There is also an opportunity to determine whether there are any temporal changes in dietary and lifestyle behaviours using data collected from two year follow up visits. Findings from this study will be able to provide insights into the relationship between poor diet and mental health in an at-risk population. Additionally, findings may also provide the framework for targeted intervention strategies. This project would suit a student interested in women's and mental health. Suitable for Honours, Masters, PhD or MPH studies.

43. Risky behaviours in females with Type 1 Diabetes aged 16-25 years - *also offered as MBiomedSc*

Supervisors: Prof John Wark, Prof Suzanne Garland, Ms Alexandra Gorelik, Dr Asvini Subasinghe.
Project Site: Department of Medicine, (RMH) Parkville Campus
Contact: Prof John Wark E: jdwark@unimelb.edu.au

There is strong evidence to show that the prevalence of risky behaviours in young adults with chronic diseases, such as diabetes, is greater than in those without diabetes. The Young Female Health Initiative (YFHI) Diabetes Study is a comprehensive female health study conducted on 16-25 year old females with Type 1 diabetes. Students will have the opportunity to investigate the prevalence of risky behaviours in this cohort and compare behaviour profiles to those of a young healthy female population. Findings from this study will be able to provide insights into the problem of risky behaviours in a young female cohort with diabetes and provide evidence for targeted intervention strategies. This project would suit a student interested in women's health. Suitable for Honours, Masters, PhD or MPH studies.

44. Metabolic health of females with Type 1 Diabetes aged 16-25 years - *also offered as MBiomedSc*

Supervisors: Prof John Wark, Prof Suzanne Garland, Ms Alexandra Gorelik, Dr Asvini Subasinghe.
Project Site: Department of Medicine, (RMH) Parkville Campus
Contact: Prof John Wark E: jdwark@unimelb.edu.au

Though there is strong evidence to show that individuals with Type 1 diabetes are at risk of various metabolic and cardiovascular diseases, there is limited evidence to show these associations in adolescent and young adult females. The Young Female Health Initiative (YFHI) Diabetes Study is a comprehensive female health study conducted on 16-25 year old females with Type 1 Diabetes. Students will have the opportunity to investigate the prevalence of metabolic and cardiovascular risk factors and associated behavioural and lifestyle factors in a young female cohort with type 1 diabetes. Findings from this study will be able to shed light on the health profiles of young females with diabetes and provide evidence for targeted intervention strategies for females in this age group. This project would suit a student interested in endocrinology and cardiovascular health. Suitable for Honours, Masters, PhD or MPH studies.

45. Vitamin D status and mental health outcomes in females aged 16-25 years participating in a randomized controlled trial - *ONLY offered as MBiomedSc*

Supervisors: Prof John Wark, Prof Suzanne Garland, Ms Alexandra Gorelik, Dr Asvini Subasinghe.
Project Site: Department of Medicine, (RMH) Parkville Campus
Contact: Prof John Wark E: jdwark@unimelb.edu.au

There is a large body of evidence supporting a relationship between Vitamin D and poor mental health. Students will have the unique opportunity to investigate the association between Vitamin D and several indices of mental health in females recruited into the intervention component of the Safe-D study (Part B). Participants with 25 OHD levels 25 to 75 nmol/L are randomized to one of three groups in 1:1:1 ratio: a mobile phone–based application designed to encourage safe sun exposure, vitamin D supplementation (1000 IU/day), and a control group. Data collection points are at baseline, 4 and 12 months post baseline with the major endpoints being at 4 months. A wide range of information is collected from participants throughout the course of this study including validated and self-reported information relating to mental health status and lifestyle behaviours. Students will have the fantastic opportunity to investigate a number of relationships between Vitamin D status and indices of mental health. There is also an opportunity to determine whether there are any temporal changes in these associations at 4 months and 12 months after baseline. Findings from this study will help provide an insight into the effects of improving vitamin D levels on several health outcomes, particularly mental health. This project would suit a student interested in mental health. Suitable for Masters, PhD or MPH studies.

46. Vitamin D status and musculoskeletal outcomes in females aged 16-25 years participating in a randomized controlled trial - *ONLY offered as MBiomedSc*

Supervisors: Prof John Wark, Prof Suzanne Garland, Ms Alexandra Gorelik, Dr Asvini Subasinghe.
Project Site: Department of Medicine, (RMH) Parkville Campus
Contact: Prof John Wark E: jdwark@unimelb.edu.au

Low vitamin D levels are associated with an increased risk of numerous chronic health conditions, including poor musculoskeletal health and osteoporosis. However, few researchers have investigated these relationships in young females. We present a novel opportunity for students to investigate these associations in 16-25 year old females participating in a randomized clinical trial as part of the Safe-D study. Participants with 25 OHD levels 25 to 75 nmol/L are randomized to one of three groups in 1:1:1 ratio: a mobile phone–based application designed to encourage safe sun exposure, vitamin D supplementation (1000 IU/day), and a control group. Data from comprehensive surveys, blood tests,

bone densitometry, body composition scans, and Leonardo mechanography tests are available on participants at baseline and at 12 months post baseline. Therefore, students will also have the opportunity to investigate these associations longitudinally. Findings from this study will help provide an insight into the effects of improving vitamin D levels on several health outcomes, particularly musculoskeletal health. Findings from this study will help provide an insight into the effects of improving vitamin D levels on musculoskeletal disorders. This project would suit a student interested in musculoskeletal health. Suitable for Masters, or PhD.

47. Longitudinal analysis of health outcomes in 16-29 year old females - *also offered as MBiomedSc*

Supervisors: Prof John Wark, Prof Suzanne Garland, Ms Alexandra Gorelik, Dr Asvini Subasinghe.
Project Site: Department of Medicine, (RMH) Parkville Campus
Contact: Prof John Wark E: jdwark@unimelb.edu.au

The Young Female Health Initiative (YFHI) and Safe-D studies are comprehensive female health studies conducted with 16-29 year old females. Data are collected via online surveys and clinical site visits for the YFHI study at baseline and at 2 years post baseline. Survey data are available on the following health domains: general health and lifestyle behaviours, mental health, sexual and reproductive health, bone and joint health, cardiovascular and metabolic health, and dietary behaviours. Clinical data include fasting blood tests, anthropometric measurements, sexual health samples, bone mineral density, and body composition scans obtained through site visits. Students will have the novel opportunity to investigate a research question of interest in a representative sample of young Australian females as well as determining variations in health outcomes longitudinally using data collected from two year follow up visits. This project would suit a student interested in women's health. Suitable for Honours, Masters, or PhD.

BRAIN BIONICS

48. 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 – 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.

49. 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 – 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 design and evaluate hemodynamic responses to implanted devices and will assist in optimization of fabrication materials and methodologies

50. 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 – 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.

BRAIN INJURY

51. Treatment with an interleukin 1 receptor antagonist in a novel model of multi-trauma

Supervisors: Dr. Sandy Shultz, Prof. Terence O'Brien, Dr. Bridgette Semple, Dr. Stuart McDonald
Project Site: Department of Medicine RMH, Melbourne Brain Centre, Kenneth Myer Building
Contact: Dr. Sandy Shultz, E: sshultz@unimelb.edu.au

Project description: Traumatic brain injury (TBI) is a leading cause of death and morbidity, and there is no treatment to improve TBI outcomes. Although many TBI patients suffer concurrent bone fractures, pre-clinical TBI research utilises 'single-hit' models not featuring the pathophysiological complexities induced by multi-trauma, which may account for failures in translating pre-clinical findings to the clinical setting.

To address this, Dr. Shultz and his team recently developed an internationally unique mouse model of multi-trauma and identified the pro-inflammatoy cytokine interleukin-1β (IL-1β) as an important factor in the neuropathogenesis of these devastating injuries. This project will now employ this novel mouse model to assess the therapeutic benefits of an IL-1 receptor antagonist (IL-1ra) in multi-trauma. This project will involve advanced neuroimaging, behavioral, cellular, and molecular methods.

52. Biomarkers of brain concussin in Australian Rules Footballers

Supervisors: Dr. Sandy Shultz, Prof. Terence O'Brien, Prof. Andrew Kaye
Project Site: Department of Medicine RMH, Melbourne Brain Centre, Kenneth Myer Building
Contact: Dr. Sandy Shultz, E: sshultz@unimelb.edu.au

Project description: Brain concussion, a common form of mild traumatic brain injury (TBI), is a serious medical and societal issue. Of particular concern are individuals who are at high risk of suffering multiple concussions – such as athletes playing collision sports – because repeated concussions may contribute to chronic neurological impairments and neurodegenerative disease. There is evidence that the long-term adverse effects of repeated concussion are due to the recurring insults occurring before the brain has recovered from the initial concussion and is still in a period of increased vulnerability. Currently there are no reliable markers that indicate when the brain is no longer in this state of increased vulnerability, but the identification of such biomarkers would allow them to be used to guide medical decisions, so as to reduce the effects of repeated concussion.

There are a number of promising concussion biomarker platforms. Physical, psychological, and cognitive symptoms are common after concussion, and symptom scales and neuropsychological testing are currently used in concussion management. Magnetic resonance imaging (MRI) is a non-invasive tool that may identify changes in the brain after a concussion, and monitor the recovery of these changes. Blood samples can be used to measure markers that may provide information about the pathophysiology, progression, and recovery of concussion.

In this project we will us advanced and multimodal MRI, proteomic, behavioural, cellular and molecular methods, to assess the pathophysiology of concussion, and identify MRI, blood, and behavioural biomarkers that can detect these changes and estimate recovery. This will be done in Melbourne University Football club athletes (i.e. amateur Australian Rules Football).

CANCER

53. Examination of circulating pre-treatment biomarkers of patient response to bone marrow transplantation

Supervisors: Rachel Koldej, Joanne Davis, Eric Wong
Project Site: ACRF Translational Research Laboratory, Victorian Comprehensive Cancer Centre
Contact: Rachel Koldej E: rachel.koldej@mh.org.au

Project description: The Royal Melbourne Hospital (RMH) is one of the largest providers of allogeneic haematopoietic cell transplantation (alloHCT) in Australia. AlloHCT is a complex but potentially curative procedure for patients with haematologic malignancies or bone marrow failure syndromes. The fundamental principle of alloHCT is that a donor's haematopoietic stem cells (or graft), when infused into the recipient, will develop into a new set of immunologically active cells that recognise tumour cells as foreign and contain or destroy them. Retrospective studies in alloHCT have been pivotal in unlocking key pieces of knowledge that have shaped and continue to shape transplant clinical practice.

The RMH Bone Marrow Transplant Service already possesses a comprehensive, HREC-approved clinical databank which contains detailed pre- and post-transplant data including crucial outcome measures and the ACRF Translational Research Laboratory (located at the Victorian Comprehensive Cancer Centre) has HREC-approved access to an existing set of archival post-transplant patient samples. We are now examining these samples for markers that predict pre-treatment

how a patient will respond to alloHCT. This would allow the patients treatment to be modified to prevent adverse outcomes including acute or chronic graft-versus-host disease. Markers currently under evaluation include circulating microRNAs, cytokine levels and the presence of single nucleotide polymorphisms in either the transplant donor or recipient. The potential biomarkers to be examined in this project include the chemokine CXCL10 (Ahmed et al, 2015, Bone Marrow Transplantation) and soluble DNAM-1 (Kanaya et al, 2016, PLOS One).

This project combines both laboratory and clinical correlative research and has HREC approval. All samples and clinical data required for the successful completion of the project are available.

54. Psychosocial and behavioural outcomes of women at high pedigree based risk of breast and/or ovarian cancer.

Supervisors: Dr Lesley Stafford, Prof Bruce Mann, Prof Geoff Lindemann
Project Site: Centre for Women's Mental Health, Royal Women's Hospital
Contact: Dr Lesley Stafford. E: Lesley.Stafford@thewomens.org.au T: 61 03 8345 3909

Project description: Data has been collected from 372 women (193 affected by cancer and 178 unaffected by cancer) at high pedigree based risk for breast and/or ovarian cancer who have either had genetic testing for a deleterious gene mutation (BRCA 1 or BRCA 2) with an uninformative result, or who cannot be personally tested for a range of reasons.

It is not well understood how these women perceive their risk of cancer, manage their disease risk or adjust psychologically in the context of a lack of established risk management guidelines.

The cross-sectional data collected relate to risk management practices for breast/ovarian cancer including screening, surgery and lifestyle modification; and psychological morbidity in the form of depression, anxiety, cancer-specific distress and worry. Other psychological data collected include levels of neuroticism and cognitive representations of illness.

55. Glioma stem cells: biology and molecular targets

Supervisor: Dr Andrew Morokoff
Co-Supervisors: A/Prof Kate Drummnod, Prof Andrew Kaye.
Location: Department of Surgery, Royal Melbourne Hospital
Contact: Dr Andrew Morokoff (morokoff@unimelb.edu.au) T: 9035 8586

Project Description: Giomas are common malignant brain tumours with an extremely poor survival because of their highly invasive nature and high recurrence rate. Recently a subpopulation of cells with stem-cell like properties has been identified in gliomas and these cells are thought to be related to recurrence and treatment resistance. Furthermore, certain molecular pathways that lead to invasion, apoptosis and drug resistance effects may be 'switched on' specifically in glioma stem cells. This project involves establishing stem cell cultures directly from surgical brain tumour samples and isolating cancer stem cells in neurspher cultures in vitro. These cell lines will be assessed for alterations of molecular signalling pathways including be new techniques such as next-generation whole genome and transciptome sequencing. These celll lines and mouse xenograft models utilising bioluminescence will be used to test novel compounds targeting these pathways.

56. Twist as a Regulator of EMT in Gastric Cancer and its role in invasion

Supervisors: A/Professor Alex Boussioutas. Co-supervisor: Dr Rita Busuttil
Project Site: Peter MacCallum Cancer Centre
Contact: A/Professor Alex Boussioutas T: +61 03 9656 1287 E: alexb@unimelb.edu.au or alex.boussioutas@petermac.org; Dr Rita Busuttil T: +61 03 9656 1287 E: Rita.Busuttil@petermac.org

Gastric cancer (GC) is often diagnosed at advanced stages, giving patients a 5-year survival of less than 20%. Advanced stage GC is directly correlated with increased local invasion of the cancer through the gastric wall and, at more advanced stages into adjacent structures.

Epithelial Mesenchymal Transition (EMT) is one mechanism which has been proposed as a modulator of invasion in GC as well as other cancer types. This project seeks to expand on previous work in our laboratory exploring the role of TWIST, a master regulator of EMT, in gastric cancer. We have previously shown that TWIST is more highly expressed at the invasive front of the tumor compared to its core indicating that EMT is occurring in this area. It is conceivable that reducing TWIST expression could be used as a means to decrease the invasive capacity of a cancer.

This project will aim to further explore the role of TWIST in the invasion of GC and its potential utility as a therapeutic target. A broad range of techniques including bioinformatics, cell culture, shRNA lentivirus mediated gene knockdown, and molecular biology will be applied.

We are looking for motivated students (both Honours and PhD students) to strengthen our group.

57. Validation of candidate genes involved in the progression of gastric cancer

Supervisors: A/Professor Alex Boussioutas. Co-supervisor: Dr Rita Busuttil
Project Site: Peter MacCallum Cancer Centre
Contact: A/Professor Alex Boussioutas T: +61 03 9656 1287 E: alexb@unimelb.edu.auH
Dr Rita Busuttil T: +61 03 9656 1287 E: Rita.Busuttil@petermac.org

Project Description: Gastric cancer (GC) is the fourth most common cancer globally and in many western countries is usually only diagnosed at advanced stage giving patients a 5-year survival rate of less than 20%. GC has distinct premalignant stages that have significant propensity to progress. The premalignant cascade consists of easily identifiable histological stages from chronic atrophic gastritis (ChG), intestinal metaplasia (IM) and dysplasia. The progression through these stages, particularly IM, takes years, offering a large window of opportunity to intervene. However not all patients with IM will progress and selection of patients for high-risk surveillance would reduce the burden of unnecessary screening, patient anxiety and improve outcomes due to early detection of disease.

Relatively little is known about the key genetic events leading to IM. Our laboratory is currently in the process of completing the first comprehensive analysis of IM in the world and seeks to identify candidate genes involved in the progression of IM to GC that can be used to reliably predict the progression to GC in humans by using a genomics based approach. Identification of such genes offers an opportunity to study the molecular mechanisms involved and pinpoint targets for prevention and therapy. The aim of this project is validate these candidate genes using an independent data set and then characterizing these genes using functional assays and animal models.

We are looking for motivated students (both Honours and PhD students) to strengthen our group. The project will use broad range techniques including bioinformatics, cell culture, animal models and molecular biology.

58. Role of the Tumour Microenvironment in Gastric Cancer

Supervisors: A/Professor Alex Boussioutas. Co-supervisor: Dr Rita Busuttil
Project Site: Peter MacCallum Cancer Centre
Contact: A/Professor Alex Boussioutas T: +61 03 9656 1287 E: alexb@unimelb.edu.auH
Dr Rita Busuttil T: +61 03 9656 1287 E: Rita.Busuttil@petermac.org

Project Description: Gastric cancer (GC) is the fourth most common cancer globally and 7th in incidence in Australia. It has a poor survival rate which can be attributed to the advanced stage at diagnosis in most patients. The molecular and cellular mechanisms underlying the development of GC are not well described.

Traditionally cancer research involved studying the cancer cell itself. More recently, there has been growing interest in studying the normal cells and molecules which surround the cancer cell. This tumour microenvironment consists of a variety of stromal cell types including cells such as fibroblasts. It is believed that the dynamic communication between tumour cells and the surrounding cell types may play a major role in cancer initiation, progression and establishment of metastatic disease. The aim of this project is to investigate tumour-stromal interactions in gastric cancer utilizing established and primary cell lines. Once the molecular pathways by which a tumour cell progresses has been elucidated it is possible that these processes could be exploited in the development of novel therapeutics.

This project will use a broad range of techniques such as live cell microscopy, cell culture techniques and siRNA to interrogate the function of gene products that influence tumour-stroma communication.

Our previous genomic experiments has provided us with a number of exciting candidate genes that may be involved in this interaction. This is novel research that may have a major benefit to our understanding of cancer and improve patient outcomes.

59. Elucidating the role of mesenchymal stem cells in promoting metastasis of ovarian cancer cells – also offered as MBiomedSc

Supervisors: Dr Bill Kalionis (Pregnancy Research Centre, RWH), Dr Nuzhat Ahmed (The Fiona Elsey Cancer Research Institute, Ballarat).
Project Site: Work will be conducted at the laboratories of the Royal Women's Hospital
Contact: Dr Bill Kalionis, Pregnancy Research Centre, RWH. T: 8345 3748
E: bill.kalionis@thewomens.org.au

Hypothesis- Mesenchymal stem cells (MSC) residing in ovarian stroma or in non-ovarian tissues can promote ovarian cancer metastasis.

Specific aims- (i) To determine whether MSC derived from ascites of ovarian cancer patients or those derived from human placenta can alter the growth, invasive and ovcasphere forming abilities of ovarian cancer cell lines in vitro; & (ii) to determine if MSC can alter the response of ovarian cancer cell lines to chemotherapy.

Background/Rationale: MSC within tumour stroma are derived from the resident tissue or from the circulation or recruited from tissues not related to the tumour. Few recent reports have shown MSC to promote cancer metastasis by initiating paracrine signalling or through enriching the population of 'tumour initiating cells' commonly known as 'cancer stem cells'. About 75% of ovarian cancer patients diagnosed at an advanced-stage have peritoneal dissemination in the form of ascites containing single cells and tumour cellular aggregates. Recent data in our laboratory suggests that MSC forms an important component of ascites of ovarian cancer patients. This warrants the need to study the biological alterations (phenotype) induced by MSC on the growth, invasiveness and response to chemotherapy in ovarian cancer cell lines in vitro.

Outcomes/Benefits: This proposal will compare the inherent traits and chemotherapy response of ovarian cancer cells in the presence and absence of MSC. MSC will be isolated from the ascites of ovarian cancer patients as well as from the placenta of women undergoing caesarean section. Differences in the biological phenotype of ovarian cancer cells in the presence and absence of MSC will be assessed by methods such as Western blot, quantitative PCR, immunofluorescence, flow cytometry, MTT and ^{3}H-thymidine uptake assays. The identification of these changes/molecules may lead to the development of novel therapeutic targets either independently or by inhibiting the effects of MSC on ovarian cancer cells. Human ethics application (HEC#09/09) has been approved by the Royal Women's Hospital Human Ethics Committee.

60. TGF- signalling and cancer development

Supervisors: Dr. Hong-Jian Zhu, Dr. Rodney Luwor, Bo Wang, Catherine Winbanks
Project Site: Cancer Signalling Laboratory, Department of Surgery (5th Floor, Clinical Sciences Building, The Royal Melbourne Hospital)
Contact: Dr Hong-Jian Zhu T: 8344 3025 E : hongjian@unimelb.edu.au;
Dr Rodney Luwor T: 8344 3027 E: rluwor@unimelb.edu.au

Project description: Traditionally, key-lock or on-off models dominate the molecular understanding of cellular signalling and disease development, with most studies focusing on linear molecular signalling cascades. With the advent of large scale molecular techniques such as proteomics and microarrays, cross-talk between signalling networks has been implicated to play critical roles in cancer development. It challenges the physiological validity of the switch on-off model. Our lab, using molecular, cellular and gene targeted animal models as well as human patient samples, has established that the moderation of signalling sensitivity by other pathways, rather than a black-white switch on-off, specifically of the TGF (Transforming Growth Factor-) signalling pathways determines cancer progression. These findings have been published in top-ranking biomedical journals including **Nature Medicine** (11:845-52, 2005). Given the medical significance, current works in our lab are supported by 4 NHMRC and 1 Cancer Council grants totalling more than $2 million.

This lab aims to understand the molecular fundamentals of TG signalling mis-regulation and its causation effect on early tumor development and late tumor invasion and metastasis. In particular, we focus on the few major oncogenic molecular pathways' cross-talk with TGF signalling in various stages and types of cancer development. Concurrently, we are also devising strategies utilizing our unique molecular insights to convert tumor-causing signalling to directly tumor-killing.

The following projects are designed for students to participate in forefront cancer research and to achieve excellent novel results in a relative short time frame (9-10 months).

- Project A: Converting oncogene signalling to tumor killing in brain cancer
- Project B: Stat3 mediated impairment of TGF - signalling in head&neck and breast cancer
- Project C: Targeting TGF - signalling expansion in brain tumor invasion

Project D: Regulation of TGF - signaling by Wnt pathway in the development of colon cancer

Techniques to be used: Cell culture, reporter assays (gene expression), adenoviral work, molecular biology, Western and Northern blotting (protein and mRNA respectively), thymidine assays (cell proliferation), real-time PCR, immunofluorescence and immunohistochemistry, siRNA (gene silencing), animal imaging.

Preferred background and quality of student: biochemistry, pathology, medical sciences; good nature as a person, passionate and dedication in research, perseverance in problem solving.

61. Integrated Genomics of metastatic, lethal Prostate Cancer - also offered as MBiomedSc

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. Must have done very well academically.

62. Double Jeopardy – dead prostate cancer cells can't recur – also offered as MBiomedSc

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.

63. STAT3-mediates Resistance to EGFR targeted therapy in Cancer

Supervisors: Dr Rodney Luwor
Project Site: Dept of Surgery, Royal Melbourne Hospital
Contact: T: 8344 3027, E: rluwor@unimelb.edu.au

Project description: During physiological processes the intracellular protein Signal Transducer and Activator of Transcription 3 (STAT3) is activated by many growth factors and cytokines (e.g. EGF, IL-6, IL-11…etc) resulting in transcription of many genes involved in a multitude of cellular processes. However, uncontrolled or un-attenuated STAT3 phosphorylation and activation results in cancer initiation, progression and metastasis of many tumour types. Therefore, understanding how STAT3 is regulated or controlled within the cell is pivotal for cancer biology and may allow greater scope for therapeutic intervention into STAT3-driven tumourigenesis. Recently, we have shown that many colon cancer cell lines are resistant to a clinically approved anti-EGFR monoclonal antibody, Cetuximab. However, blocking STAT3 activation could re-sensitize these tumour cells to the growth inhibitory effects of cetuximab. Therefore we hypothesise that activation of STAT3 provides an alternative mechanism for resistance to EGFR targeted therapy and targeting IL-6, IL-11 or STAT3 can overcome this resistance. Our Honours/Masters program offers students a choice of projects within our STAT3 signalling research. This project seeks to evaluating novel regulators of STAT3 and determining whether these regulators have a role in driving STAT3-mediated resistance to anti-EGFR therapy. We will also assess the potential of

delivering novel inhibitors to STAT3 to inhibit cancer growth and resistance to anti-EGFR agents. Furthermore, this project has the scope to evolve into a PhD project starting in 2018/19 pending the ability of the incumbent student.

Skills acquisition: Cell biology techniques including Cell transfections, western blotting, immunofluorescence staining and confocal microscopy, luciferase reporter assays, RT-PCR and potentially animal handling and injecting

64. The Molecular Determinants of Brain Tumour Progression and Resistance to Therapy

Supervisors: Dr Rodney Luwor, and Dr Theo Mantamadiotis
Project Site: Dept of Surgery, Level 5, Clinical Sciences Building, Royal Melbourne Hospital (also Dept of Dept of Pathology, University of Melbourne)
Contact: Dr Rodney Luwor; T: 8344 3027, E: rluwor@unimelb.edu.au

Project description: Glioblastoma Multiforme (GBM) is the most devastating and aggressive tumour of the central nervous system accounting for approximately 50% of all primary brain tumours. Surgery, followed by irradiation and concomitant and adjuvant temozolomide is now considered the standard of care for GBM patients. However, the overall prognosis remains abysmal for GBM patients with a median survival of only 15 months. The presence of pre-existing intrinsic resistance and the ability of GBM tumours to develop or acquire resistance represents a major challenge to successful treatment. Resistance to temozolomide is common; however the exact mechanisms and key molecules that mediate resistance are not clearly elucidated.

Our Honours/Masters program offers students a choice of projects within two major themes based on our GBM-orientated research. Firstly, projects will be designed to explore novel molecular mediators of GBM proliferation, migration and invasion and potentially evaluate treatment strategies to overcome GBM progression. Alternatively, students will perform projects that seek to explore potential molecular candidates in mediating resistance to current therapy. Both these project directions will ultilise a large set of brain tumour cell lines and human brain tumour tissue and serum archived within our department. Furthermore, this project has the scope to evolve into a PhD project starting in 2018/19 pending the ability of the incumbent student.

Skills/Techniques acquired: Cell biology techniques including Cell transfections, western blotting, immunohistochemistry, confocal microscopy, luciferase reporter assays, RT-PCR, migration and invasion assays and potentially animal handling and injecting.

65. Defining the Epidermal Growth Factor Receptor Signaling Network in Brain Tumour Stem Cells

Supervisors: Rodney Luwor and Dr. Theo Mantamadiotis
Location: Dept of Surgery RMH and Dept of Pathology
Contact: Dr Rodney Luwor E: rluwor@unimelb.edu.au
Dr. Theo Mantamadiotis: theom@unimelb.edu.au;

Project description: Aberrant cell signalling underlies the loss of growth control, enhanced survival, inappropriate migration and drug resistance in tumour cells. In malignant brain tumours such as Glioblastoma Multiforme (GBM), a number of key components of signaling pathways are known to be inappropriately activated due to mutations. The epidermal growth factor receptor (EGFR) is mutated in about 30% of GBM patients. The downstream effects of the EGFRvIII mutation in brain tumour cells leads to a spectrum of cell signaling events which promote the transcription of many genes which orchestrate pro-tumorigenic cell characteristics. A key transcription factor which lies downstream of the EGFR pathway is CREB, which has recently been shown to have a role in regulating cell human brain tumour cell growth. In this project, the activation of CREB, in a variety of human tumour cell lines, including cancer stem cells which express wild-type EGFR and EGFRvIII, will be examined using cell and molecular techniques. The CREB-dependent transcriptome will also be investigated to understand whether there is a distinct set of EGFRvIII CREB-dependent target genes compared to wild-type EGFR.

66. Regulation of invadopodium function and involvement in cancer cell invasion

Supervisors: 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.

67. Molecular biomarkers for Human Papillomavirus-related cancer progression

Supervisors: Dr Alyssa Cornall, Professor Suzanne Garland
Project Site: Women's Centre for Infectious Diseases (RWH), Bio21 Institute
Contact: Dr Alyssa Cornall: alyssa.cornall@mcri.edu.au

Project description: The majority of cancers of the cervix (>99%) and the anal canal (>80%) are associated with Human Papillomavirus (HPV) infection, yet not all HPV infections lead to cancer. Cancer development is preceded by certain molecular changes; these include epigenetic modifications such as methylation of viral gene promoters, and changes to the expression of viral and cellular gene products. Using techniques such as laser capture microdissection (LCM), HPV genotype sequencing, quantitative PCR, sequencing of methylation patterns and analysis of p16 expression, this project will involve the characterization of pre-cancerous lesions based on molecular changes to viral gene regulation, in order to identify molecular markers that can more accurately predict progression to cancer.

68. Human Papillomavirus (HPV) prevalence in Australia following a national vaccination program

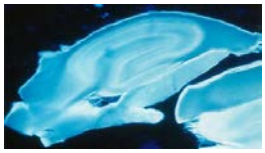
Supervisors: Dr Dorothy Machalek, Dr Alyssa Cornall, Professor Suzanne Garland
Project Site: Department of Microbiology and Infectious Diseases, RWH, Parkville Campus
Contact: Dr Dorothy Machalek: Dorothy.machalek@mcri.edu.au;
Dr Alyssa Cornall: alyssa.cornall@mcri.edu.au

Project description: Human Papillomavirus (HPV) is the causative agent for cervical and a proportion of other anogenital cancers, and of genital warts. In 2007, Australia became the first country to introduce a fully government-funded National HPV Vaccination Program and is now vaccinating boys and girls against HPV genotypes 6, 11, 16 and 18.

Following the introduction of the vaccination program, surveillance of HPV genotypes in the population is required to monitor the impact of the vaccination program in a real world setting. This project will involve genotype testing and analysis of clinical samples collected as part of the National HPV Monitoring Program (called IMPACT). Self-collected genital samples from 18 to 35 year old men and women attending IMPACT sentinel clinics will be tested for the presence of HPV DNA. Data from women will help evaluate the direct effect of the vaccine on vaccinated and unvaccinated female populations, while data from men (most of whom will not have been vaccinated) will provide valuable baseline data on HPV prevalence in men. This project will involve sample logging and processing, DNA extraction, quality control testing, PCR and genotyping, data management and epidemiological data analyses

69. In vitro brain tumour model – studying epileptic seizure development and sensitivity to anti-cancer therapy.

Supervisors: Dr Chris French, Dr Andrew Morokoff, Dr Rodney Luwor
Professor Terence O'Brien
Project Site: Department of Surgery, Department of Medicine RMH,
Melbourne Brain Centre
Contact: Dr Chris French - frenchc@unimelb.edu.au



Project description: Malignant brain tumours are notoriously difficult to treat and are often complicated by severe epileptic seizures. Research into therapies has been hampered by a limited range of model systems to explore pathogenesis and treatment of these tumours. We have developed an *in vitro* model of aggressive brain tumours using a rat brain culture technique. This uses several well-characterised human tumour cell lines as well as tumour "stem-cells" available in our laboratories. These are seeded into a section of brain maintained in tissue culture. The project has two aims – to examine the effects of conventional and novel treatments on the tumours as well as the development of epileptic seizure activity in the system. Seizure development will be assayed by electrophysiological recordings.

This novel technique in this project has the potential to provide important insights into the pathophysiology and treatment of brain tumours and tumour-related epilepsy.

70. Priorities and needs of women living with advanced cancer - *also offered as MBiomedSc*

Supervisors: Dr Jennifer Marino and Dr Michelle Peate
Project Site: Royal Women's Hospital
Contact: E: 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.

CANCER – FERTILITY PRESERVATION

71. Fertility issues in children and adolescents with cancer

Supervisors: Dr Yasmin Jayasinghe, Dr Lisa Orme, Dr Leanne Super
Project site: The Royal Children's Hospital and The Royal Women's Hospital, Melbourne
Contact: E: yasmin.jayasinghe@unimelb.edu.au

Project description: Fertility loss is one of the side effects of cancer treatment. Advances in reproductive technologies may one day offer children and adolescents with cancer, the possibility of future fertility through ovarian or oocyte tissue retrieval and storage prior to commencement of cancer therapy. However such treatments are regarded as investigational in children due to immaturity of gonadal tissue, and also pose unique clinical and ethical dilemmas with respect to informed consent and beneficience for the young person. It is now recommended that where cancer treatment poses a fertility risk, fertility preservation should be discussed with all patients, and with parents or guardians. Long-term survivors report dissatisfaction with the quality of such discussions, or have no memory of them. Over 95% of paediatric oncologists surveyed in Australia and New Zealand believe that centre-specific clinical protocols are necessary to establish standards of care. However such guidelines rarely exist. Furthermore there is little information on recovery of gonadal function post chemotherapy in children and adolescents, to further guide discussions regarding fertility options after chemotherapy.

Several sub-studies are available which may assist with the development of Fertility Preservation guidelines and improve patient outcomes at the Royal Children's Hospital Melbourne, which include:

1. An audit of fertility preservation consultations for patients seen at The Royal Children's Hospital between 2002 and 2014. This project is ethics approved. Specifically the audit will report the proportion of subjects who underwent such discussions, the procedures offered, barriers to uptake of the procedures, and complications. .
2. Evaluation of a 'Fertility Preservation Toolkit'. This is a recently introduced resource for health providers, patients and families which aims to improve knowledge and awareness of fertility preservation options for patients and families by providing information in a standardized manner.
3. Mining the haematology oncology database at the Royal Children's Hospital to examine recovery of gonadal function according to cancer treatment in the young.

Benefits to student: A multi-collaborative project encompassing basic research and clinical interaction. Publication.
Requirements for students: Dedicated, passionate, sensitive and committed. Has done well academically.

72. Fertility after cancer predictor (FoRECAsT) study – also offered as MBiomedSc

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

Project description: Breast cancer is the most frequently diagnosed cancer in reproductive aged women and many women are diagnosed before they have started or completed their families. Fortunately, survival from early breast cancer is almost at 90%. These women then need to deal with the consequences of treatment, such as potential infertility. Research has shown that fertility is a priority amongst these women and concerns about how cancer treatment impacts fertility may influence cancer treatment decisions. Thus, being able to provide women with information about how their fertility will be affected by treatment is important. This can help them to make decision around fertility preservation prior to starting adjuvant treatment. Whilst there is general information about the potential effects of cancer treatments on fertility, there is no mechanism for obtaining personalised information about likely fertility outcomes. Current "calculators" consider cancer type and treatment, but do not consider this in the context of a woman's fertility prior to cancer treatment. The aim of this study is to develop an online fertility predictor targeted at young women with breast cancer. This 'calculator' will take into consideration both intrinsic individual fertility-related characteristics, and the likely impact of cancer treatment to produce a risk of infertility. This tool will be available to women in order to inform decision making around breast cancer treatments.

There are a number of projects available:

a) Exploring needs and potential barriers for the FoRECAsT tool amongst younger women with breast cancer.
b) Exploring needs and potential barriers for the FoRECAsT tool amongst medical oncologists.
c) Determine usability of the FoRECAsT tool using a series of iterated wireframes.
d) Evaluate the acceptability and usability of the functional FoRECAsT tool.

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, data collection and analysis and a goal will be to author a peer-reviewed publication.

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

CARDIOLOGY

73. Cardiac benefits by delayed reperfusion after acute myocardial infarction in mice

Supervisors: A/Prof Xiao-Jun Du, Dr Xiao-Ming Gao
Project Site: Experimental Cardiology Laboratory, Baker IDI Heart and Diabetes Institute, AMREP (Prahran)
Contact: A/Prof XJ Du. T: 85321267; E: xiao-jun.du@bakeridi.edu.au

Project Description: Acute myocardial infarction (AMI) occurs following occlusion of a coronary artery. It is important to re-open the blocked artery to re-establish blood supply to the ischemic myocardium (reperfusion) to save ischemic myocardium from necrosis, i.e. infarct size limitation. Clinically, post-ischemia reperfusion can be achieved most commonly by catheter-based percutaneous primary coronary intervention (PCI) or by thrombolytic drugs. It is usually believed that significant delay (i.e. over 12 hours after onset of ischemic symptoms) in reperfusion does not provide clinical benefits, rather, reperfusion per se may exacerbate further injury to the ischemic heart muscle.

AMI in mice can be induced surgically by coronary artery occlusion. Like human patients, mice with AMI develop cardiac wall rupture, a malignant complication due to post-infarct myocardial inflammation and damage to the extracellular matrix (ECM) architecture of the infarct myocardium. In our recent study on mice, reperfusion was done following 1, 2 or 4 hours after coronary artery occlusion. We observed that the onset of cardiac rupture was completely prevented not only by early, but also by delayed reperfusion (Gao XM, et al: 2012. Due to significantly high metabolic rate in mice, reperfusion following a 4-hour period of ischemia in mice is equivalent to a major delay of reperfusion to humans). This finding clearly indicates benefits achieved by delayed reperfusion. This project is designed to explore the mechanism responsible for such cardiac protection by delayed reperfusion focusing on the extent of inflammation and ECM damage.

The specific aims of this project are:

- To compare delayed reperfusion versus non-reperfusion on the extent of inflammation in the infarct myocardium;
- To determine the extent of ECM damage by biochemical and histological means, between hearts without and with delayed reperfusion;
- To measure the degree of post-infarct ventricular remodelling by non-invasive echocardiography.

Skills: The project will enable the student to gain skills in: understanding the principal of reproducing heart disease models in mice, quantitative histology, biochemical assays, echocardiography in mice, data analysis using a variety of statistical methods.

References

Gao XM, White DA, Liu Y, Dart AM, Du XJ. Post-infarct cardiac rupture: Recent research progress on the pathogenesis and therapeutic interventions. *Pharmacol Ther* 2012;134(2):156-179.

74. Do the coronary small vessels respond less well to medication in patients with diabetes or renal failure – *also offered as MBiomedSc*

Supervisors: Professor Judy Savige and A/Prof Deb Colville
Project Site: NWAC, Northern Hospital, Epping.
Contact: ProfessorJudy Savige, T 8344 3260, j.savige@unimelb.edu.au

Project description: Most research into the causes of heart disease has focused on disease in the coronary arteries but the importance of small vessel disease is recognized increasingly. However the coronary small vessels are difficult to study. Nevertheless whenever the small vessels in the heart are affected, small vessels are diseased throughout the body. This includes the vessels in the retina, which are very accessible using a retinal camera and photography. So we propose to examine the retinal small vessels as a model for the coronary arterioles and determine whether renal failure or diabetes means these vessels are diseased and respond less well to medication.

This study involves recruiting patients from the wards with renal failure or diabetes and testing the effect of a tablet that usually dilates small vessels. You will help the patient fill out a questionnaire and also take their blood pressure and retinal photographs, and then review the photographs under the supervision of an ophthalmologist. In addition the retinal photos will be sent to the Centre for Eye Research Australia for the vessel diameters to be measured precisely. The aim of this project is then to determine whether small vessels are less responsive in diabetes and renal failure, and whether medication doses should be increased. The analysis includes univariate and multivariate statistics and backwards linear regression (we will help you with the statistics).

Techniques to be used and skills acquired: This project involves a lot of patient contact, going onto the wards and getting to know hospital staff, learning how to take retinal photographs, and how to interpret abnormalities, as well as statistics.
Feasibility: We already have Human Research Ethics Committee Approval for this project and many of the medical students who have undertaken similar projects during an AMS yyear have achieved a publication from their work.

75. Natural History of Coronary Plaque Evolution Through Optical Coherence Tomography– *ONLY offered as MBiomedSc*

Supervisor/s: A/Prof. Peter Barlis, Dr. Vikas Thondapu; Prof Andrew Ooi, Dr. Eric Poon
Project Site: Department of Mechanical Engineering, Parkville
Contact: Dr Vikas Thondapu E: vthondapu@gmail.com

Project description: Despite groundbreaking advances in cardiology over the past several decades, cardiovascular disease remains the most common cause of death worldwide. The unfortunate reality is that many coronary plaques remain asymptomatic until acute rupture and vessel occlusion, forming a clear impetus for the earlier identification and treatment of high-risk lesions. Intracoronary optical coherence tomography (OCT), a light-based analog of intravascular ultrasound, provides a tenfold improvement in resolution, allowing *in vivo* imaging of coronary plaques with near-histologic clarity.

This project aims to evaluate the natural history of coronary plaque over 6 months through analysis of angiographic and OCT-derived plaque features. Students will also have the opportunity to engage in state-of-the-art computational fluid dynamic modeling to better understand the role of local micro-hemodynamics in plaque evolution. This work will improve our fundamental understanding of plaque evolution, better define the role of intravascular imaging in the identification of high-risk plaques, and has a potentially high impact in the prospective diagnosis and treatment of coronary artery disease.

Baseline and follow-up angiography and OCT imaging has already been completed in a series of 60 patients. Students will be trained in quantitative coronary angiography and OCT plaque analysis. Those interested in computational modeling will be guided in 3D coronary artery reconstruction and computational fluid dynamic methods.

76. Evaluation of Coronary Stent Apposition and Intimal Healing Through Opitcla lCoherence Tomography – *ONLY offered as MBiomedSc*

Supervisor/s: A/Prof. Peter Barlis, Dr. Vikas Thondapu; Prof Andrew Ooi, Dr. Eric Poon
Project Site: Department of Mechanical Engineering, Parkville
Contact: Dr Vikas Thondapu E: vthondapu@gmail.com

Project description: Stent placement is the standard of care in the treatment of occlusive coronary artery disease. The vast majority of patients show improvement and remain asymptomatic after stent placement, however a small but significant subset of patients are prone to adverse long-term complications such as in-stent restenosis and stent thrombosis. The causes of these potentially catastrophic late outcomes remain unclear, but early evidence points to features such as incomplete stent strut apposition and persistently uncovered stent struts. Optical coherence tomography, a high-resolution intravascular imaging technique, offers unprecedented *in vivo* visualization of individual stent struts and tissue coverage patterns, and is thus an ideal tool to evaluate potential risk factors for late adverse stent complications.

This project aims to compare the stent apposition and late tissue healing characteristics of two commonly used second-generation drug-eluting stents. Students will also have the opportunity to explore the effect of stent malapposition on local micro-haemodynamics through state-of-the-art computational fluid dynamic modeling. Given that over 4 million stents are placed annually around the world, this high-impact project has potentially great clinical significance.

Baseline and follow-up angiography and OCT imaging has already been completed in a series of 60 patients. Students will be trained in quantitative coronary angiography and OCT stent analysis. Those interested in computational modeling will be guided in 3D coronary artery reconstruction and computational fluid dynamic methods.

CARDIOVASCULAR

77. Sex Hormones and Cardiovascular Disease in Postmenopausal Women - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeke E: cszoeke@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 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.

78. Lipoproteins and Cardiovascular Risk from Mid-to-Late-Life in Women - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeke E: cszoeke@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.

79. The Relationship of Physical Activity, Body Composition and Cardiovascular Risks in Older Women - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeke E: cszoeke@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, giving clinical skills experience
- There is opportunity for a publication

CLINICAL RESEARCH – SLEEP AND THE URINARY TRACT

80. Non-respiratory effects of CPAP in persons with sleep disordered breathing

Supervisor: Dr Jeremy Goldin and Dr Wendy Bower
Project Site: Dept of Respiratory and Sleep Medicine, City Campus Royal Melbourne Hospital
Contact: Dr Wendy Bower T: 61 3 83872194 E: wendy.bower@mh.org.au

Project Description: Sleep Disordered Breathing (SDB) with recurrent upper airway obstructions induces acute and chronic haemodynamic effects. During the obstructive phase negative intrathoracic pressures increase myocardial oxygen consumption and change ventricular load. Arterial blood pressure rises at the end of the apnoea episode with parallel repetitive bradycardia and tachycardia episodes occurring during sleep. Over time patients can develop systemic hypertension, inflammation and atherosclerosis. The beneficial impact of positive pressure ventilation on respiratory patterns in people with sleep apnoea is well known. Recently, however, it has been observed that comorbidities in these patients also improve after CPAP. To date there has been a lack of baseline data quantifying symptoms such as hypertension, postural hypotension, sleep dysfunction, mood disorders, nocturia, urinary urgency and urge incontinence episodes. The aim of this project is to capture baseline variables likely to be reflective of brainstem function and to measure change over the duration of CPAP therapy. This is a nested study that will include all aspects of the research process, culminating in a national level presentation and peer-reviewed publication.

CLINICAL RESEARCH – SURGICAL

81. The utility of colonoscopy in women of child bearing age

Supervisors: Ms Karen L Barclay
Project Site: Melbourne Medical School, Epping Hospital
Contact: E: karen.barclay@nh.org.au or kbarclay@unimelb.edu.au;

Project description: To establish the outcomes of colonoscopies performed for women of child-bearing age and attempt to assess the utility of haematinics and occult-blood testing in prioritization.

Colonoscopy is a scarce resource and has potential risks. Women of child-bearing age are more likely to have abnormal haematinic indices which may result in referral for colonoscopy. In our clinical setting, the outcomes of colonoscopy performed for this indication are unknown, as is the utility of laboratory measures.

The student would review colonoscopies performed at the Northern hospital in women of child-bearing age and match the results with clinical and laboratory measures. The information would be used to provide evidence for or against tests and colonoscopy in this group.

Potential students are requested to forward a CV, Academic transcript and statement of interest.

82. Opportunities to diagnose Colorectal Cancer – are we missing them?

Supervisors: Ms Karen L Barclay
Project Site: Melbourne Medical School, Epping Hospital
Contact: E: karen.barclay@nh.org.au or kbarclay@unimelb.edu.au;

Project description: To establish the proportion of people treated for CRC at TNH for whom an opportunity for earlier diagnosis may have been present

The researcher would conduct a retrospective clinical record review of patients managed for Colorectal Cancer and establish which patients have been present within the institution within the last few years in order to see if earlier diagnosis may be possible by the introduction of a generalised screening process. Patients with Colorectal Cancer would be identified from the colorectal database and clinical records and databases used to identify hospital attendances. The information would be recorded and analysed to assess the proportion of patients for whom a generalised screening process may allow earlier diagnosis of CRC.

Potential students are requested to forward a CV, Academic transcript and statement of interest.

83. A scoring system for the assessment of process in rectal cancer management

Supervisors: Ms Karen Barclay
Project Site: Melbourne Medical School, Epping Hospital
Contact: Ms Karen Barclay karen.barclay@nh.org.au

Project description: Standards of care are critical in any type of oncologic surgery. In the management of rectal cancer, key processes in the pathway of care have been shown to lead to improved outcome. Although audit processes are in place in most centres of repute, it is difficult to demonstrate due process simply and quickly. The current study looks at an original scoring system for assessing key areas of practice. The aim is to show the scoring system is easy, reproducible and a simple way of showing practice standard is adequate or highlighting areas for improvement.

Potential students are requested to forward a CV, Academic transcript and statement of interest.

84. The presentation of colorectal cancer in the era of screening

Supervisors: Ms Karen Barclay
Project Site: Melbourne Medical School, Epping Hospital
Contact: Ms Karen Barclay karen.barclay@nh.org.au

Project description: Since the introduction of the National Bowel Cancer Screening Programme in 2006, little information is available about the effect on presentation of Colorectal Cancer (CRC). With an increase in awareness of screening and numbers of people offered screening over time, it could be expected that more people would be presenting with screen-detected rather than symptomatic tumours. This project looks at the presentation of CRC over time to see whether this has occurred or not.

Potential students are requested to forward a CV, Academic transcript and statement of interest.

COLORECTAL MEDICINE AND GENETICS

85. Serrated Polyposis Syndrome - *also offered as MBiomedSc*

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

86. Prospective studies on penetrance for cancer in Lynch Syndrome – *also offered as MBiomedSc*

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

87. CAPP3: a randomized controlled trial of aspirin dosage in Lynch Syndrome – *also offered as MBiomedSc*

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 si an international study lead from Newcastle UK, with Australian leadership from RMH. Students will learn about multi centre, multi national RCTs, be immersed in aspirin science and cancer genetics, and participate in the clinical aspects of management of Lynch Syndrome.

88. 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.

89. 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).

90. PillCam Colon and IBD – *also offered as MBiomedSc*

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 intereobserver stusies, and comparing any changes in clinical management as a result of the information provided by the capsule.
This project is attractive to Scholarly Selective students; Honours students need to express interest early!

91. 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- 8417 9900 or 03- 9342 7584 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, IL1β and TNFα. 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.

ELECTROPHYSIOLOGY

92. How do Anti-Epileptic Drugs Work? - *also offered as MBiomedSc*

Supervisor: Dr Chris French
Project Collaborators – Prof T O'Brien, Prof D Williams
Project Site: Department of Medicine (RMH), Royal Melbourne Hospital
Contact: Dr Chris French T: 8344 3276 E: frenchc@unimelb.edu.au
Website: http://sites.google.com/a/hfbg1.net/crf_lab/

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

93. How do Antipsychotic Drugs Trigger Seizures? - *also offered as MBiomedSc*

Supervisor: Dr Chris French
Project Collaborators – Prof T O'Brien, Prof D Williams
Project Site: Department of Medicine (RMH), Royal Melbourne Hospital
Contact: Dr Chris French T: 8344 3276 E: frenchc@unimelb.edu.au

Project Description: The treatment of psychosis and schizophrenia has been greatly improved with the use of anti-psychotic drugs such as chlorpromazine, haloperidol and newer drugs such as clozapine. One significant side effect of these drugs is that they tend to lower the threshold for epileptic seizures to occur. The aim of this project is to quantify enhanced seizure activity with this type of drug using the in vitro brain slice technique. Seizure provocation threshold, synaptic transmission and single neuron properties will be assessed using rat hippocampal brain slices after acute application of these drugs.

94. Multi-Electrode Recording in the Rat Brain - *also offered as MBiomedSc*

Supervisor: Dr Chris French
Project Collaborators – Prof T O'Brien, Dr P O'Brien
Project Site: Department of Medicine (RMH), Royal Melbourne Hospital
Contact: Dr Chris French T: 8344 3276 E: frenchc@unimelb.edu.au

Project Description: Although immense advances have occurred in recording electrical signals from the CNS, these observations tend to be of single cells in a matrix of many millions of neurons and hence give very limited information about how the whole highly interconnected network functions. One solution to this problem is to use banks of tetrodes, bundles of four 10-20 micron diameter electrodes to record many cells simultaneously, either from a single region or from different parts of the brain. Up to 32 electrodes can be implanted with our system, and sophisticated spike detection and analysis algorithms are available to organize the complex multiple signals recorded. This recording technique can also be easily adapted to exploring epileptiform discharges in models of both focal and generalised epilepsy (including drug effects), which will the main aim of this project. This project provides opportunity to learn cutting-edge electrophysiological and computing analysis techniques for assessment of function of the mammalian nervous system.

EPILEPSY AND NEUROPHARMACOLOGY

95. Neuropharmacological strategies for disease modification and prevention of the development of epilepsy – also offered as MBiomedSc

Supervisors: Dr Pablo Casillas-Espinosa, Dr Kim Powell, Prof Terence O'Brien, Dr. Sandy Shultz, A/Prof. Nigel Jones.
Project Site: The Department of Medicine, The Royal Melbourne Hospital, and The Melbourne Brain Centre, Parkville.
Contact: Pablo Casillas-Espinosa E:pablo.casillas@unimelb.edu.au; Kim Powell E:kpowell@unimelb.edu.au

Project description: Current therapies for epilepsy are symptomatic, only suppressing the symptoms (seizures), but do not impact the development or progression of disease. Many groups around the world, including ours, are testing novel therapies to impact epileptogenesis, intervening very early in epilepsy development to limit the severity of disease, with some preclinical success. But most patients present at the clinic already experiencing seizures, so a more practical strategy would be to attempt to modify epilepsy disease progression.

For this project, we will investigate whether our novel treatments can reverse epilepsy severity in a rat model of acquired epilepsy in cases of established epilepsy. We then evaluate if the animals are having less seizures, behavioural comorbidities and neuroimaging changes after the completion of treatment. If the results are positive, they would have major clinical implications in patients with already established acquired epilepsy. Moreover, the experimental drugs that we will be tested have a favorable safety profile in early phase clinical trials facilitating the translation of the results of this preclinical study into a clinical trial.

Skills: The skills expected to be learnt from this projects include: Small animal handling and neurosurgery (electrode implantations), animal models of temporal lobe epilepsy, behavioral neuroscience, magnetic resonance imagining interpretation and analysis.

Projects available

1. *Anti-epileptogenic effects of novel T-type calcium channel blocker.*
2. *Behavioural changes and Imaging the during the epileptogenic process*

96. Biomarkers of epileptogenesis and epilepsy disease progression – also offered as MBiomedSc

Supervisors: Dr Pablo Casillas-Espinosa, Dr Kim Powell, Dr. Sandy Shultz, A/Prof. Nigel Jones. Prof Terence O'Brien
Project Site: The Department of Medicine, The Royal Melbourne Hospital, and The Melbourne Brain Centre, Parkville.
Contact: Pablo Casillas-Espinosa E:pablo.casillas@unimelb.edu.au; Kim Powell E:kpowell@unimelb.edu.au

Project description: A biomarker is an objectively measured characteristic of a normal or pathologic biological process. The development of novel interventions to treat, cure, and prevent epilepsy would benefit greatly from the identification and validation of such biomarkers. In addition, identification of biomarkers may facilitate the development of novel interventions to prevent epilepsy; to prevent the occurrence of epileptic seizures, reverse progression of epilepsy, and potentially even cure epilepsy after it is established. This project will investigate blood- and brain-derived biomarkers of epileptogenesis (the development of epilepsy) and of disease progression of epilepsy using small animal models.

Skills: The skills expected to be learnt from this project include: Small animal handling and neurosurgery (electrode implantations), models of acquired epilepsy, blood and cerebrospinal fluid (CSF) collection, EEG recordings and analysis, and biochemical and molecular analysis (subcellular fractionation, western blotting), magnetic resonance imagining interpretation and analysis.

Project: **Serum, cerebrospinal fluid and neuroimaging biomarkers of epilepsy**

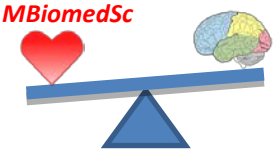
97. Reducing Epilepsy Deaths – Learning from the NCIS (National Coronial Information System)

Supervisors: Dr Rosemary Panelli
Project Site: The Melbourne Brain Centre, The Department of Medicine (RMH)
Contact: Dr Rosemary Panelli E: rpanelli@unimelb.edu.au

Project Description: The most common epilepsy-related cause of death remains a mystery. Epilepsy carries a risk of premature death that is 2-3 times higher than for the general population and a risk of sudden death 20 times higher. The mean age of death is low and the number of Years of Life Lost is high. Sudden Unexpected Death in Epilepsy (SUDEP) is the term now used to describe these unexplained deaths but recognition and appropriate reporting is inconsistent internationally and the incidence is difficult to assess.

The Australian National Coronial Information System is unique internet-based data storage and retrieval system and research access to such a comprehensive database is rare in the international context.The objective of this study is to identify and analyse all information held in the NCIS database concerning epilepsy-related deaths. The NCIS data is extensive and valuable due to the large number of these deaths which occur in the community setting. A systematic examination of the NCIS documents (police reports, post-mortem results, toxicology, and coroners' findings), will allow the researchers to clarify the frequency of SUDEP and to identify any patterns or common factors associated with the deaths, thus enabling a more informed characterisation of epilepsy-related death and risk in this country. The project will include extensive assessment and interpretation of forensic and police reports, database development, critical analysis of the data, and preparation of information for publication.

98. Keeping the Brain and the Heart in Sync – HERG channels in the CNS - *also offered as MBiomedSc*



Supervisors: Dr Chris French,
Project Site: Melbourne Brain Centre
Contact: Chris French frenchc@unimelb.edu.au

Project description: (H)ERG ("human ether a go-go") ion channels are important in for pacing the heart. Genetic disorders of this channel or drug inhibition lead to serious cardiac arrhythmias. It is known that (H)ERG channels are also in the mammalian CNS, but there is almost no data on their effects on neural function. Recent studies in this lab have disclosed evidence of electrical activity of these channels in rat hippocampus, and that they are exquisitely sensitive to antipsychotic drugs. Additionally, computer simulations show activity of this channel may modulate brain rhythms known to be important in epilepsy and schizophrenia. The project will involve further characterization of these channels in single neurons, as well as looking at how brain rhythms and epileptic activity in brain slices are affected by these channels, especially their modulation by antipsychotic drugs. Additionally, we will have the unique opportunity of studying these channels in human brain tissue obtained from neurosurgical procedures.

99. Modelling Epilepsy and Epilepsy Drug Effects–Computational Neuroscience Project

Supervisor: Dr Chris French
Project Site: Department of Medicine , MBC Neurosciences Building, Parkville
Contact: Dr Chris French T: 9035 6376 E: frenchc@unimelb.edu.au

Project Description: It is unclear how large scale electrical oscillations in the CNS are produced with epileptic seizures. Simple hyper-excitability of individual ion channel types and abnormalities of synaptic transmission are undoubtedly important. However, at the network level, recurrent excitation and inhibition from interneurons must be crucial, and may explain why some anti epileptic drugs (AED's) produce paradoxical exacerbation of seizures. This project involves modelling small networks (initially just 2 neurons) to examine the dynamics of seizure production, as well as how certain anti-epileptic drugs suppress or occasionally exacerbate network oscillations. This modelling involves incorporating novel experimental data from this laboratory on normal and drug affected ion channel mechanisms, as well as the effect of glial (supporting cells) cell interactions. The program "Neuron" will be mainly used for the simulations. Some programming experience is necessary, but the modelling language is relatively simple. This project provides an opportunity to gain an in-depth understanding of ion channel kinetics and non-linear behaviour of individual neurons and networks, with a strong clinical relevance.

100. Sodium Channels in Epilepsy - *also offered as MBiomedSc*

Supervisors: Dr Chris French, Prof Terence O'Brien
Project Site: Department of Medicine (RMH), MBC Neurosciences Building, Parkville
Contact: Dr Chris French T: 9035 6376 E: frenchc@unimelb.edu.au

Laboratory Overview. The O'Brien Laboratory in the Department of Medicine, University of Melbourne, has a wide range of research activities related to the neurological disorder epilepsy. Projects include molecular biological studies, *in vivo* and *in vitro* electrophysiology, advanced imaging techniques, animal behaviour models, pharmacogenomics as well as comprehensive clinical

Project Overview. The project will be to study voltage-gated sodium channels, membrane proteins that are the basis of almost all electrical signaling in the nervous system, and so of the greatest significance in normal function, as well as disease states including epilepsy. Properties of normal channels in rat brain cells and cloned channels in tissue culture will be studied, as well as the effects of common anti-epileptic drugs (AED's). We are particularly interested in examining how minor genetic variations impact on AED action. Opportunities for mathematical modeling and computational simulations of nerve cell activity are also available.
The project thus offers a very wide range of possibilities for advanced skill acquisition, including molecular biological techniques, patch-clamping and computational neuroscience. Several publications are anticipated. Additionally, a very high priority is placed on basic research skill acquisition, including experimental design and analysis, statistical techniques, familiarity with common molecular biological methods, as well as public presentation of research findings.

101. Long-term outcome of newly diagnosed epilepsy - *also offered as MBiomedSc*

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: Seventy million people have epilepsy with 34–76 per 100,000 developing the condition every year. To formulate rational treatment plans, it is important to understand the different clinical courses and patterns of response to antiepileptic drugs, ideally by following outcomes from the point of treatment initiation.

This project will perform analysis focusing on response to the initial therapies and their relationship with long-term treatment outcomes and development of pharmacoresistance in newly treated epilepsy patients. The project will be based on the expanding database of new onset epilepsy at RMH. The student will be involved in recruiting and following up eligible patients. Basic knowledge and skills in biostatistics is preferred.

102. Does epilepsy cause a secondary cardiac channelopathy?

Supervisors: Dr. Kim Powell, Prof Terence O'Brien, Dr. Marian Todaro
Project Site: The Department of Medicine, The Royal Melbourne Hospital and Melbourne Brain Centre, Parkville
Contact: Dr KimPowell E: kpowell@unimelb.edu.au; Prof Terence O'Brien E: obrientj@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 results in secondary changes in cardiac ion channel expression and function that could contribute to an increased risk of cardiac arrhythmias and therefore SUDEP.

Aims: To investigate whether patients with chronic epilepsy have alterations in cardiac electrophysiology and ion channel expression compared to matched non-epileptic control subjects.

Methods: This will be investigated by examining cardiac tissue from patients with chronic epilepsy collected during open heart surgery at the Royal Melbourne Hospital and Melbourne Private. This tissue collected will be atrial muscle, which is routinely excised, and discarded as part of the routine cannulation of patients that are being placed on cardiopulmonary bypass for cardiac surgery. These patients would be identified by using a screening questionnaire given to all patients during the pre-admission clinic assessment. Identified patients will then be given a more detailed interview collecting data about their epilepsy syndrome, aetiology, duration, seizure frequency, and medication history. Control subjects will be patients without a history of epilepsy matched to the epilepsy patients for age, sex, cardiac disease status in a ratio of 1:3 (i.e. three controls for each patient with epilepsy). The mRNA and protein levels for the ion channels, HCN2 and 4 channels, which are expressed both in the hearth and the brain will be measured, and compared between the epilepsy and control patients. The patients' ECG recordings will also be compared for significant electrophysiological difference. Any significant molecular or electrophysiological changes identified will be correlated with the epilepsy syndrome (i.e. genetic vs. acquired), the duration of epilepsy and the seizure frequency. Parrellel studies are being undertaken in animal models of chronic epilepsy to enable the mechanisms causing the epilepsy-associated cardiac changes to be better elucidated.

Outcome: This study has the potential to identify the mechanism responsible for epilepsy-associated cardiac dysfunction and thereby provide an opportunity to target interventions that can prevent the cardiac dysfunction, and mitigate the risk of SUDEP.

103. Investigating molecular and physiological determinants of Sudden Unexplained Death in Epilepsy in acquired and genetic animal models of epilepsy - *also offered as MBiomedSc*

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

Project Description: Epilepsy is associated with an increased risk of sudden unexplained death (SUDEP), possibly due to cardiac arrhythmias, although the precise mechanism remains unknown. SUDEP is considered the most important direct epilepsy-related mode of death and accounts for up to 30% of all deaths in the epilepsy population, being particularly prevalent amongst young patients with uncontrolled or drug-resistant, frequent and severe generalized tonic-clonic seizures.

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)).

Several projects will be offered to investigate different aspect of SUDEP and cardiac dysfunction in animal models of genetic and acquired epilepsy

Project 1: To investigate the molecular mechanisms contributing to the cardiac dysfunction on genetic and acquired animal models of epilepsy.

Project 2: To investigate if decreased HCN2 expression translates to a decrease in HCN channel current (*If)* in cardiomyocytes in animal models of genetic and acquired epilepsy.

Project 3: To investigate if by pharmacologically suppressing seizures we can alleviate the altered cardiac electrophysiological function and HCN2 and T-type calcium channel transcriptional repression

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).

104. Stargazin and AMPA receptor expression at cortical synapses in epileptic rats - *also offered as MBiomedSc*

Supervisors: Dr Kim Powell, Dr Pablo Casillas-Espinosa and Prof Terence 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: Absence seizures, one of the most common seizure types in humans with idiopathic generalised epilepsy (IGE), are generalised non-convulsive events characterised by recurrent episodes of staring with unresponsiveness. Absence seizures most commonly affect children and adolescents who can experience hundreds of seizures per day and if left untreated can lead to disruptions in learning. Despite the important recent identification of genetic mutations in some rare families with IGEs showing a monogenic inheritance, in the common situation (>95% of sufferers) with complex inheritance patterns the genetic determinants of the absence seizures are still unknown. These epilepsies are presumed to be polygenic, with more than one genetic variation contributing to the phenotype, but the nature of these variations and how they interact to result in epilepsy remains to be determined**.** GAERS are a strain of rats which spontaneously develop generalized absence seizures.

AMPA receptors are ionotropic transmembrane receptors for the excitatory neurotransmitter glutamate, which mediates fast synaptic transmission in the central nervous system. Stargazin is the archetypal member of a family of proteins called Transmembrane AMPA Receptor regulatory Proteins (TARPs), and is critical for the trafficking and anchoring of AMPA receptors to synaptic membranes. Stargazin also influences electrophysiological properties of AMPA receptors including the slowing of deactivation and reducing desensitization rates. This newly identified TARP role for stargazin may have major functional implications on the homeostatic balance of neuronal excitation, and potentially for the pathophysiology of epilepsy. Recent work from our lab has shown increased expression of stargazin at neuronal membranes in the somatosensory cortex of epileptic GAERS animals, a brain region thought to be involved in the generation of absence seizures. These animals also show increased membrane AMPA receptor expression, which may be driven by elevated stargazin levels. Stargazin is known to interact with other synaptic proteins to localise AMPA receptors to the post-synaptic density (PSD), the region of the postsynapse opposite sites of neurotransmitter release.

The specific aims of this project are

- To biochemically isolate the PSD from the somatosensory cortex of epileptic GAERS and non-epileptic control (NEC) rats
- To compare PSD localization of stargazin, AMPA receptor subunits and other synaptic proteins in GAERS and NECs
- To correlate membrane and synaptic expression of stargazin and AMPA receptors with seizure parameters

Skills: The skills expected to be learnt from this project include: Small animal handling and neurosurgery (electrode implantations), EEG recordings and analysis, and biochemical and molecular analysis (subcellular fractionation, western blotting).

105. Investigating the role of a Cav3.2 calcium channel mutation in contributing to the epileptic phenotype using congenic rat strains and a knock in mouse model - *also offered as MBiomedSc*

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

Project Overview: Absence seizures, one of the most common seizure types in humans with genetic generalised epilepsy (GGE), are generalised non-convulsive events characterised by recurrent episodes of staring with unresponsiveness. Absence seizures most commonly affect children and adolescents who can experience hundreds of seizures per day and if left untreated can lead to disruptions in learning. Despite the important recent identification of genetic mutations in some rare families with IGEs showing a monogenic inheritance, in the common situation (>95% of sufferers) with complex inheritance patterns, the genetic determinants of the absence seizures is still unknown. These epilepsies are presumed to be polygenic, with more than one genetic variation contributing to the phenotype, but the nature of these variations and the mechanisms by which they act to result in epilepsy remains to be determined. In an important, well characterised model of GGE with absence seizures, the Genetic Absence Epilepsy Rats from Strasbourg (GAERS), our research group has discovered a homozygous, missense, single nucleotide (G to C) mutation in the $Ca_v3.2$ T-type calcium (Ca^{2+}) channel gene (Cacna1h) resulting in an amino acid from arginine to proline (R1584P). The R1584P mutation correlates with the epileptic phenotype in GAERS doubled crossed with Non-Epileptic Control (NEC) rats. Additionally, the R1584P mutation increases the rate of recovery from channel inactivation in a splice variant specific manner, producing a predicted gain-of-function phenotype.

We have a knock-in mouse model of the R1584P $Ca_v3.2$ mutation as well as two congenic rat strains; a NEC strain expressing the R1584P mutation and a GAERS strain without the R1584P mutation which we will use as tools to investigate the neurobiological mechanisms by which the R1584P mutation results in is pro-absence effects. These experiments will explore further the specific role played by the R1584P mutation in the absence phenotype of GAERS and the effect of genetic background.

Project 1: To examine the expression of spike-wave-discharges (SWD) in two different congenic rat strains, an NEC congenic strain expressing the R1584P mutation and a GAERS congenic rat strain without the R1584P mutation.

Project 2: To characterise the epileptic phenotype of a knock-in mouse expressing the R1584P mutation and to investigate the effect of genetic background.

Skills: The skills expected to be learnt from this project include: Small animal handling and surgery, EEG recording and analysis.

106. Investigations into the role of neuropeptide y in a genetic rat model of absence epilepsy - *also offered as MBiomedSc*

Supervisor: Prof Margaret Morris, Prof Terence O'Brien, Dr Kim Powell
Project Site: Department of Medicine (RMH), MBC Neurosciences Building, Parkville.
Contact : Dr Kim Powell T : 9035 6394 E : kpowell@unimelb.edu.au

Project Description: The Genetic Generalised Epilepsies (GGE) account for approximately 30% of all epilepsy patients, and patients may manifest a variety of different seizure types. Absence seizures are one of the most common seizure type in GGE and are characterised by a classical 3Hz generalised spike-and-wave discharge (SWD) on EEG resulting in abrupt episodes of interrupted consciousness. SWDs develop from natural neural oscillations within the thalamocortical circuitry, which is comprised of three structures; somatosensory cortex (SCx), ventrobasal nucleus and reticular nucleus (nRT) of the thalamus**.** The underlying aetiology for this disorder is still unknown. However, there is rapidly accumulating evidence for an anti-seizure role of Neuropeptide Y (NPY) in animal models of both focal and of generalised epilepsies. NPY is a 36-amino acid neuropeptide that acts as a neurotransmitter in the brain and has several different functions including increasing food intake and storage of energy as fat, reducing anxiety and stress, reducing pain perception, affecting the circadian rhythm, lowering blood pressure, and controlling epileptic seizures.

This study will investigate the efficacy of enhancing NPY expression focally in selected thalamocortical brain regions using a recombinant adenovirus viral vector in suppressing seizures in Genetic Absence Epilepsy Rats of Strasbourg (GAERS) model of GGE.

Skills: Small animal handling and neurosurgery (electrode implantations, microinjection catheter implantations), rat electroencephalography recordings, brain perfusion, fixation and histological preparation, immunohistochemistry.

107. Serotonin in epilepsy

Supervisorr: A/Prof. Nigel Jones ncjones@unimelb.edu.au
Project Site: Department of Medicine RMH, MBC Neurosciences Building Parkville
Contact: A/Prof Nigel Jones E: ncjones@unimelb.edu.au

Project description: Any type of brain injury can result in epilepsy, a chronic neurological condition associated with seizures or 'fits'. The pathological processes occurring in the brain which drive the development of epilepsy following brain injury are not clear, but certain drugs acting at serotonin receptors, including SSRI antidepressants, accelerate these processes. Using animal models, this project will investigate serotonin signalling in epilepsy, and attempt to understand why SSRIs accelerate the development of disease following injury. We will utilise a variety of techniques, including assessment of serotonin levels, molecular consequences of serotonin activity, immunocytochemical identification of serotonin receptors, and pharmacological manipulation of the serotonin system, all in the context of epilepsy. Available as Honours, Masters or PhD projects

Skills: Small animal handling; animal models of epilepsy; small animal surgery and EEG recording; pharmacology; microdialysis; fast-scan cyclic voltammetry; molecular biology techniques, such as real-time qPCR, Western blotting; histology, including immunocytochemistry.

THE ION CHANNELS AND DISEASE LABORATORY

Our laboratory is located on the first floor in the Melbourne Brain Centre, Kenneth Myer Building, and is fully equipped with state-of-the art neurophysiological and imaging capabilities. We are a 20 person multidisciplinary team working on individual and joint projects in the neurosciences. Our primary interest is in diseases and therapies that involve ion channels with a particular focus on epilepsy. In epilepsy our work begins with clinical and genetics collaborators who identify gene mutations. Many of these are in ion channels and we seek to understand how these mutated genes lead to behavioural seizures. We use a range of methods, appropriate to the scale of investigation and combine, genetic, molecular, biophysical, computational, neurophysiological and behavioural approaches. In addition, our laboratory houses the Australian Optogenetics Repository and we are well positioned to exploit this exciting new method. The projects below give a sample of the work being undertaken and available for suitable candidates.

108. Elucidating the pharmacology and mechanism of action of phrixotoxin on voltage-gated sodium channels – also offered as MBiomedSc

Supervisors: Dr Geza Berecki and Prof Steven Petrou
Project Site: Epilepsy and Ion Channels Group, The Florey Institute of Neuroscience and Mental Health, Kenneth Myer Bldg
Contact: Dr Geza Berecki E : geza.berecki@florey.edu.au

Project description: Voltage-gated Nav1.2 sodium channel mutations are associated with a number of neurological disorders such as epileptic encephalopathies. Clinically used drugs and experimental compounds can target Nav1.2 channels and modulate neuronal excitability. Among these, phrixotoxin-3 (PTx3) from the venom of the tarantula Grammostola rosea blocks the inward Nav1.2 channel current (INa) by altering Nav1.2 channel gating. Remarkably, PTx3 is one of the most potent and selective peptide modulators of Nav1.2 channels, with a half-maximum inhibitory concentration of 0.6 nM and ~100 fold selectivity for Nav1.2 over other neuronal voltage-gated Nav channels. Therefore PTx3 could emerge as a valuable research tool capable of selectively targeting Nav1.2 channels.

The goal of this project is to elucidate the effect of PTx3 on neuronal human Nav1.1, Nav1.2, and Nav1.6 channels stably expressed in mammalian cell lines using the conventional voltage-clamp (VC) technique, and to study the effect of PTx3 on neuronal firing using the novel dynamic-clamp (DC) technique. The biophysical properties of these Nav channels, including current-voltage characteristics, voltage-dependence of (in)activation, and recovery from inactivation will be determined in the absence and presence of PTx3. In DC configuration, Nav1.2, Nav1.2, or Nav1.6 currents will be implemented as external current input to a realistic cortical pyramidal neuron model cell. This model cell incorporates all major neuronal channel currents; however its Nav channel current is replaced with external Nav1.2, Nav1.2, or Nav1.6 current. The model cell's membrane potential is continuously computed in real time and used to clamp the membrane voltage of the mammalian cell expressing the Nav channel under investigation. This unique DC recording configuration provides a dynamic voltage environment capable of mimicking the physiology of the cell and provides a direct readout PTx3 modulation on neuronal model cell excitability.

109. Electrophysiological properties of patient derived stem cell neurons harbouring SCN2A mutations – also offered as MBiomedSc

Supervisors: Dr Geza Berecki, Ben Rollo and Prof Steven Petrou
Project Site: Epilepsy and Ion Channels Group, The Florey Institute of Neuroscience and Mental Health, Kenneth Myer Bldg
Contact: Dr Geza Berecki E : geza.berecki@florey.edu.au

Project description: Epileptic encephalopathies (EE) are a group of devastating disorders with poor prognosis and complex etiology presenting in childhood. De novo mutations in the SCN2A gene encoding for the voltage-gated Nav1.2 sodium channel represent a relatively common cause of EE. Recent landmark technological advances enable patient-specific cells reprogramming to pluripotency by creating induced pluripotent stem cells (iPSC). iPSCs can then be differentiated into neurons, resulting in stem cell (SC) neurons. These patient-derived SC neurons can serve as models of EEs and help clarify the contribution of Nav1.2 channel mutations to these conditions.
In this project, the candidate will study the electrophysiological properties of SC neurons derived from patients with R1882Q or R853Q mutations in SCN2A, whereas SC neurons resulting from CRISPR/Cas9 gene correction of the R853Q mutation to wild-type (wt) and SC neurons generated from healthy subjects will serve as controls. It has been suggested that the R1882Q mutation may result in Nav1.2 channel gain in function, whereas the R853Q mutation may be associated with loss of function and presence of aberrant so-called omega currents, facilitated by the movement of the mutated voltage-sensor S4 segments. Nevertheless, the effects of such altered Nav1.2 functions on the overall neuronal activity are unknown.
Conventional whole-cell current-clamp and voltage-clamp techniques will be used to characterize the activity and action potential (AP) characteristics of various SC neurons, including firing frequency, rheobase, and threshold for AP initiation, AP amplitude, and AP waveform. These experiments will deliver a direct readout of the impacts of Nav1.2 dysfunction on SC neuron excitability and will provide the basis for a detailed understanding of disease mechanisms and allow the development of effective therapies.

110. *Wetware* in a loop: voltage-clamp and dynamic-clamp studies of SCN2A sodium channel mutations underlying childhood epilepsy – also offered as MBiomedSc

Supervisors: Dr Geza Berecki and Prof Steven Petrou
Project Site: Epilepsy and Ion Channels Group, The Florey Institute of Neuroscience and Mental Health, Kenneth Myer Bldg
Contact: Dr Geza Berecki E : geza.berecki@florey.edu.au

Project description: Epileptic encephalopathies (EE) are a group of devastating disorders with poor prognosis and complex etiology presenting in childhood. De novo mutations in the SCN2A gene encoding for the voltage-gated sodium (Nav) channel, type II α subunit (Nav1.2), represent a major cause of EE. Prior to understanding and treatment of a particular EE, the contribution of Nav1.2 channel mutations to individual neuronal excitability need to be determined.

In this project the candidate will use both conventional voltage-clamp (VC) and novel dynamic clamp (DC) techniques to investigate the pathogenicity of selected SCN2A mutations affecting Nav1.2 channel function. Transiently expressed human Nav1.2 channels carrying K905N and D1598G mutations (associated with severe EE), R937C and R1902C mutations (associated with autism and milder epileptic syndromes), and wild-type (wt) Nav1.2 channels (control) will be studied in transfected mammalian cells. Sodium currents through wt or mutant Nav1.2 channels will be recorded in VC mode and applied as external current input to a realistic cortical pyramidal neuron model cell in real time. This model cell incorporates all major neuronal channel currents; however its Nav channel current is replaced with external wild-type or mutant Nav1.2 current. The model cell's membrane potential is continuously computed in real time and it is used as a voltage clamp command for the HEK cell expressing wt or mutant Nav1.2 channels. This unique DC recording configuration provides a dynamic voltage environment capable of mimicking the physiology of the cell and provides a direct readout of the impacts of Nav1.2 dysfunction on neuronal excitability. This is a significant advance over conventional electrophysiological and computational modelling approaches that are the only option currently available, and DC should improve the throughput of mutation analysis and quality of predictions.

111. Multielectrode array analysis of neuronal networks derived from an epilepsy mouse-model – also offered as MBiomedSc

Supervisors: Dr. Snezana Maljevic, Prof Steven Petrou
Project Site: Florey Institute of Neuroscience & Mental Health, Division of Epilepsy, Kenneth Myer Bldg
Contact: Snezana Maljevic, Steve Petrou E-mail: snezana.maljevic@florey.edu.au, steven.petrou@florey.edu.au

Project description: A recurrent mutation, Arg320His, in the KCNC1 gene, encoding voltage-gated potassium channel Kv3.1, has been recently identified as one of the main causes of progressive myoclonus epilepsy (PME), a rare, inherited disorder manifesting with myoclonus, tonic-clonic seizures, and ataxia. *In vitro* analysis in *Xenopus laevis* oocytes revealed that the mutation causes a loss of channel function (Muona et al., Nat Genet 2015).

To provide in-depth analysis of disease mechanisms, we generated knock-in mouse model carrying Arg320His mutation. The project aims at examining properties of neuronal networks derived from this mouse model using multielectrode array (MEA) analysis. To this end, primary neuronal cultures will be plated on MEA dishes and their activity analysed at different time points. We will also examine the effects of elevated temperature on the network activity, as clinical data suggest improvement of symptoms in patients with fever. This platform will be further used to test the efficiency of different drugs, including specific Kv3.1 channel openers, by assessing their impact on the signatures of network activity altered by the mutation.

Apart from cell culture methods and MEA analysis, the project will include Ca imaging of neuronal network activity, as well as immunostaining to assess the localization of mutant channels in neurons. We expect that the obtained results will lead to the clinical translation and precision medicine approaches in the treatment of the affected individuals.

112. Epilepsy in a Dish – Disease Modelling and Treatment of Severe Epileptic Encephalopathies – also offered as MBiomedSc

Supervisors: Dr Ben Rollo, Dr Snezana Maljevic, Prof Steve Petrou
Project Site: Epilepsy and Ion Channels Group, The Florey Institute of Neuroscience and Mental Health, Kenneth Myer Bldg
Contact: Ben Rollo ben.rollo@unimelb.edu.au

Project description: The Ion Channel and Disease Laboratory are investigating new treatments for a class of severe genetic epilepsy known as epileptic encephalopathies (EE). In most cases EE are caused by mutations in genes coding for membrane-bound ion channels, such as the sodium and potassium channel proteins SCN2A and KCNT1, respectively. Since EE patients do not respond to mainstream anti-epileptic treatments our laboratory has created patient-derived neurons for the purpose of creating a disease model to test novel anti-epileptic therapeutics.

Specifically, we have generated induced pluripotent stem (iPS) cells from EE patients who carry point mutations in the sodium channel gene *Nav1.2* (which codes for the SCN2A protein). Cortical neurons have been generated from these iPS cells by neural differentiation protocols using either small molecules or forced expression of neural genes. These EE patient-derived cortical neurons are capable of firing action potentials and forming functional synapses in culture. In this project we will investigate the action of a novel anti-epileptic therapy which will utilize gene-targeting anti-sense oligonucleotides (ASOs). ASOs designed to bind *Nav1.2* will be studied for their ability modulate the behavior of SCN2A and restore normative behavior to EE patient-derived neurons. The functional outcomes of ASO treatment will be assessed by single cell patch clamping, and for network analysis by multi electrode arrays (MEAs). In addition, this project will require the techniques of *in vitro* cell culture, immunohistochemistry (including western blot and single cell immunofluorescence) and gene expression analysis using real time PCR.

113. Evaluating the impact of dietary C10 and C8 fatty acids on spontaneous seizures and behavior in mouse models of epilepsy – also offered as MBiomedSc

Supervisors: Nikola Jancovski-PhD and Professor Steve Petrou
Project Site: Florey Institute of Neuroscience & Mental Health, Division of Epilepsy, Kenneth Myer Building
Contact: Nikola Jancovski: nikola.jancovski@florey.edu.au/jancovski.n@unimelb.edu.au

Project description: Increasing evidence suggests that medium-chain triglyceride (MCT) diet is one of the most effective therapeutic approaches in patients with drug-resistant epilepsy. Octanoic acid (C8) and decanoic acid (C10) are major constituents in the diet and research has shown increased quantities of these compounds in plasma of children with intractable epilepsy treated with the diet. The antiepileptic properties of MCT diet might be attributed to C10 and C8, and recent studies reported acute anticonvulsant effects of C10 and C8 in several seizure tests in mice. Although it is suggested that C10 acid exerts direct inhibition of excitatory neurotransmission and therefore decreases seizure activity, the exact mechanisms of action remain elusive. Further studies with C10 and C8 acids using animal models are needed to evaluate the role of these acids in seizures control. It is very important to complete important pre-clinical work in rodent models of epilepsy before these diets are used in clinical trials.

In this project the student will have the possibility of using a range of experimental techniques; from behavioural studies using different mouse models of epilepsy to recording electrical activity of the brain. The results might lead to developing of new therapeutic approaches for patients with drug-resistant epilepsy.

114. "CLARITY" based glass brain mapping in health and disease – also offered as MBiomedSc

Supervisors: Dr Tim Karle, Dr Kay Richards, Prof Steve Petrou,
Project Site: Florey Institute
Contact: Prof Steven Petrou E: spetrou@unimelb.edu.au;

Project description: Histochemical optically clearing of whole tissue samples and the development of new microscopes that can image deep within the tissue have created unprecedented insight into the wiring of neural networks. Changes in the wiring of cortical neurons, in particular, have been implicated in a number of disorders such as epilepsy,

schizophrenia, autism and depression. In this project the candidate will clear whole brains; allowing imaging of neurons, which have been labelled with fluorescent tags. Multi-photon excitation and custom laser light-sheet based microscopy will allow acquisition and reconstruction of exquisite 3D images in key regions of the mouse cortex. The workflow will include chemical clearing, optical microscopy and software deconvolution of the big data sets which will be generated. By comparing normal and epilepsy models this work will begin to unravel the changes that occur prior to and after the occurrence of seizures. This will shed important light on the scale on which structural changes occur in epilepsy and will guide future experimental and clinical work.

115. Multiphoton imaging of induced pluripotent-stem cell derived brainoids – also offered as MBiomedSc

Supervisors: Dr. Tim Karle, Dr. Snezana Maljevic, Prof Steven Petrou
Project Site: Florey Institute of Neuroscience & Mental Health, Division of Epilepsy, Kenneth Myer Bldg
Contact: Dr Tim Karle, Dr Snezana Maljevic E: tkarle@florey.edu.au, snezana.maljevic@florey.edu.au

Project description: Development of induced pluripotent stem cell (iPSC) approaches has enabled studies of epilepsy mechanisms in patient –based models. This can be achieved by generating 3-D iPSC-derived neuronal cultures, so called brainoids, which present self-organised neuronal assemblies. Video rate imaging of neuronal activity in these millimetre sized assemblies is made possible using short intense pulses of infrared light to image inside the living tissue. Scanning the light rapidly through the tissue causes fluorescence of genetically tagged populations of neurons, expressing Calcium sensitive fluorescent indicators. This allows multiphoton optical mapping of electrical activity in the neural networks. This project combines stem cell biology with novel imaging techniques to aid the understanding of genetic epilepsy mechanisms.

116. Pharmacological modulation of KCNT1 by quinidine in a genetic mouse of epilepsy – also offered as MBiomedSc

Supervisors: Melody Li, Nikola Jancovski, Kay Richards, Steven Petrou
Project Site: Florey Institute of Neuroscience & Mental Health
Contact: Dr Melody Li E: melody.li@florey.edu.au, Prof Steven Petrou E: steven.petrou@florey.edu.au

Project description: Pathological mutations in the gene, *KCNT1*, are the primary cause of a spectrum of severe epilepsies characterized by early disease onset, often with cognitive and developmental impairments. Recently, we identified a clinically used anti-arrhythmic, quinidine, could reverse the pathological effects of *KCNT1* mutations *in vitro*. While clinical trials resulting from our *in vitro* work showed clear benefits of quinidine, the effects were not as dramatic as expected, presumably as a consequence of poor blood brain barrier penetration and the late age of treatment initiation.

This project aims to address the above factors of quinidine administration in a KCNT1 epileptic mouse model. Techniques will involve: [1] administering quinidine directly to brain using intra-cerebroventricular injection, [2] examining the potential correlation between seizure and age of treatment initiation using pro-convulsant assay and/or electroencephalogram (EEG). Outcomes from this study are expected to inform future clinical studies on the quinidine dosing regimen in patients.

117. Evaluating the efficacy of antisense oligonucleotides in a mouse model of Epilepsy of Infancy with Migrating Focal Seizures (EIMFS) – also offered as MBiomedSc

Supervisors: Melody Li, Nikola Jancovski, Kay Richards, Snezana Maljevic, Steven Petrou
Project Site: Florey Institute of Neuroscience & Mental Health
Contact: Dr Melody Li E: melody.li@florey.edu.au,
Prof Steven Petrou E: steven.petrou@florey.edu.au

Project description: Antisense oligonucleotide (ASO) has recently emerged as a novel therapeutic strategy and several ASOs have entered Phase I clinical trials for neurological disorders and cancer. ASOs are chemically modified short strand of nucleotides that are designed to “switch off” a gene of interest. Using cell-based assay, we identified increased *KCNT1* gene function as the key disease mechanism in several types of epileptic encephalopathies. Thus, ASOs that are designed to downregulate *KCNT1* is a promising therapeutic strategy.

This study aims to evaluate the effect of ASOs designed by a pharmaceutical company in the KCNT1 EIMFS mouse model. Specific techniques will involve [1] intra-cerebroventricular administration [2] electroencephalogram (EEG) [3] pro-convulsant assay.

This is an important pre-clinical test that aims to motivate precision medicine application of ASO technology in genetic epilepsy

118. Functional characterization of KCNA2 epilepsy – causing mutations – also offered as MBiomedSc

Supervisors: Dr. Snezana Maljevic, Prof. Steven Petrou
Project Site: Ion Channels and Human Diseases Group, The Florey Institute of Neuroscience and Mental Health
Contact: E: snezana.maljevic@florey.edu.au,

Project description: Increasing number of genetic variants affecting ion channel genes and associated with different forms of epilepsy has been identified in the recent years. One of the important steps in understanding if and how these variants contribute to the disease phenotype is their functional characterization using different in vitro and in vivo approaches. The initial screen of detected variants is often performed in *Xenopus laevis* oocytes or HEK cells and involves site-directed mutagenesis, RNA production and injection, cell culture methods and two-microelectrode or patch clamp technique. In addition, biochemical methods and immunocytochemistry are applied to examine the expression and localization of affected channels. Positions are currently available for examining several novel mutations detected in the *KCNA2* and *KCNC1* gene, encoding voltage-gated potassium channel Kv1.2 and Kv3.1, respectively. Both genes have recently been associated with different forms of epilepsy, and we aim to examine the common disease mechanisms and select variants for further in depth analysis using mouse and stem cell models

119. Problematic pumps: the mechanistic basis of Na K-ATPase **mutations – also offered as MBiomedSc**

Supervisors: Ian C Forster, Melody Li, Steve Petrou
Project Site: Florey Institute of Neuroscience & Mental Health
Contact: E: ian.forster@florey.edu.au

Project description: Mutations in the ubiquitous Na-K-ATPase (sodium potassium pump) have been implicated in several neurological disorders such as rapid-onset parkinsonism and alternating hemiplegia. Understanding the molecular basis for these clinical disorders is key to developing appropriate treatments as well as gaining deeper insights into the physiological role and molecular mechanism of the wild-type protein. We will use real-time biophysical assays, combining conventional electrophysiology and fluorometry, to elucidate the mechanistic dysfunction. Interested applicants will gain first-hand experience with molecular biology, electrophysiology, fluorometry and computational biology. Some basic knowledge of molecular biology techniques and basic laboratory practices would be desired.

120. Structure function studies on phosphate transporters – also offered as MBiomedSc

Supervisors: Ian C Forster, Melody Li, Steve Petrou
Project Site: Florey Institute of Neuroscience & Mental Health
Contact: E: ian.forster@florey.edu.au

Project description: Sodium-coupled phosphate transporters provide the main means by which dietary phosphate is absorbed in the gut and reabsorbed in the kidney, to achieve phosphate homeostasis. Understanding the molecular basis of the transport mechanism at the molecular level is essential for developing clinically effective drugs to target phosphate transporters in clinically prevalent conditions such as end-stage kidney disease. We will use biophysical assays, combining conventional electrophysiology and fluorometry, to study the transport dynamics in real time and elucidate potential drug interaction sites. Interested applicants will gain first-hand experience with molecular biology, electrophysiology, fluorometry and computational biology. Some basic knowledge of molecular biology techniques and standard laboratory practices would be desired.

121. Zinc and seizures

Supervisors: A/Prof Chris Reid, A/Professor Steve Petrou, Dr Paul Adlard - ***also offered as MBiomedSc***
Project Site: Florey Institute of Neuroscience & Mental Health, Division of Epilepsy, Kenneth Myer Bldg
Contact: Chris Reid E : careid@unimelb.edu.au

Project description: Zn^{2+} is an essential element having a multitude of biological functions throughout the body. Our research has demonstrated that low brain Zn^{2+} can increase seizure susceptibility (Hildebrand et al 2015 Sci Rep). This highlights Zn^{2+} supplementation as a potentially good therapeutic strategy for seizure conditions. Before clinical trials can begin we need to complete important pre-clinical work in rodent models of epilepsy. We also need to better understand the mechanisms through which Zn^{2+} modulates neuronal excitability. In this project the student will learn a range of experimental techniques aimed at understanding the role Zn^{2+} plays in changing neuronal excitability. This will include using established rodent models to test diet and drug manipulations of brain Zn^{2+} levels on seizure susceptibility and electrophysiological investigations looking at how neuron excitability is changed by Zn^{2+}. The results have particularly relevance for developing countries, where epilepsy rates are high and nutritional supplementation is a potential practical therapy

122. Novel antiepileptic drug targets based on HCN channel antagonists - *also offered as MBiomedSc*

Supervisors: A/Prof Chris Reid, A/Professor Steve Petrou
Project Site: Florey Institute of Neuroscience & Mental Health, Division of Epilepsy, Kenneth Myer Bldg
Contact: Chris Reid E : careid@unimelb.edu.au

Project description: About 30% of epilepsy patients are not controlled on currently available antiepileptic drugs. Our laboratory has discovered a novel anti-epileptic drug target. HCN channels are an ion channel in the brain that regulates rhythmic behaviour which is a hallmark of a seizure. In collaboration with Italian scientists we have demonstrated that a compound that blocks a certain subtype of this channel reduces seizures. Based on this the NIH Anticonvulsant Screening Program in USA will test this compound on a range of seizure models. In this project we want to begin to understand how blockers of this channel reduce seizures. We have assembled a range of state-of-the-art tools to answer this question. This includes a viral-based knock-down strategy, a conditional knock-out mouse model and pharmacological tools. In this project the student will have the possibility of using a range of experimental techniques; from behaviour to recording single neuron activity. These channels are also thought to be important to the generation of pain and drugs based on this target may be useful in this condition as well.

123. How does pH change brain excitability? - *also offered as MBiomedSc*

Supervisors: Christopher A. Reid, Nikola Jancovski, Steven Petrou
Project Site: Florey Institute of Neuroscience & Mental Health, Division of Epilepsy, Kenneth Myer Bldg
Contact: Chris Reid E: Christopher.reid@florey.edu; careid@unimelb.edu.au

Project description: Brain pH levels have long been known to modify seizure susceptibility. Breathing too quickly results in brain alkalosis and can trigger seizures. In contrast, acidic shifts in brain pH induced by respiration of increased CO_2 concentrations can reduce seizure susceptibility. In fact, a gas found in emergency departments called carbogen (5% CO_2 – 95% O_2), is a rapid and effective anti-seizure therapy that could be used clinically. Our laboratory is working on how pH causes change in neuronal excitability. We have already discovered that pH impacts excitatory and inhibitory neurons differently. This project will investigate the impact of pH in a mouse model that is missing an acid sensitive channel. It will involve testing the behaviour of the mouse and looking at neuron and network excitability. By understanding these mechanisms we will be better able to develop more targeted therapeutic strategies for stopping seizures.

124. Functional characterization of the temperature sensitive component of the KCNCI epilepsy causing mutation R320H

Supervisors: Dr Carol Milligan & A/Professor Steve Petrou
Project Site: Florey Institute of Neuroscience & Mental Health, Division of Epilepsy, Kenneth Myer Bldg
Contact: Steven Petrou T : 9035 3628 E : spetrou@unimelb.edu.au;
Carol Milligan E : carol.milligan@florey.edu.au

Project Description: A *KCNC1* gene mutation (p.Arg320His) has recently been identified in 20 cases of progressive myoclonus epilepsy (PME), a distinctive epilepsy syndrome characterised by myoclonus, generalised tonic-clonic seizures and progressive neurological deterioration. *KCNC1,* not previously associated with human disease, encodes the voltage-gated potassium channel $K_V3.1$ which is expressed predominantly in inhibitory interneurons. This recurrent, loss of function missense mutation is pathogenic in the heterozygous state (Muona et al., Nat Genet 2015). Unexpectedly, transient improvement in gait and myoclonus with fever was noted in six cases, typically lasting just hours or a few days while the subject was ill.

This project aims to explore the mechanism of action of this fever effect on both homomeric and heteromeric channels, using *in vitro* high throughput automated electrophysiology and temperature. The candidate will first have to produce mutant cDNAs then transiently transfect into HEK293 cells prior to analysis on the automated platforms. Candidates will be trained in the necessary molecular biological methods and then in ion channel electrophysiology and will work closely with a senior member of the team to ensure success

GASTROENTEROLOGY

125. Barrett's Oesophagus – *also offered as MBiomedSc*

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.

GENOMICS

126. GAERS versus NEC: Genetics of epileptic and non-epileptic rat strains– *also offered as MBiomedSc*

Supervisor: Dr. Slave Petrovski and Prof. Terence J. O'Brien
Project Site: Department of Medicine RMH, Kenneth Myer Bldg
Contact: Slave Petrovski E: slavep@unimelb.edu.au

Project description: Whole genome sequence data is available for the GAERS epilepsy rat and its sibling strain the NEC non-epileptic rat. Moreover, whole-genome sequencing is available for four F2 pups born from breeding GAERS and NEC strains. This project will explore the whole genomes of these strains to identify potential genetic aberration markers of epilepsy. This project will require interest in genetics, bioinformatics and big data.

127. When synonymous mutations aren't silent – *also offered as MBiomedSc*

Supervisor: Dr. Slave Petrovski
Project Site: Department of Medicine RMH, Kenneth Myer Bldg
Contact: Slave Petrovski E: slavep@unimelb.edu.au

Project description: Synonymous mutations are generally dismissed as neutral 'background' mutations. Yet, there are many examples of cryptic splice synonymous mutations that cause severe genetic disorders. This project will compare catalogs of synonymous mutations ascertained from patients with epilepsy, autism, schizophrenia and severe ID and compare them to catalogs of mutations from healthy controls of convenience. The aim will be to use in silico tools to pinpoint potentially pathogenic cryptic splice variants followed by functional splicing assessment.

128. Neurocognitive complaints and epilepsy prognosis – *also offered as MBiomedSc*

Supervisor: Dr. Slave Petrovski and Prof. Terence J. O'Brien
Project Site: Department of Medicine RMH, Kenneth Myer Bldg
Contact: Slave Petrovski E: slavep@unimelb.edu.au

Project description: It has been previously reported that patient's with pre-treatment neuropsychiatric symptomatology are less likely to respond efficaciously to anti-epileptic drug (AED) therapy. Given what we already know about the potential for neurocognitive side-effects induced by AEDs, this study extends the original observation to investigate whether patient-reported neurocognitive adverse drug reactions (ADRs) within the first three months of therapy along with pre-treatment neuropsychiatric symptomatology could together provide a more sensitive and specific prediction of pharmacoresponse in this population of newly-treated patients.

129. Genomics of adverse response to antiepileptic drugs - *also offered as MBiomedSc*

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.

GLOBAL HEALTH

130. Global gastroenterology – *also offered as MBiomedSc*

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 buden of pancreatico-biliary disease in Fiji Islands, with a view to justifying training in biliary endoscopy and later, introduction of a biliary enbdoscopy 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

131. Longitudinal Effect of physical activity on cortical thickness in people at risk of dementia – *ONLY offered as MBiomedSc*

Supervisors: Prof.Patricia Desmond, Prof.Nicola Lautenschlager, Dr.Vijay Venkatraman, Dr.Chris Steward
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: Dementia is a leading cause of death, accounting for 6% of all deaths in 2010. Despite these already high and increasing prevalence rates, there is no curative treatment for dementia. Therefore the identification of individuals who are at increased risk of dementia and the implementation of preventive interventions is necessary until a treatment is found. . More recently a growing body of literature is focusing whether physical activity could also have a positive impact on brain ageing with exploring healthy brain ageing as well as on cognitive impairment and dementia. Increasingly research into underlying mechanisms in relation to physical activity and brain ageing identify biomarker candidates with especially neuroimaging measurements being more used in trials with humans. In this study, we look at one such biomarker of cortical thickness as a measure of brain plasticity and effect of physical activity over 2 years period in participants at risk of dementia.

132. Development of novel neuroimaging biomarkers in Neurological diseases- *also offered as MBiomedSc*

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.

133. Neuroimaging

Supervisors: Dr Chris Steward, Professor Patricia Desmond, Dr Brad Moffat
Project Site: The Brain Imaging Laboratory, Department of Radiology, Level 2, 1B building, Royal Melbourne Hospital.
Contact: Dr Chris Steward T: 9342 8337 E: csteward@unimelb.edu.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 (MI) 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 clinicans 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. The following are a subset of possible projects:

Project 1: Diffusion tensor MRI techniques for clinical assessment of white matter integrity in mild cognitive impairment and healthy aging.

Project 2: MRI in healthy aging (also available as MBiomedSc)

134. Network Activity in Brain Tissue Recorded with Combined Calcium and Voltage-Sensitive Dye Imaging and Electrophysiology - *also offered as MBiomedSc*

Supervisor: Dr Chris French
Project Collaborators – Prof T O'Brien, Prof D Williams
Project Site: Department of Medicine (RMH), Royal Melbourne Hospital
Contact: Dr Chris French T: 8344 3276 E: E: frenchc@unimelb.edu.au
Website: http://sites.google.com/a/hfbg1.net/crf_lab/

Project Description: Understanding the normal function as well as pathophysiological states of neural systems requires sampling information from many points in the network simultaneously. One way to do this is using optical methods that allow the activity of many neurons to be imaged simultaneously. Calcium-senstive fluorescent dyes can be loaded into neurons, so that the "firing" of neurons can be observed as a change in fluorescence in real time across many neurons. Voltage-sensitive dyes have the advantage of better time resolution, but the signal obtained is much smaller than calcium indicators. This project involves imaging groups of neurons in rat hippocampal brain slice in normal and epileptic states, with concomitant elctrophysiological recording to better understand epileptogenesis in this structure. Additionally, the effects of anti-epileptic drugs will be examined at the network level using these techniques. In particular, we will be looking for key parameters that permit the stable network to enter oscillatory modes. Confocal and multi-photon imaging will be used for imaging the neurons loaded with dyes, combined with patch-clamp recording.

135. High resolution connectivity mapping to examine epileptogenic tuber structure in Tuber Sclerosis Complex - *also offered as MBiomedSc*

Supervisors: Kay Richards and Steve Petrou.
Project Site: Melbourne Brain Centre
Contact: Kay Richards kay.richards@florey.edu.au

Project description: Tuber Sclerosis Complex (TSC) is a genetic disease where pathogenesis includes development of multiple benign cortical tubers in the developing brain and throughout the whole body. The focus of this study is to examine the epileptogenic tuber in the context of the whole brain connectivity; the working hypothesis is cortical tuber connectivity forms the basis of seizure generation. The project will involve analysis of anatomical and diffusion weighted MRI data from several TSC patients before and after removal of epileptogenic tubers. In addition, utilizing high-resolution MRI data of the resected tissue obtained using a 16T MRI system; detailed analysis of tuber circuitry will also be explored. In addition, there is scope to further analyze details about cellular architecture of the tuber, including neuronal sub-types, their population density and morphology obtained using immunohistochemistry methods. Overall, the project is an important step in determining the mechanism of seizure genesis from tuber focus to whole brain dysfunction and will guide future therapeutic strategies including surgical approach

136. Morphometric analysis of a Dravet Syndrome mouse model - *also offered as MBiomedSc*

Supervisors: Kay Richards, David Raffelt, Alan Connelly and Steven Petrou
Project Site: Melbourne Brain Centre
Contact: Kay Richards kay.richards@florey.edu.au

Project description: Dravet Syndrome is a devastating neurological disease with early onset at approximately 6 months of age. In Dravet Syndrome patients, seizures predominate and are difficult to treat; patients also have severe learning disabilities and a reduced lifespan. This project will examine disease mechanisms using a genetic epilepsy mouse model that has the Scn1a gene mutation, which has been found in over 85% of Dravet Syndrome patients. The purpose of the current project is to provide evidence of the structural mechansism/s causing seizures and possible therapeutic strategies by examining whole brain anatomy and connectivity by utilising high resolution diffusion MRI and glass brain imaging. In addition, microcircuitry will be explored using immunohistochemistry and electron microscopy techniques.

137. Early detection of age associated diseases using imaging - *ONLY offered as* MBiomedSc

Supervisor: Professor Patricia Desmond, A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Dept of Medicine, Centre for Medical Research, Royal Melbourne Hospital, UoM, Parkville, Vic 3052.
Contact: A/Professor Cassandra Szoeke T: 61 3 8344 1835
E: cszoeke@unimelb.edu.au / Cassandra.szoeke@mh.org.au

Project description: Australia's population is ageing at a dramatic rate with about two million people aged over 70 years at present. As populations age, the disabilities of the oldest age groups become increasingly important. 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.

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

138. Describing the molecular epidemiology of vancomycin resistant enterococcus (VRE) at the Royal Melbourne Hospital

Supervisors: Associate Professor Caroline Marshall, Associate Professor Ben Cowie, Professor Ben Howden
Project Site: Peter Doherty Institute for Infection and Immunology/Royal Melbourne Hospital
Contact: Caroline Marshall caroline.marshall@mh.org.au

Project description: Vancomycin resistant enterococcus (VRE) has become an established hospital acquired pathogen since the 1990s. It may colonise asymptomatic patients, but also may be a major cause of morbidity and mortality. In Australia, up until recently, the predominant genotype has been *vanB* VRE, however, in recently years, we have seen increasing numbers of the *vanA* genotype. At The Royal Melbourne Hospital, *vanB* VRE is now endemic, despite many years of attempting to control its spread, and we have recently had an outbreak of *vanA* VRE affecting several wards. This outbreak was controlled by using strict infection control precautions, yet these seemed to have no effect on the rates of *vanB* VRE. We have collected data on our VRE isolates for many years, including antibiotic sensitivity patterns, ribotyping and other clinical, infection control and epidemiological data.

This study will involve describing the molecular epidemiology of VRE at the Royal Melbourne Hospital to document the effect of our interventions on both *vanA* and *vanB* VRE. It will involve correlating ribotyping data with clinical and epidemiological information and performing statistical analysis of the outbreak. This project will use skills in microbiology, molecular typing, epidemiology and statistics.

139. Monitoring the efficacy of a training program in gastroenterology in the Pacific - *also offered as MBiomedSc*

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 quantitavely, 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).

INJECTING DRUG USE

140. Exploring the similiarities and differences of hepatitis C treatment and opiate substitution treatment therapy in people who inject drugs to inform increasing access HCV treatment in this population

Supervisors: Prof Margaret Hellard, Dr Peter Higgs
Project Site: Burnet Institute
Contact: E: peterh@burnet.edu.au E: margaret.hellard@burnet.edu.au

Project description: Pharmacotherapy, when used with regard to substance dependence refers to the replacement of a person's drug of choice with a legally prescribed and dispensed substitute. Known as opioid substation therapy (OST) in Victoria over 14,000 people are currently being dosed daily with methadone or suboxone for their heroin dependency.

Currently few PWID receive treatment but the advent of new direct-acting antiviral (DAA) treatment provides opportunity for increased uptake of therapy which will have the duel benefit of curing the PWIDs HCV and also potentially reducing HCV transmission (through treatment as prevention (TasP)) leading to HCV elimination in Australia.

Working with participants from the Treatment and Prevention (TAP) Study, a world first study of community based treatment for PWID and HCV elimination, this honours project will explore the PWIDs attitudes and understandings of the new DAA HCV treatment, the best mechanism to provide DAAs to the – separate to or with OST. The overall aim is to identify mechanism to increase PWIDs access to DAAs and compliance with DAA treatment so as to inform HCV elimination in Australia and globally.

The study will use qualitative methods including in-depth semi-structured interviews to achieve the research aims. An interview guide will be developed to map broad areas of investigation and to lead the semi-structured interview process, which will be inductive to allow for the generation of new ideas and knowledge that may otherwise remain uncovered.

141. The outcomes of transitioning between prison and community for people with a history of injecting drug use

Supervisors: Prof Paul Dietze, A Prof Mark Stoove
Project Site: Burnet Institute
Contact: Paul Dietze E: paul.dietze@burnet.edu.au

Project description: Injecting drug use contributes disproportionately to the health and social burden of illicit drug use in Australia. Sustained patterns of problematic injecting drug use are influenced by a complex interaction of social, health, structural, and policy factors, including the ongoing criminalisation of drug use and the routine incarceration of people for drug-related crime.

People who inject drugs (PWID) are vastly over-represented in the prison and broader criminal justice system. Transition out of prison represents a particularly vulnerable period for PWID that is characterised by challenges associated with social reintegration, housing, employment, accessing health and other support services, and relationships with significant others. Return to dependent patterns of drug use following prison release is also common, resulting in very high rates or mortality, morbidity, recidivism and re-incarceration in this population.

Burnet Institute is undertaking Australia's first prison-to-community prospective cohort study of people with injecting drug histories. This study provides an opportunity for analysis pre- and post-release data collected from 500 participants in the weeks preceding prison release and in the first three months following their release. A range of post-release outcomes are available for investigation, including but not restricted to patterns of drug use, engagement and retention in treatment and health care, overdose, housing stability and blood borne virus risk. Univariate descriptive and prospective analyses examining the pre- and post-release predictors of outcomes will be undertaken to help inform policy and practice in the Justice and Health arenas.

142. The persistence of risk among people who inject drugs - *also offered as MBiomedSc*

Supervisor: Professor Paul Dietze, Co-Head , Alcohol & Other Drug Research, Centre for Population Health, Burnet Institute
Project Site: Burnet Institute
Email: Paul Dietze E: paul.dietze@burnet.edu.au

Project Description: The prevalence of risk behaviours such as sharing of injecting equipment among people who inject drugs (PWID) has been well described in the Australian context. However, little is known about transitions in risk behaviours among PWID over time and whether Australian PWID moderate their behaviours in response to their changing circumstances. In this study data from the Melbourne Injecting Drug User Cohort Study (MIX) will be examined to determine the extent to which risk behaviours change over time in the cohort and what impact any changes have on key health outcomes such as blood borne virus transmission.

INNATE IMMUNITY

143. Train your monocytes with treats: understanding how glycosaminolyscans can modulate monocyte biology - *also offered as MBiomedSc*

Supervisors: Dr. Louise Randall (Medicine RMH, Doherty Inst), A/Prof Anthony Jaworowski (Burnet Inst)
Project Site: Doherty Institute and Burnet Institute
Contact: Dr Louise Randall E: louise.randall@unimelb.edu.au

Project description: Glycobiology is an exciting and rapidly expanding field of science. Glycosaminoglycans consist of repeating chains of disaccharide (2 sugar) units and are generally attached to a protein core, thereby forming a proteoglycan. These molecules have important structural roles but new functions, including roles in cell signaling and the immune system, have now been described. Monocytes are key cells of the immune system with diverse roles, which include responding to infection and aiding in repair. Data generated in our laboratories suggest that specific glycosaminoglycans can modulate the response of monocytes to pathogen products, including the malaria-causing parasite *Plasmodium falciparum*. This new project aims to examine the mechanisms involved in this glycosaminoglycan-

dependent education of monocytes by focusing on signaling pathways within the cells. The techniques available for this project include cell culture of primary cells and cell model systems, flow cytometry, ELISA, protein analyses and realtime RT-PCR.

144. Immune Cell Signalling Regulation During Inflammation - *also offered as MBiomedSc*

Supervisors: Dr Rodney Luwor and Dr Paul Licciardi
Location: Dept of Surgery RMH and Murdoch Children's Research Institute
Contact: Dr Rodney Luwor; T: 8344 3027, E: rluwor@unimelb.edu.au

Project Description: Infections with *Streptococcus pneumoniae* (pneumococcus) are a major cause of morbidity and mortality in children <5 years of age globally with ~1.5 million deaths per year due to invasive pneumococcal diseases (IPD) such as pneumonia, meningitis and sepsis. There has been recent interest in understanding the host response to pneumococcal infection, particularly on innate immunity and inflammation. Following infection, recognition of *S. pneumoniae* (and their bacterial components) occurs by pattern recognition receptors such as Toll-like receptors (TLRs-2,4) on monocytes and neutrophils as well as on airway epithelial cells. Activation of TLRs lead to inflammation characterised by cytokine and chemokine secretion (e.g. TNF-α, IL-1β, IL-6, IL-8) which further recruit innate immune cells mainly under the control of NFκB. In addition, large multi-protein complexes known as inflammasomes regulate caspase-1-mediated IL-1β and IL-18 release and are critical in this response. Recent studies have shown that the NLRP3/NALP3 inflammasome is integral in the host inflammatory response to pneumococcal infection but can also contribute to the associated pathology. Therefore, novel anti-inflammatory therapies that target the inflammasome would be effective in limiting the pathological consequences of pneumococcal infections. Dietary short-chain fatty acids (SCFAs) such as butyrate are widely recognised to possess potent anti-inflammatory effects. SCFAs are also produced probiotic bacteria, and represent a possible mechanism by which they exert their reported beneficial effects on inflammation, immune modulation and pathogen colonisation. This study aims to assess the biological role of butyrate on NFkB- and inflammasome-driven responses using a bacterial infection model recently developed in the laboratory.

Skills/Techniques acquired: Cell biology techniques including Cell transfections, western blotting, luciferase reporter assays, RT-PCR and potentially animal handling and injecting.

INNATE PHAGOCYTOSIS & NEURODEGENERATION

145. Leukocyte surface and functional biomarkers for prognosis of age-related macular degeneration

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

Project description: Age-related macular degeneration (AMD) is a multifactorial disease and is a leading cause of irreversible vision loss in Australia. AMD at its early stage is characterized by accumulation of debris (lipid rich drusen) in retina, which is believed due to reduced clearance capacity. While AMD can be easily diagnosed with high resolution retina imaging, early prognosis biomarkers are needed to identify people with high risk for preventive treatment. Our previous study has shown that genetic variants leading to defective phagocytosis are risk factors for AMD. In this study, we will measure the phagocytosis ability of monocytes and monocyte subsets from AMD patients as well as age-matched healthy controls, using a real-time tri-colour flow cytometry method developed by our group. Meanwhile, the monocyte surface expression of scavenger receptors, e.g. P2X7, TREM-2, SCARA1 and CD36, will be examined. Cell surface biomarkers will be examined on peripheral blood leukocytes from patients and healthy controls. The sensitivity and specificity of promising parameters will be analysed and validated in a follow-up study. This study will not only identify a useful pattern for early prognosis of AMD, but also provide insights on the pathogenesis and development of this disease.

146. Identification of serum glycoproteins inhibiting innate immunity - *also offered as MBiomedSc*

Supervisors: Dr Ben Gu, Professor James Wiley
Project Site: Ion channel & Human Disease, Florey Neuroscience Institutes, Level 1, Kenneth-Myer Building, Parkville
Contact: Ben Gu T: 03 9035 6317 E: ben.gu@florey.edu.au James Wiley E: james.wiley@florey.edu.au

Project description: Innate immunity is the first line defense of host against invading pathogens. Phagocytosis of non-opsonized particles (bacteria or viruses not coated by immunoglobulin, complement, etc) is an important part of innate immunity. Our recent findings show that innate phagocytosis is completely abolished by a group of serum glycoproteins, i.e. serum inhibits innate immunity. These proteins play an important role in regulation of innate immunity and the most potent protein remains unknown. Identifying this protein will lead to a new therapies to boost resistance against infectious diseases.

Techniques involved are chromatography, cell culture, flow cytometry, electrophoresis, western blotting and mass spectrometry.

147. How does the brain remove the excess number of neurons during development and ageing - *also offered as MBiomedSc*

Supervisors: Dr Ben Gu, Professor James Wiley
Project Site: Ion channel & Human Disease, Florey Neuroscience Institutes, Level 1, Kenneth-Myer Building, Parkville
Contact: Ben Gu T: 03 9035 6317 E: ben.gu@florey.edu.au James Wiley E: james.wiley@florey.edu.au

Project description: Many more neurons are produced during development than are present in the adult brain. Also many neurons are lost during aging, however the process of innate phagocytosis, which removes unwanted and superfluous neurons is poorly defined. The unwanted neurones enter apoptosis but subsequent clearance of these dying cells is important for our body to avoid autoimmunity or inflammation in the brain. Apoptotic cells express unique markers which enable them to be recognized and engulfed by phagocytes. The knowledge of these unique markers is limited at present to certain cell membrane lipids, e.g. phosphatidylserine. Recent novel finding from our laboratory suggests that a unique protein epitope is expressed early in apoptosis and this is recognized by P2X7 receptors on phagocytes. This project will examine how apoptotic cells are recognized and cleared by phagocytes both in health and in disease. This result will have relevance to many neurological diseases as well as early neurodevelopment.

Techniques involved are cell culture, immunoprecipitation, western blotting, flow cytometry, peptide screen, molecular biology and mass spectrometry.

148. Identify the transcriptional regulatory factors of the P2X7 receptor - *also offered as MBiomedSc*

Supervisors: Dr Ben Gu, Professor James Wiley
Project Site: Ion channel & Human Disease, Florey Neuroscience Institutes, Level 1, Kenneth-Myer Building, Parkville
Contact: Ben Gu T: 03 9035 6317 E: ben.gu@florey.edu.au
James Wiley E: james.wiley@florey.edu.au

Project description: P2X7 is an ATP-gated purinergic receptor and plays a broad role in infection, inflammation, autoimmunity, neurodegeneration and oncogenesis. Several isoforms of P2X7 have been identified to be associated with cancer or other diseases. High expression of non-functional P2X7 has also been found in a broad range of tumour tissues. However, the transcriptional regulatory factors leading to these isoforms and non-functional P2X7 are unclear. This project will identify the transcriptional factors in the P2X7 promoter region, and how these transcriptional factors regulate production of P2X7 isoforms and non-functional P2X7. The results will provide insights on how cancer cells avoid removal by innate immunity.

Techniques involved include molecular biology, including primer extension, transfection, fluorescent super electrophoresis mobility shift assay and chromotin-immunoprecipitation, as well as cell culture, flow cytometry.

149. Do circulating microvesicles from patients with multiple sclerosis (MS) disrupt the blood-brain barrier (BBB)? - *also offered as MBiomedSc*

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

Project description: Breakdown of the blood brain barrier (BBB) precedes clinical symptoms of new lesions of MS and it is possible that high numbers of microvesicles in multiple sclerosis (MS) plasma are related to episodes of disruption of the BBB. The integrity of BBB will be studied using an *in vitro* model examining lymphocyte transmigration across confluent monolayers of cultured endothelial cells. Human umbilical vein endothelial cells (HUVECs) are grown to confluent monolayers in tissue culture plates and peripheral blood lymphocytes added to each well and incubated for 2-4 h. The HUVEC layer is washed 5 times with saline media, then fixed and examined by phase-contrast microscopy. Cells beneath the monolayer appear phase dark while adherent cells above appear phase light. The number of adherent and migrated cells are counted to give an index of efficiency of migration. To assess if microvesicles impair the integrity of the endothelial monolayer, the migration assay will be performed both in the absence and presence of plasma containing known concentrations of platelet derived microvesicles. Meanwhile, the lysosomal β-hesosaminidase activity will be measured in platelet poor plasma from 20 MS patients and 20 controls using a standard colourimetric assay. The microvesicle counts, β-hesosaminidase activity and the impact on lymphocytes transendothelial migration will be analysed in correlation. Results could provide evidence for a mechanism by which peripheral blood leukocytes infiltrate to brain in MS.

Techniques involved include cell culture, ultra-centrifugation, flow cytometry, fluorescent microscopy and biochemistry.

MALARIA

150. Hiding out in the Placenta. Investigating how glycosaminoglycans can modulate the immune system during malaria and pregnancy – *also offered as MBiomedSc*

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.

Techniques involved: enzyme-linked immunosorbent assay (ELISA), cell culture, measurement of cytokines, real-time PCR.

151. Development of an ultra-sensitive non-invasive point-of-care immunosensor for malaria elimination – *also offered as MBiomedSc*

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).

152. Investigating the effects of GM-CSF and M-CSF derived human macrophages on phagocytosing *P. falciparum* infected erythrocytes and cytokine production - *also offered as MBiomedSc*

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.

153. A role for Adipose Tissue in Malaria? - *also offered as MBiomedSc*

Supervisors: Dr Elizabeth Aitken & Professor Stephen Rogerson
Project Site: Department of Medicine (RMH), Peter Doherty Institute
Contact: Dr Elizabeth Aitken T: 03 8344 1972 E: Elizabeth.aitken@unimelb.edu.au and Professor Stephen Rogerson T: 03 8344 3259 E: sroger@unimelb.edu.au

Project description: The pathology associated with malaria is partly caused by a strong inflammatory immune response to the Plasmodium parasite. Adipose (fat) tissue has recently been shown not to be an inert energy store, but a tissue which actively regulates the immune response. Interestingly, we know that the parasite likes to sequester in the adipose tissue

but we don`t know much else. With increasing obesity worldwide, this could be important for development of severe malaria. In this project you will study adipose tissue from people and mice infected with Plasmodium parasites. You will discover where in the adipose tissue the parasites are, if (and which) immune cells are also there and if there are any other changes in adipose tissue associated with infection. Techniques will include: Immunohistochemistry, light microscopy, image analysis software.

154. Investigating the acquisition and maintenance of immunity to malaria in infants and pregnant women

Supervisor: Dr Freya Fowkes, Head, Malaria Epidemiology Group, Centre for Population Health, Burnet Institute
Project Site: Burnet Institute
Email: E: Fowkes@burnet.edu.au

Project Description: Immunity to infectious diseases during pregnancy remains an intriguing area with immunologic and physiologic changes during pregnancy rendering pregnant women to be more susceptible to, and more severely affected by, infectious diseases. Malaria is one of the most important pathogens in pregnancy and world-wide it is estimated that 50 million women living in malaria endemic areas become pregnant. Despite acquiring substantial pre-existing blood-stage immunity pregnant women typically develop higher parasite densities compared to non-pregnant adults, placental infection and associated complications. Very little is known about antibody acquisition, maintenance and boosting during or after gestation. Furthermore little is known about maternal transfer of antibodies and subsequent maternal antibody decay and infant antibody acquisition in infants born in malaria endemic areas.

We have samples from several established longitudinal cohorts of pregnant women and infants that can address questions of antibody acquisition and maintenance through antibody assays and epidemiological analyses. Findings will help us understand how immunity develops and is maintained against infectious diseases.

155. Understanding the targets and mechanisms of human immunity to malaria

Supervisor: Professor James Beeson, Dr Jack Richards
Project site: Burnet Institute
Email: E: beeson@burnet.edu.au Richards@burnet.edu.au

Project Description: This project will focus on identifying the key antigens that are targets of protective immunity against malaria and understanding the mechanisms mediating immunity, which includes antibodies and cell-mediated responses. This knowledge is crucial for the development of effective vaccines against malaria. The project may combine detailed studies of immune responses with clinical and population studies in Africa, Asia, and Papua New Guinea. It will examine how immune responses protect children from malaria, or protect pregnant women and their developing babies from the devastating consequences of malaria in pregnancy. The studies would particularly focus on understanding antibody acquisition, maintenance and boosting and how antibodies neutralize and clear malaria parasites in the blood, and examine interactions with monocytes/macrophages and dendritic cells, and understanding the nature and specificity of antibody responses.

For all queries please contact Arzum, arzum.cubuk@burnet.edu.au

156. Vaccines against malaria

Supervisor: Professor James Beeson, Dr Jack Richards
Project site: Burnet Institute
Email: E: beeson@burnet.edu.au jack.richards@burnet.edu.au

Project Description: The aim of this project is to evaluate candidate antigens as potential malaria vaccines, understand what combinations of antigens could be use to generate the most effective immune responses, and understand the protective activity of vaccine-induced immune responses. These studies will focus on several leading candidate antigens (AMA1, EBAs, PfRh, MSP2), and other promising antigens. They will use novel approaches in molecular biology, cell biology and immunology to address these aims. In addition, the project could include working on optimising vaccine approaches to induce potent protective immune responses (e.g. improving antigen presentation). The project could focus on vaccines for P. falciparum and P. vivax, which are the two main causes of human malaria.

For all queries please contact Arzum, arzum.cubuk@burnet.edu.au

157. Identifying targets and mechanisms of the acquired immunity to severe malaria in children

Supervisors: Professor James Beeson, Dr Jack Richards, Professor Stephen Rogerson
Project Site: Burnet Institute
Contact: Professor James Beeson E: beeson@burnet.edu.au jack.richards@burnet.edu.au; sroger@unimelb.edu.au

Project description: Malaria caused by Plasmodium falciparum is a leading cause of mortality and morbidity globally, particularly among young children. After repeated exposure, individuals develop effective immunity that controls blood-stage parasitaemia, thereby reducing clinical symptoms and life-threatening complications. Antibodies are important

mediators of this acquired immunity. The demonstration that naturally acquired antibodies are associated with protection from malaria is one of the criteria used to objectively prioritize malaria antigens for malaria vaccine development.

We have recently completed a case-control study of severe malaria in children living on the North coast of Papua New Guinea. Cases were identified at Madang hospital and were defined as having severe malaria according to the World Health Organization criteria. Each case of severe malaria was matched to a healthy community control. Blood samples were taken from cases at the time of hospital admission and when the patient had recovered. For controls, samples were taken at the time of enrolment into the study. We would like to determine levels of antibodies to a range of malaria antigens by Enzyme-linked immunosorbent assay (ELISA), flow cytometry and functional antibody assays. The levels of these antibodies will then be related to clinical outcome using statistical analysis including regression techniques.

These findings will help us understand how immunity contributes to protection from severe malarial disease progression. The findings are valuable for advancing vaccine development by providing evidence supporting certain malaria antigens as targets of protective immunity.

For all queries please contact Arzum, arzum.cubuk@burnet.edu.au

158. Healthy Mothers, Healthy Babies in Papua New Guinea – The impact of Nutrition, Malaria and STIs on pregnant women and infants

Supervisors: Professor James Beeson, Dr Freya Fowkes, Dr Philippe Boeuf
Project Site: Burnet Institute
Contact: beeson@burnet.edu.au freya.fowkes@burnet.edu.au; Philippe.boeuf@burnet.edu.au

Project description: In many resource-poor regions globally, pregnant women experience high rates of malaria, under-nutrition and sexually transmitted infections (STIs) which can lead to maternal morbidity and mortality and in infants, low birth weight (LBW) resulting in a significant number of infant deaths each year. In these settings, LBW is due to fetal growth restriction and preterm delivery. However the link between nutrition, malaria and STIs and these birth outcomes have yet to be elucidated.

At the Burnet Institute, we have initiated a unique research program in rural PNG, called Health Mothers Health Babies, in partnership with the PNG Institute of Medical Research, East New Britain Provincial Goverment, University of PNG, the National Department of Health, and others. We have undertaken a longitudinal study of 700 pregnant women attending antenatal care, and followed them through to delivery. Among these women we will measure markers of nutrition and evaluate micronutrient deficiencies, determine malaria and STIs. The association of nutrition, malaria, and STIs during pregnancy with respect to birth outcomes will then be assessed using epidemiological techniques. The objective of this project is to determine the major preventable causes of poor maternal health and LBW to enable the development of future interventions to improve health and pregnancy outcomes. This project is offered as a laboratory or epidemiological project, or a combination of the two depending on student interests.

For all queries please contact Arzum, arzum.cubuk@burnet.edu.au

159. Development of novel point-of-care diagnostics tests and surveillance tools

Supervisors: Professor James Beeson, Dr Philippe Boeuf, Associate Professor David Anderson
Project Site: Burnet Institute
Contact: beeson@burnet.edu.au Philippe.Boeuf@burnet.edu.au anderson@burnet.edu.au

Project description: There is an urgent need for diagnostic and surveillance tests that could be used in resource-poor settings. These include vaccine antibody testing (malaria, measles, HBV, pneumonia and others) to assess vaccine coverage in populations, and sero-surveillance tools for monitoring and tracking major infectious diseases. The limited resources and health care infrastructure in many disease-endemic countries means that tools for evaluating the vaccine status of patients, vaccine coverage in populations and for disease surveillance need to be simple to perform without a requirement for laboratory facilities or advanced equipment. The tests need to be being semi-quantitative, have a long shelf-life, stable for periods at ambient temperature, and easy to perform and interpret to ensure their suitability to the specific conditions to resource-poor settings. This project will work towards the development of novel semi-quantitative point-of-care rapid tests and investigate different approaches to improve sensitivity and quantitation. This will build on Burnet's extensive expertise in diagnostic test development and strong links to communities that experience a high burden of disease and have an urgent need for new point-of-care tests. The development of new low cost point-of-care tests for major diseases would facilitate major advances in disease control in resource-limited settings.

For all queries please contact Arzum, arzum.cubuk@burnet.edu.au

160. Developing new assays to identify mechanisms of human immunity to malaria

Supervisor: Dr Philippe Boeuf, Professor James Beeson, Dr Jack Richards
Project site: Burnet Institute
Contact: E: philippe.boeuf@burnet.edu.au; james.beeson@burnet.edu.au ; jack.richards@burnet.edu.au

Project Description: Malaria caused by *Plasmodium falciparum* is a leading cause of mortality and morbidity globally, particularly among young children. After repeated exposure, individuals develop effective immunity that controls blood-stage parasitaemia, thereby reducing clinical symptoms and life-threatening complications. Antibodies are important mediators of this acquired immunity. The demonstration that naturally-acquired antibodies are associated with protection from malaria is one of the criteria used to objectively prioritize malaria antigens for malaria vaccine development.

This project will focus on developing new assays to identify the antibody-dependent mechanisms that mediate protective immunity against malaria. This knowledge is crucial for the development of effective vaccines against malaria. The project may combine detailed studies of immune responses with clinical and population studies in Africa, Asia, and Papua New Guinea. It will examine how immune responses protect individuals from malaria; especially how antibodies interact with immune cells to neutralize and clear malaria parasites in the blood.
(For all queries, please contact Arzum, arzum.cubuk@burnet.edu.au)

161. Screening for anti-malarial drugs that block trafficking in parasites

Supervisors: Dr Paul Gilson, Dr Ben Dickerman, Dr Freya Fowkes
Project Site: Burnet Institute, 85 Commercial Rd, Melbourne
Contact: E: paul.gilson@burnet.edu.au

Project description: Malaria is a devastating parasitic disease that infects hundreds of millions of people each year, tragically killing about half a million, mainly children. Anti-malarial drugs are the main weapons used to combat infection but alarmingly parasites are starting to become resistant to the latest frontline drugs. For this reason new drug targets need to be identified and new medicines developed to for future use. One potential suite of targets are the protein trafficking pathways used by parasites to shuttle proteins around not only their own cells but also those of the human host cells they infect. This project will involve screening libraries of parasite killing drugs to identify compounds that block protein trafficking. Parasites treated with the trafficking drugs will then be studied to determine where the drugs block trafficking and what their potential enzyme targets might be. This work could form the basis for the future development of novel anti-malarial chemotherapies.

Techniques involved: Cell culture, luciferase based growth assays, live cell microscopy of parasites.

162. Host cell modification in malaria parasites – *also offered as MBiomedSc*

Supervisors: Dr Paul Gilson, Dr Hayley Bullen, Dr Sarah Charnaud, Dr Freya Fowkes
Project Site: Burnet Institute, 85 Commercial Rd, Melbourne
Contact: E: paul.gilson@burnet.edu.au

Project description: Malaria parasites extensively modify the red blood cells they infect to enable them to grow rapidly and to avoid host immunity. To modify their host cells, the parasites make and then export hundreds of proteins into the host compartment. These proteins traffic to different regions within the host and form a number of complexes and structures that contribute to parasite virulence. We have made a number of key discoveries regarding the methods used by parasites traffic their virulence proteins and this project hopes to extend this work further to assess the value of the trafficking systems as future targets for anti-malarial drugs.

Techniques involved: Cell culture, luciferase based growth assays, live cell microscopy of parasites.

MEDICATION SAFETY

163. Safe and appropriate medication prescribing of older patients with chronic obstructive pulmonary disease (COPD) – *also offered as MBiomedSc*

Supervisors: Professor Elizabeth Manias, Dr Snezana Kusljic and Ms Alexandra Gorelik
Project Site: Royal Melbourne Hospital, Parkville Campus; Melbourne School of Health Sciences, The University of Melbourne
Contact: Professor Elizabeth Manias T: 0450 308 060 E: emanias@unimelb.edu.au

Project description: Chronic obstructive pulmonary disease (COPD) is a progressive and disabling condition that leads to chronic and recurrent airflow obstruction. COPD is an umbrella term used for two pathological lung conditions: chronic bronchitis and emphysema. According to national figures, COPD affects 5.7% of older Australians aged 55 and over, with the main cause being active smoking although some people with COPD have never smoked. The mainstay of therapy

includes administration of bronchodilators and corticosteroids. Furthermore, older individuals in general have a number of other co-morbidities, such as diabetes and hypertension for which they require regular medications. The use of multiple medications in older patients to treat a range of conditions adds to the complexity of their medication regimen and also increases the burden of care and cost of treatment.

In this study, the STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment) criteria will be applied to a random sample of older patients admitted to hospital for an exacerbation of COPD. Use of these screening tools will determine what medications have been inappropriately commenced in older patients and what medications have been inappropriately stopped or not commenced in older patients. The adverse events experienced by older patients will also be examined to determine whether the medications they are prescribed may be associated with these adverse events. Medical histories of older patients will be examined retrospectively on admission, at two days following admission and at discharge. Following completion of the study, recommendations will be made about the safety and appropriateness of medication prescribing for older patients with COPD.

164. Safe and appropriate medication prescribing of older patients with dementia – *also offered as MBiomedSc*

Supervisors: Professor Elizabeth Manias, Dr Snezana Kusljic and Ms Alexandra Gorelik
Project Site: Royal Melbourne Hospital, Parkville Campus; Melbourne School of Health Sciences, The University of Melbourne
Contact: Professor Elizabeth Manias T: 0450 308 060 E: emanias@unimelb.edu.au

Project description: With increasing aging of the Australian population, the proportion of older patients with dementia is expected to increase markedly over time. About one in ten patients aged over 65 years and about three in ten patients over the age of 85 years have dementia. Dementia is a leading cause of death in older patients, and it is associated with increased burden of care, and prolonged illness and disability. Many older patients with dementia also have a number of other chronic conditions, such as depression, osteoarthritis, and diabetes, which escalates the complexity of their medication regimen.

In this study, the STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment) criteria will be applied to a random sample of older people with dementia admitted to hospital for treatment of an acute condition. Use of these screening tools will determine what medications have been inappropriately commenced in older patients with dementia and what medications have been inappropriately stopped or not commenced in these patients. The adverse events experienced by older patients with dementia will also be examined to determine whether the medications they are prescribed may be associated with these adverse events. Medical histories of older patients will be examined retrospectively on admission, at three days following admission and at discharge. Following completion of the study recommendations will be made about the safety and appropriateness of medication prescribing for older people with dementia in hospitals.

MOTOR NEURON DISEASE

165. Neurodegeneration – Stimulating autophagy to improve intracellular proteostatis in MND

Supervisors: Dr Bradley Turner, Dr Rebecca Sheean
Project Site: Florey Institute, Kenneth Myer Building
Contact: Bradley Turner E: Bradley.turner@florey.edu.au T: 9035 6521

Project description: Motor neuron disease (MND) is a neurodegenerative and protein misfolding disorder linked to defects in proteostasis pathways, or protein homeostasis, within affected motor neurons. MND is associated with cytoplasmic accumulation and aggregation of key proteins (SOD1, TDP-43 and FUS) which are implicated in motor neuron death. Strategies that improve proteostasis and clear these misfolded proteins in motor neurons are therefore an attractive candidate therapeutic approach for MND. Our group is interested in autophagy, the main catabolic pathway in neurons that eliminates misfolded proteins, aggregates and damaged organelles by targeting these substrates to lysosomes for digestion.

This project will investigate the therapeutic effect and action of stimulating autophagy in genetic cell culture and mouse models of MND. The effects of newly identified autophagy enhancing drugs will be evaluated on clinical progression, neuropathology and misfolded and aggregated protein load in mouse models of MND. This project will employ transgenic mice, behavioural studies, advanced microscopy, immunohistological and biochemical techniques

166. Neurodegeneration – Development of survival motor neuron gene therapy for spinal muscular atrophy

Supervisors: Dr Rebecca Sheean, Dr Bradley Turner
Project Site: Florey Institute, Kenneth Myer Building
Contact: Rebecca Sheean E: rebecca.sheean@florey.edu.au T: 9035 6567

Project description: Spinal muscular atrophy (SMA) is a progressive neuromuscular disorder and the leading genetic cause of infant death. SMA results from inactivation of the survival motor neuron 1 (*SMN1)* gene and retention of the *SMN2* gene, leading to ubiquitous SMN protein deficiency and selective spinal motor neuron loss and muscle weakness. SMN is an essential factor for motor neurons regulating gene splicing and axonal functions important for motor neuron development. SMN gene replacement or upregulation using viral vectors or antisense oligonucleotides show promise in mouse models of SMA.

This project involves testing a novel non-viral SMN gene therapy approach for SMA using immunogenes. Immunogenes consist of motor neuron targeting antibodies complexed with gene expression plasmids. The therapeutic effects of SMN immunogenes will be evaluated on clinical progression, neuropathology, and SMN splicing and axonal functions in a mouse model of SMA. This project will employ knockout mice, behavioural studies, confocal microscopy, immunohistochemical and biochemical techniques

167. Development of bifunctional peptide-oligonucleotide conjugates as a novel RNA based therapy for C9orf72 amyotrophic lateral sclerosis

Supervisors: Dr Fazel Shabanpoor, Dr Bradley Turner
Project Site: Florey Institute of Neuroscience and Mental Health
Contact: Dr Fazel Shabanpoor T: 9035 7273 E: fazel.shabanpoor@unimelb.edu.au

Project description: Amyotrophic lateral sclerosis (ALS) is an incurable disease of motor neuron degeneration in the brain and spinal cord, leading to paralysis of voluntary muscles and death by respiratory failure within a median of 3 years from onset(*1*). The expansion of a GGGGCC (G4C2) hexanucleotide repeat in the first intron/promoter of C9orf72 gene has been reported to be the most common genetic cause of familial and sporadic ALS and frontotemporal dementia (FTD)(*2, 3*). A gain-of-function as a results of sequestration of RNA-binding protein by toxic RNA resulting from the expanded G4C2 repeat has also been proposed (*4*). Another causal mechanism is the repeat-associated non-ATG (RAN) translation of the intronic G4C2 repeat expansion in both sense and antisense direction which can generate up to five different dipeptide repeats proteins that can form toxic aggregates (*4*) (Figure. 1A).

The **aim** of this project is to use oligonucleotide-based therapeutic approach to selectively degrade C9orf72 sense and antisense RNAs with repeat expansion (Fig. 1B) The sense and antisense oligonucleotides will be conjugated to a single cell-penetrating peptide for their simultaneous intracellular delivery. Using this novel therapeutic strategy, the level of repeat-expanded C9orf72 RNA transcripts will be reduced. This approach will mitigate the main pathological hallmark of ALS, repeat-expanded RNA and aggregated protein toxicities.

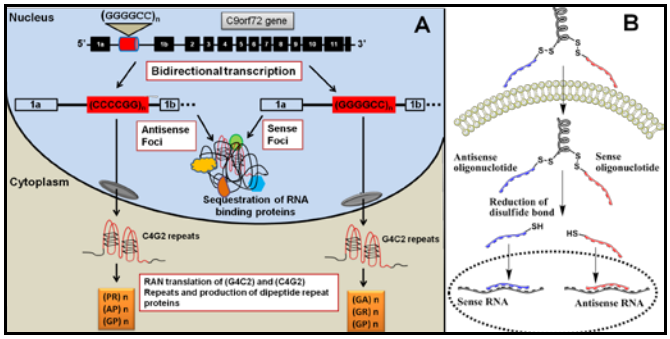


Figure.1: (A) Schematic illustration of bidirectional transcription of chromosome 9 open reading frame (*C9orf72*) gene. Formation of sense and antisense foci and RAN translation of the G4C2 and C4G2 repeats. **(B)** Delivery of sense and antisense oligonuclotides conjugated to a single cell-penetrating peptide for simultaneous knockdown of sense and antisense C9orf72 RNAs with repeat expansion.

Skill acquisition: A broad range of skills will be acquired. Students will be trained in synthesis of peptides, conjugation of peptides to oligonuclotides, HPLC purification, mass spectrometry characterization. Cell culture, RNA extraction, RT-qPCR, protein purification and western-blotting and immunohistochemistry.

168. Development of autophay-inducing peptides as therapy for neurodegenerative diseases

Supervisors: Dr Fazel Shabanpoor, Dr Bradley Turner
Project Site: Florey Institute of Neuroscience and Mental Health
Contact: Dr Fazel Shabanpoor T: 9035 7273 E: fazel.shabanpoor@unimelb.edu.au

Project description: The altered protein degradation and accumulation of misfolded, aggregate-prone proteins is one of the main hallmark of neurodegenerative diseases. Autophagy is an intracellular process which plays a major role in clearance of misfolded/aggregate-prone protein. Motor neurons are in particular very vulnerable to the accumulation of

misfolded proteins. Due to their inherent low autophagy capacity, motor neurons can clear their aggregated protein and undergo degeneration (*1*).

Recent identification of an autophagy-inducing peptide (Fig. 1) has provided a platform for development of autophagy-inducing peptide drugs with potential therapeutic application for neurodegenerative diseases (*2*). However, these newly discovered peptides have low efficacy and also poor cell-permeability. They are not capable of crossing cell membrane to reach their target in the cytosol (Fig. 1). Therefore, the **aim** of this project is to **(i)** develop analogues of beclin 1 peptide with higher autophagy-inducing efficacy and **(ii)** to enhance their cell uptake by conjugating them to cell-penetrating peptide.

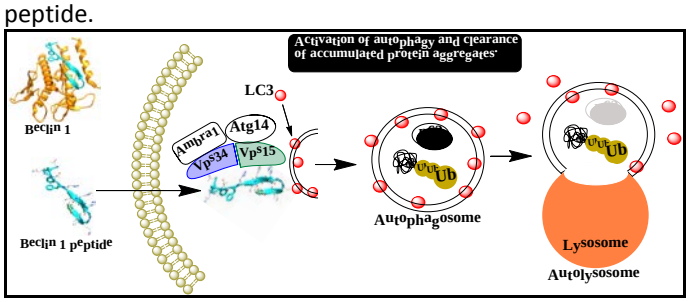


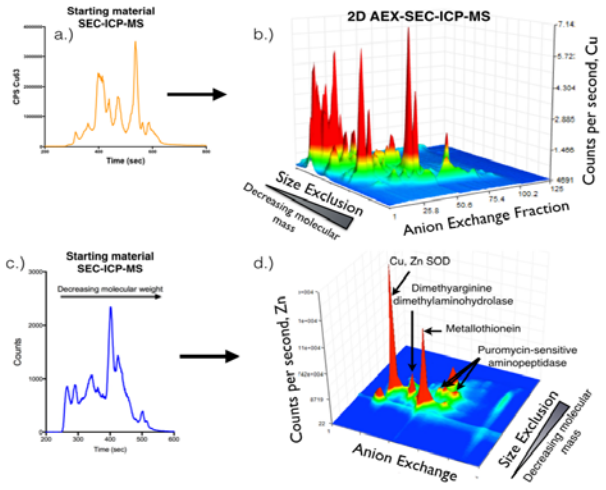
Figure.1: Cellular uptake of Beclin 1 peptide, activation of autophagy and clearance of aggregated proteins.

Skill acquisition: A broad range of skills will be acquired. Students will be trained on synthesis peptides, HPLC purification, mass spectrometry characterization. Cell culture, protein purification, western-blotting, immunofluorescent and immunohostochemistry.

169. Bioanalytical tools to investigate the role of metalloproteins in Alzheimer's disease and amyotrophic lateral sclerosis

Supervisors: Dr. Blaine Roberts
Project Site: Florey Inst. Neuroscience-Melbourne Brain Centre
Contact: Dr. Blaine Roberts blaine.roberts@florey.edu.au

Project description: Trace elements are an essential requirement for life. Transition elements, including copper (Cu), iron (Fe) and zinc (Zn), are used to catalyse a wonderful array of reactions throughout all kingdoms of nature. It is then no surprise that the most complex organ to have evolved, the brain, is a rich source of transition metal chemistry. However, we still lack the detailed understanding of how transition elements and the biomolecules that rely on them are involved in the function of the brain. Alzheimer's disease and amyotrophic lateral sclerosis both have a rich history indicating a critical role of trace elements Cu, Fe, and Zn in their pathophysiology. My lab has implemented bioanalytical tools that allow us to investigate the role metalloproteins have in neurodegeneration. This has project will investigate the role of metalloproteins in the neurodegenerative process.



NEUROLOGY/DEMENTIA/ALZHEIMER'S DISEASE

170. Can statins protect against cognitive decline associated with dementia? - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Dept of Medicine, Centre for Medical Research, Royal Melbourne Hospital, UoM, Parkville, Vic 3052.
Contact: A/Professor Cassandra Szoeke T:61 3 8387 2224 F : 61 3 9387 9384
E: cszoeke@unimelb.edu.au

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 will help us identify the short term and long term effects of cholesterol-lowering medication on cognition, and whether statins can be used 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.

171. Nutrient intake and cognitive decline - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Dept of Medicine, Centre for Medical Research, Royal Melbourne Hospital, UoM, Parkville, Vic 3052.
Contact: A/Professor Cassandra Szoeke T:61 3 8387 2224 F : 61 3 9387 9384
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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 (Aβ) peptide deposition in the brain, resulting in formation of plaques. However little is known about the possible association between nutrient intake and Aβ plasma. In this study, we will examine whether dietary intake of nutrients (data already collected from a food frequency questionnaire) is associated with plasma Aβ levels in a cross-sectional analysis of women aged 65 years and over. Aβ levels will be examined using Positron Emission Tomography (PET) scans (data already collected) in collaboration with imaging experts.

A major benefits 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.

172. Lifestyle Factors and Cognitive Health - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeke E: cszoeke@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 and alcohol consumption 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 factors on cognitive performance and health.

The main opportunities for this project are:

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

173. Examining neuropsychological trajectories using data collected from a longitudinal study - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeke E: cszoeke@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.

174. Subjective memory complaints, frailty and dementia - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Centre for Medical Research, Royal Melbourne Hospital
Contact: A/Professor Cassandra Szoeke, E: cszoeke@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

175. What causes a neuron to die? Investigating the essential role of selenium nutrition in neurodegenerative disease including Alzheimer's

Supervisors: Dr. Blaine R. Roberts
Project Site: Florey Inst. Neuroscience, Melbourne Brain Centre
Contact: Dr. Blaine R. Roberts blaine.roberts@florey.edu.au

Project description: Selenium is an essential trace element required for normal development. Curiously, out of the entire human genome of ~22,000 genes we only have 25 genes that encode for selenium containing proteins. This indicates an evolutionarily conserved function for selenium proteins. We have recently connected a newly discovered pathway for cell death known as ferroptosis to a key antioxidant selenium enzyme. The enzyme is known as glutathione peroxidase 4 (GPX4) and is a master regulator of ferroptoisis. Ferroptosis was discovered as a new form of cell death in cancer cells. Oxidative stress and selenium nutrition are intimately linked to the incidence and progression of cancer. The brain has a unique requirement for selenium and the levels of selenium in brain tissue are implicated in the pathogenesis of Alzheimer's disease.

This project involves the use of modern cutting edge 'omics' technology (e.g. Proteomics and Metallomics) to investigate the role of selenium containing proteins in human Alzheimer's disease tissue.

NEUROLOGY/MULTIPLE SCLEROSIS

176. Validation of computerized tools for the assessment of tremor severity in Multiple Sclerosis - *also offered as MBiomedSc*

Supervisors: Dr Anneke van der Walt, Dr Thushara Perera
Project Site: Department of Medicine, Royal Melbourne Hospital and Bionics institute
Contact: Dr Anneke van der Walt, Anneke.vanderwalt@mh.org.au

Project description: Tremor in MS (MST) is difficult to treat and the development of new interventions is limited by the absence of universal measuring systems. At present, therapeutic outcomes are measured by a variety of clinical rating scales that are subjective and lack sufficient sensitivity. With increasing use of interventional treatments such as Botulinum toxin injections or Deep Brain Stimulation for MST, it has become critical to develop precise measurement instruments.

This project aims to compare two computerized techniques used to measure MS tremor severity. The first is a 3D motion tracker, called TREMBAL, developed by the Bionics institute. The second is a simple joystick-based computer game. The aim of the project is to demonstrate that the simple joystick computer game is equivalent to the 3D motion tracker analysis.

During the project, you will be able to analyse data from MS patients with and without tremor, using both methods. This project requires MATLAB and statistical skills.

177. Functional MRI of speech in multiple sclerosis: understanding the organisation of speech production and its relation to cerebellar dysfunction

Supervisors: Dr Anneke van der Walt, Dr Scott Kolbe, Dr Adam Vogel
Project Site: Department of Medicine at Royal Melbourne Hospital, UoM,
Centre for Neuroscience of Speech at The University of Melbourne
Contact: Dr Anneke van der Walt, Anneke.vanderwalt@mh.org.au

Project description: Dysarthria is the most common communication disorder in MS, with a prevalence ranging from 40% to 55%. Yet, it has not often been the focus of MS studies. There are virtually no studies investigating the correlation of other cerebellar scores with dysarthria severity in MS. The underlying pathophysiology of dysarthria in MS is also not well understood with mixed reports of cerebellar, brainstem pathology and cortical pathology contributing to the changes in voice production.

To explore this, we have recruited and assessed patients with MS with and without arm tremor by performing a functional Brain MRI during which participants performed several reading, speaking and listening tasks.

This study aims to 1) analyse functional brain MRI and 2) understand the network changes observed by comparing it to clinical speech analysis and cerebellar disability scores. We hypothesize that the affected functional brain networks will be different in patients with and without other cerebellar features (such as arm tremor).

During this project, you will gain experience in analysing functional MRI images and develop the neuroanatomical knowledge to interpret these results. You will become familiar with statistical approaches to correlative analyses. This work will add to the current knowledge about communication problems in people with M

178. Measuring long-term disability outcomes in multiple sclerosis - *also offered as MBiomedSc*

Supervisors: Dr Tomas Kalincik; Dr Vilija 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.

179. Therapy of progressive forms of multiple sclerosis- *also offered as MBiomedSc*

Supervisors: Dr Tomas Kalincik; Dr Vilija 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: 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 in 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.

NEPHROLOGY

180. Finding genetic mutations in new types of inherited kidney disease – *ONLY offered as MBiomedSc*

Supervisors: Professor Judy Savige and Dr Yanyan Wang
Project Site: Department of Medicine RMH.
Contact: Professor Judy Savige, T 8344 3260, j.savige@unimelb.edu.au

Project description: To date, more than 120 different inherited kidney diseases due to mutations in 160 different genes have been identified. However there are still many diseases where the genes are not known. We have an Inherited renal disease clinic and are referred many families with unclassified kidney diseases. We have a number where the mutant genes are not known, and in the first instance are looking at some candidate genes. The aim of this project is to help characterize the patients (many have hearing loss and eye abnormalities too) and determine the mutant gene that is responsible for the disease in each family. For example, we have 12 families with inherited focal segmental glomerulosclerosis (FSGS), and also some candidate genes. Patients with focal segmental glomerulosclerosis have protoeinuria and invariably develop renal failure, requiring life long dialysis or a renal transplant. The aim of this project is to determine which genes are affected in FSGS and some other inherited renal diseases.

Techniques to be used and skills acquired: This study involves extracting DNA from peripheral blood, designing amplification/PCR primers, amplifying DNA, purifying it, sequencing it, and determining if the DNA change is pathogenic. This work is likely to result in a publication and could easily lead on to a PhD. This project involves working with a kidney specialist (Prof Judy Savige in her clinic) and with A/Prof Deb Colville an ophthalmologist.

Feasibility: We already have DNA stored from 12 families with FSGS and have Human Research Ethics Committee Approval for this project. This project has plenty of patient contact and also good laboratory experience.

NEUROPSYCHIATRY AND STRESS BIOLOGY

181. The worldwide ENIGMA MDD consortium: detecting robust imaging markers of depression – *also offered as MBiomedSc*

Supervisors: Dr. Lianne Schmaal and Dr. Chris Davey
Project Site: Orygen the National Centre of Excellence in Youth Mental Health, University of Melbourne
Contact: D r. Lianne Schmaal, **T**: 0393422886 **E**: lianne.schmaal@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 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.

182. Understanding the heterogeneity of youth depression using machine learning methods – *also offered as MBiomedSc*

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**: lianne.schmaal@unimelb.edu.au

Project description: The conventional approach to diagnosing MDD does not reflect the complexity and heterogeneity of the disorder, and consequently, reproducible neurobiological and genetic studies remain elusive. Depression is a complex heterogeneous disorder and the diagnostic label of MDD based on the classificatory systems of the DSM and ICD is likely to encompass biologically distinct phenotypes with different aetiologies and different optimal treatment strategies. This project aims to disentangle phenotypic heterogeneity of youth depression by integrating neurobiological information with clinical and behavioural data using machine learning techniques.

This project (or potentially PhD project) will use functional magnetic resonance imaging (fMRI) and data on symptom dimensions. The student will be involved in the acquisition of the neuroimaging and clinical data, processing of neuroimaging data and using machine learning methods to stratify the patients. Patients will be recruited from Orygen Youth Health and headspace centres. 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.

183. The relationship between dietary quality, nutrient biomarkers, and major depressive disorder – *also offered as MBiomedSc*

Supervisors: Dr Jerome Sarris
Project Site: The Melbourne Clinic (Richmond)
Contact: Dr Jerome Sarris jsarris@unimelb.edu.au

Project description: Emerging data is showing there is a relationship between mental health and a person's dietary quality and nutrient status. We have novel data assessing dietary quality, in addition to serum levels of essential fatty acids, zinc, folate, and B12, in a sample of adults with current major depressive episode (*n*=150). This sub-project (from an NHMRC-funded study) will explore the relationships between these factors to determine any meaningful associations. Matched control data will be collected by the successful research student, to determine any differences between depressed and healthy people in respect to their dietary quality and nutrient status

184. Mapping the Human Schizophrenia Connectome – *also offered as MBiomedSc*

Supervisors: Dr Andrew Zalesky (Melbourne Neuropsychiatry Centre), Dr Alex Fornito (Monash Biomedical Imaging), Dr Luca Cocchi (Queensland Brain Institute), Professor Christos Pantelis (Melbourne Neuropsychiatry Centre)
Project Site: Melbourne Neuropsychiatry Centre
Contact: Dr Andrew Zalesky: azalesky@unimelb.edu.au

Project description: This project aims to comprehensively map the entire human connectome in schizophrenia. The student will complete one of the largest clinical connectome mapping studies undertaken in the world by analysing high-quality brain imaging data in more than 330 individuals with schizophrenia provided by the *Australian Schizophrenia Research Bank* (ASRB). The ASRB is the largest brain research project ever undertaken in Australia. This project will apply advanced fibre tracking algorithms to the diffusion-MRI brain imaging data acquired in each patient, with the goal of comprehensively mapping all disrupted connections comprising the entire schizophrenia connectome. VLSCI computational resources may be utilised for this purpose.

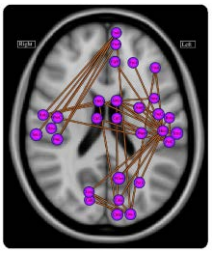


Figure: *Disruptions to functional brain connectivity in schizophrenia.*

185. Human Connectome Bioinformatics – *also offered as MBiomedSc*

Supervisors: Dr Andrew Zalesky, Professor Christos Pantelis
Project Site: Melbourne Neuropsychiatry Centre
Contact: Dr Andrew Zalesky: azalesky@unimelb.edu.au

Project description: The connectome refers to a comprehensive network description of the brain's internal wiring. Advances in magnetic resonance imaging (MRI) have enabled reliable mapping of the large-scale connectome in the living human brain. Comparing the human connectome between healthy and diseased brains has identified disease-specific anomalies in brain circuitry that may provide novel therapeutic targets and potential biomarkers to assess risk and predict patient outcomes. This project aims to develop and apply tools that capitalise on these advances.

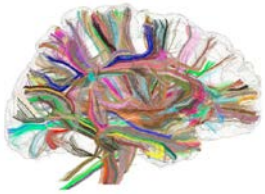


Figure: The human connectome mapped using diffusion-MRI and tractography

186. Neuroimaging in schizophrenia-spectrum disorders – *ONLY offered as MBiomedSc*

Supervisors: Dr Vanessa Cropley, Dr Andrew Zalesky, 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.

187. Effects of oxytocin genetic variants on brain and behavior in schizophrenia – *also offered as MBiomedSc*

Supervisors: Dr Cali Bartholomeusz (Orygen); Dr Chad Bousman (Melbourne Neuropsychiatry Centre); Prof Cyndi Shannon-Weickert (Neuroscience Research Australia); Prof Christos Pantelis (Melbourne Neuropsychiatry Centre)
Project site: Orygen, The National Centre of Excellence in Youth Mental Health and Centre for Youth Mental Health, 35 Poplar Road, Parkville; and Melbourne Neuropsychiatry Centre, The Alan Gilbert Building, 161 Barry Street, Carlton South.
Contact: Dr Cali Bartholomeusz Email: barc@unimelb.edu.au

Project Description: Oxytocin (OXT), a neurohypophysial hormone and neurotransmitter, is widely recognized as having an important role in human social cognition and prosocial behavior. These domains, which contribute to general social functioning, are significantly impaired in schizophrenia. Variation in OXT single nucleotide polymorphisms (SNPs) and OXT receptor (OXTR) SNPs have been linked to risk for schizophrenia. In addition, several of these SNPs have been associated with the severity of psychopathology, as well as social cognitive impairment in schizophrenia. A number of neuroimaging studies support a link between structural differences in social brain areas and OXTR variants in the healthy population, however no study has yet examined the relationship that these variants have to brain volumes in schizophrenia.

Aims: To examine the relationships between genetic load for previously identified OXT/OXTR SNPs and cognition, symptoms, and social functioning, in Australians with schizophrenia and healthy control participants. We will also investigate whether these relationships are linked to and potentially mediated by, brain volumes, particularly of the amygdala, nucleus accumbens and medial prefrontal/anterior cingulate cortices.

Method: Pre-existing data from the Australian Schizophrenia Research Bank will be utilised for the current study. Correlation statistics, and mediation analyses where appropriate, will be conducted to explore the associations between genetic variants and outcome measures and brain volumes. ANOVAs will also be conducted to explore differences between patients and healthy controls.

Outcome: This project will increase our understanding of how variants in key OXT and OXTR SNPs are related to risk for schizophrenia, symptomatology, cognition and general social functioning in an Australian sample

188. MRI volumetry and shape analysis in frontotemporal dementia and schizophrenia

Supervisors: Dr Dennis Velakoulis and Dr Mark Walterfang
Project Site: Melbourne Neuropsychiatry Centre, Royal Melbourne Hospital
Contact: Dr Dennis Velakoulis T: 93428750 E: dennis.velakoulis@mh.org.au

Project Description: It has been well recognised for over a century that some patients with schizophrenia develop a dementia but the nature of this dementia has remained unclear. Recent clinical, neuropathological and genetic studies have identified a previously unrecognised association between chronic schizophrenia and frontotemporal dementia. This project aims to examine whether the volume and shape changes identified in schizophrenia are quantitatively and qualitatively similar to patients with a frontotemporal dementia. In addition to demographic and diagnostic information a subset of the subjects have neuropsychological and bedside screening cognitive testing which can be correlated with brain structural volumes and shape.

Aims: To estimate and compare brain structure volume and shape in an existing database of MRI images of patients with chronic schizophrenia and frontotemporal dementia compared to control subjects.

Methods: Specific regions of interest to examine would include:
- Frontal and temporal lobes
- Orbitofrontal / dorsolateral / medial frontal cortex
- hippocampus
- Insula cortex
- Superior temporal gyrus

Depending on the region of interest the project would require the learning of methods for analysing the region and developing a reliable method for this assessment.

Outcome: To assess and compare the nature and pattern of brain changes in chronic schizophrenia and FTD.

189. Characterisation of physiological stress responses in patients with depression and epilepsy - *also offered as MBiomedSc*

Supervisors: Dr Dennis Velakoulis, Dr Chris Turnbull and Professor Terry O'Brien
Project Site: Melbourne Neuropsychiatry Centre, Royal Melbourne Hospital and Alan Gilbert Building, University of Melbourne
Contact: Dr Dennis Velakoulis T: 93428750 E: dennis.velakoulis@mh.org.au

Project Description: Depression and epilepsy are disabling disorders that are common in the community. Both disorders have been shown to have effects on the human body's physiological response to stress. These effects have been identified in both the autonomic nervous system (responsible for immediate responses to stress) and the hypothalamic-pituitary-adrenal axis (which mediates longer-term stress responses). However, it is not known whether these effects occur through similar mechanisms, partly because previous research has not focused extensively on patients with both disorders. This project will broaden our understanding of stress physiology in these disorders by assessing stress physiology in patients who have been admitted to hospital for assessment of seizures and have one or both disorders.

Aims: To compare the effects of depression and epilepsy, particularly temporal lobe epilepsy, human physiological stress responses and to assess whether these effects are additive or have a more complex interaction

Methods: The project will measure parameters of the physiological stress response in patients who have been admitted to investigate their epilepsy. Assessment of the autonomic nervous system will use a variety of measures of heart rate variability, and the HPA axis will be measured by the level of the hormone cortisol in saliva. Clinical data will be obtained by working with the clinical team caring for the patient and involves direct patient contact.

Outcome: To better understand stress physiology in depression (a psychiatric illness) and epilepsy (a neurological disorder) by assessing their interaction.

190. Functional disconnections and the pathophysiology of psychosis - *also offered as MBiomedSc*

Supervisors: Dr Nigel Jones and Prof Terence J O'Brien.
Project Site: Department of Medicine (RMH), MBC Neurosciences Building, Parkville
Contact: Dr Nigel Jones T: 9035 6402 E: ncjones@unimelb.edu.au

Project Description: Functional disconnections in cortico-thalamo-cortical (CTC) systems, the neuronal circuits of attention, cognition and perception, are thought to underlie dysfunctions of conscious integration such as those seen in schizophrenia. More than 80% of the neurons that make up the CTC systems are glutamatergic. There is considerable evidence to suggest that NMDA-type glutamate receptors are implicated in the pathophysiology of schizophrenia. Non-competitive NMDA receptor antagonists (PCP, ketamine, MK-801), at subanaesthetic doses, induce cognition impairment, schizophreniform psychosis, hallucinations, and exacerbate both positive and negative symptoms in schizophrenic patients. In rodents, ketamine produces a wide spectrum of abnormal behaviour relevant to schizophrenia. The neuronal mechanisms underlying transient disruption in NMDA receptor function remain to be determined. CTC circuits generate coherent synchronized gamma frequency (30-80 Hz) oscillations during conscious brain operations. Disruption of cognition-related coherences of gamma oscillations between cortical areas is a major functional abnormality in schizophrenic patients.

This project will explore the hypothesis that aberrant cortical gamma frequency activity induced by ketamine mediates alterations in behavioural activity, thereby linking NMDA-mediated dysfunction of neuronal activity to schizophrenic-like behaviour.

Research plan: Rats are surgically implanted with recording electrodes and connected to a computer facilitating measurement of the EEG and analysis of the effects of drugs on cortical brain rhythms in the gamma frequency. The resultant changes in cortical rhythms will be concurrently measured with either sensorimotor gating or working memory to establish a temporal and magnitudinal association between disruptions to gamma oscillations and behavior.
Skills: small animal surgery, EEG measurement, behavioural analysis.

191. Antidepressants in epilepsy

Supervisor: Dr Nigel Jones and Dr Sandy Shultz
Project Site: Department of Medicine (RMH), MBC Neurosciences Building, Parkville.
Contact: Nigel Jones E: ncjones@unimelb.edu.au Sandy Shultz E: sandy.shutlz@unimelb.edu.au

Project description: Patients with epilepsy also frequently suffer from psychiatric disorders such as depression. As a consequence, many patients receive antidepressants to mitigate these mood disorders. While these are generally effective, the influence of antidepressants on the severity of the epilepsy in patients, and on the risk of developing epilepsy, has been little studied. Our provocative recent data suggest that antidepressants actually promote the development of epilepsy, which could have major implications for how these drugs are prescribed to patients. Using a range of animal models, including post-traumatic epilepsy, this project seeks to characterise and understand the influence of antidepressants such as Prozac on epilepsy development. Available as Honours, Masters or PhD projects

Skills: Small animal handling; animal models of epilepsy; models of traumatic brain injury; small animal surgery and EEG recording; MRI, animal behaviour and cognition, molecular biology techniques, such as real-time qPCR, Western blotting; histology, including immunocytochemistry

192. Temporal lobe epilepsy, the HPA axis and depression - *also offered as MBiomedSc*

Supervisor: Prof Terence O'Brien, Dr Dennis Velakoulis,
Project Site: Department of Psychiatry and Medicine Royal Melbourne Hospital
Contact: Terence O'Brien T: 8344 5490 E: obrientj@unimelb.edu.au
Dennis Velakoulis T: 93428750 E: dennis.velakoulis@mh.org.au

Brief Summary: The key structures involved in mesial temporal lobe epilepsy – the hippocampus and amygdala – are critical components in the central regulation of the HPA axis. The implications of this have hardly been studied at all. Does the HPA axis function normally when someone has mesial temporal sclerosis (the usual pathology underlying TLE)? What happens to HPA axis function when a temporal lobe is excised to treat intractable TLE (temporal lobectomy)? There are good reasons to think the answers to these questions are very important for several reasons, e.g., glucocorticoids and stress have been shown in animal models of this kind of epilepsy to aggravate the disorder, to speed up its rate of development.

Project: We have a small preliminary study in progress, testing HPA function before and after temporal lobectomy. We're using the dex/CRH test, doing this about 2 weeks before and at 6 and 12 weeks after surgery. We're doing the same protocol with surgical control patients, having elective brain surgery for nonepilepsy conditions remote from the temporal lobe.

We think temporal lobectomy disinhibits the HPA axis, which may help explain the transient mood disturbance that occurs in temporal lobectomy patients in the early months following surgery.

This study will interest students interested in a topic that involves basic neuroscience and neuroendocrinology but also with a very immediate clinical relevance. It will involve contact with patients – in recruitment, obtaining informed consent, administering questionnaires and helping administer the dex/CRH test (a two hour procedure). It will also involve data analysis and writing-up in the usual way.

193. Does stress contribute to epilepsy? - *also offered as MBiomedSc*

Supervisor: Dr Nigel Jones and Prof Terence O'Brien
Project Site: Department of Medicine (RMH), MBC Neurosciences Building, Parkville.
Contact: Dr Nigel Jones T: 9035 6402 E : ncjones@unimelb.edu.au

Project description: Chronic stress is strongly linked to the development of psychiatric disturbances, such as depression and anxiety disorders. Interestingly, these disorders are prevalent in a high proportion of people suffering from epilepsy.

Recent literature suggests that environmental exposures such as stress may also contribute to the development of epilepsy. This project aims to investigate this hypothesis, with a parallel focus on anxiety and depression-like behaviour.

Using rat models, this study will determine whether exposure to repeated stressful situations leads to a vulnerability to limbic epilepsy. It will also study whether psychiatric disturbances are enhanced in subjects who have experienced the stress.

The second stage of the project will investigate molecular and plasticity changes which occur after epilepsy to determine whether the stress can influence such parameters as stress receptor expression and neurogenesis.

***Skills*:** Small animal handling and neurosurgery (electrode implantations), neurobehavioural testing and analysis, post-mortem stereology.

194. High Frequency Brain Wave Patterns in a Rodent Model of Schizophrenia

Supervisors: Dr Chris French, A/ProfAnthony Hannan, Dr Nigel Jones, Prof Terence O'Brien
Project Site: Department of Medicine RMH, MBC Neurosciences Building, Parkville
Contact: Chris French frenchc@unimelb.edu.au

Project description: High frequency ("gamma") brain wave activity has been associated with higher cognitive activity in humans and animals, and has shown to be abnormal in psychosis and schizophrenia. Phospholipase C-β1 (PLCβ1) is an enzyme that is altered in human schizophrenia and a PLCβ1 knockout mouse displays deficits (locomotor hyperactivity, sensorimotor gating and cognitive impairment) homologous to those seen in schizophrenia. Remarkably, some of these deficits can be improved with antipsychotic drugs that are efficacious in humans.
The aim of these experiments is to characterize the gamma-frequency brain wave patterns of normal and PLCβ1 knockout mice, and to investigate whether the behavioural effects of antipsychotic drugs can be correlated with brain wave patterns.

These experiments are likely to lead to a better understanding of the functional abnormalities that lead to schizophrenia in humans and to suggest new and better forms of treatment.

195. Estrogen, antipsychotics and schizophrenia – *also offered as MBiomedSc*

Supervisors: Dr Andrea Gogos and Dr Snezana Kusljic
Project Site: Hormones in Psychiatry Laboratory, The Florey Institute of Neuroscience and Mental Health
Contact: Dr Andrea Gogos E: andrea.gogos@florey.edu.au and
Dr Snezana Kusljic E: skusljic@unimelb.edu.au

Project description: A role for sex hormones in the development of schizophrenia has been hypothesized to explain the observed sex difference in the age-of-onset, with women presenting symptoms on average 3-4 years later than in men. Interestingly, clinical trials have shown that adjunctive estrogen treatment in women with schizophrenia can accelerate the beneficial effect of the antipsychotic treatment. Our laboratory aims to study the role of estradiol, progesterone and testosterone in modulating symptoms of schizophrenia and depression. We currently use both in vivo and in vitro rodent models, as well as post-mortem CNS tissue. This project aims to investigate the expression of estrogen receptors in the brain using one of the approaches commonly-used in our laboratory: radioligand receptor binding, western blot, or in situ hybridization.

DEVELOPMENTAL PSYCHOBIOLOGY @ THE FLOREY

196. Early life stress and memory development

Supervisors: Dr Heather Madsen Co-supervisor: Dr Jee Hyun Kim
Project Site: Florey Institute, Parkville
Contact: heather.madsen@florey.edu.au

Project description: Early life experiences play a pivotal role in shaping personality and psychosocial functioning into adulthood. For example, early life adversity in humans is associated with increased risk of developing mental illnesses such as depression and anxiety. Given the importance of these first few years of life, it is interesting that most adults fail to recall autobiographical events from their early childhood years. Infantile amnesia is the term used to describe this phenomenon of accelerated forgetting during infancy, and it is not unique to humans. In fact, infantile amnesia has been observed in every altricial species examined; that is, animals that undergo extensive post-gestational development.

Many investigations into infantile amnesia have used Pavlovian fear conditioning in rats as a model of learning and memory. While adult rats exhibit excellent memory retention following just a single conditioning episode, infant rats rapidly forget fear associations over short intervals. Recently it has been shown that exposure to early life stress improves retention of learned fear in infant rats. The aim of this project is to investigate the neurobiological changes that underlie this early transition to adult-like memory.

197. Regulation of emotional memory across development

Supervisors: Dr Despina Ganella, Co-supervisor: Dr Jee Hyun Kim
Project Site: Florey Institute, Parkville
Contact: despina.ganella@florey.edu.au

Project description: Most anxiety disorders emerge during childhood, and individuals with childhood onset express more severe symptoms than do individuals who have adult onset. In fact, there is growing recognition that mental disorders may actually be developmental brain disorders and, as such, treatment strategies should focus on the young population. Currently, the effective treatments for anxiety disorders are cognitive-behavioural therapies that rely on inhibition of emotional memory. This project will examine inhibition of emotional memory throughout development using Pavlovian fear conditioning as a model of anxiety disorders in rats.

198. Latent inhibition in adolescent rats

Supervisors: Dr Jee Hyun Kim
Project Site: Florey Institute, Parkville
Contact: E: jee.kim@florey.edu.au

Project description: Ever wondered why individual differences exist in developing an anxiety disorder following a similar traumatic experience (e.g., a car accident)? It turns out that having previous related experiences before the traumatic event can play a huge part. For example, a veteran driver with many years of safe driving experience will be less likely to develop an anxiety disorder following a car accident, compared to a novice driver who has not had much prior safe driving. This protection from forming fear memories due to previous safe experiences is called 'latent inhibition', and this process shares similar mechanisms to 'extinction' that refers to safe experiences following the traumatic event. In the present project, we'd like to investigate latent inhibition in adolescent vs adult rats, as we know that extinction is different across the two ages. Examining latent inhibition in adolescence may help us to understand why adolescence is a particularly vulnerable age to experience anxiety disorders.

NEUROVASCULAR

199. Imaging predictors of neurological recovery post acute stroke intervention

Supervisors: A/Prof. Bernard Yan, A/Prof. Peter Mitchell, A/Prof. Rick Dowling
Project Site: Royal Melbourne Hospital
Contact: Bernard.Yan@mh.org.au

Project Description: Stroke is the second leading cause for death and the leading cause for disability worldwide. It accounts for significant financial burden up to $5 billion on health care costs associated with stroke in Australia in 2012 alone. Rapid treatment with thrombolysis (s clot busting medication), within 4.5 hours of ictal onset, increases the chance of blood flow restoration to the ischemic area and decreases the risk of disability and dependence. This benefit diminishes and approaches parity at approximately 6 hours from stroke onset. CT scan is a widely used imaging modality for the initial evaluation of stroke. The Alberta Stroke Program Early CT Score (ASPECTS) tool was developed to provide a standard CT scan with a reproducible grading system. It is a semi-quantitative method of defining infarct extent in the middle cerebral artery (MCA) territory.[11] However, very few studies have examined the impact of time on outcome as adjudicated by ASPECTS. The aim of this retrospective analysis study on an existing prospective database is to assess the

impact of time on ASPECTS score and its correlation to functional outcome at 3 months after an acute ischemic stroke. We hypothesize that, in patients with acute ischaemic stroke treated with IV tPA, the predictive capacity of ASPECTS score of clinical outcome increases with time from stroke onset.

200. Continuous monitoring of motor recovery post acute stroke rescue: development of a broadband-based portable motion detector (REWIRE system) - *also offered as MBiomedSc*

Supervisors: A/Professor Bernard Yan, A/Professor Peter Mitchell, A/Professor Richard Dowling
Location: Department of Neurology & Department of Radiology, Royal Melbourne Hospital
Contact: A/Professor Bernard Yan, Neurointerventionist, Neurovascular Research Group, Department of Neurology, Royal Melbourne Hospital,
T: +61 3 9349 2477 / F: +61 3 9349 4489, Email: bernard.yan@mh.org.au

Project Description: Acute stroke is caused by a blockage of one of the arteries in the brain resulting in interrupted blood supply. Brain cells deprived of oxygenated blood die rapidly unless blood supply is restored. The clinical manifestation is acute loss of neurological function e.g. paralysis of arms and legs.

One of the milestones of modern management of acute stroke is the administration of a thrombolytic (clot-busting medication) in order to unblock the blocked artery. A proportion of patients will experience recanalization (reopening) of blocked arteries with consequent recovery of arm and leg movements (motor recovery).

The monitoring of motor recovery is by clinical observation is critical in the management of stroke patients. Patients who do not exhibit early motor recovery post thrombolysis may benefit from more aggressive treatment. However, the current clinical observation paradigm is time consuming and subjected to inter-observer bias. We aim to validate the clinical utility of a novel portable motion detector (REWIRE system) which allows for continuous monitoring of motor recovery in stroke patients treated with thrombolysis. The findings of the study may inform future decision to mandate continuous motor monitoring of patients post thrombolysis. We envisage that the study findings may lead to investigations of the REWIRE system in other neurological diseases e.g. Epilepsy.

Research Plan: Human Ethics Committee approval has been obtained. The first phase of the project has been completed with 10 healthy controls. The second phase of the project aims to study the motor recovery of stroke patients. We hypothesize that the motion detector (REWIRE system) is able to better detect motor recovery compared to standard clinical observations. Inclusion criteria: acute stroke patients admitted to RMH Stroke Care Unit. Methods: study subjects will wear the REWIRE system on each limb for 4 hours. Accelerometry raw data will be continuously transmitted by WIFI to a base station for analysis. Study subjects are also examined by standard clinical examination for comparison.

201. Acute stroke rescue: clot retrieval. Does imaging characteristics predict the histophathology of clot composition? - *also offered as MBiomedSc*

Supervisors: A/Professor Bernard Yan, A/Professor Peter Mitchell, A/Professor Richard Dowling
Location: Department of Neurology &Department of Radiology, Royal Melbourne Hospital
Contact: A/Professor Bernard Yan, Neurointerventionist, Neurovascular Research Group, Department of Neurology, Royal Melbourne Hospital,
T: +61 3 9349 2477 / F: +61 3 9349 4489, Email: bernard.yan@mh.org.au

Project Description: Acute stroke is caused by a blockage of one of the arteries in the brain by clot(s). The clinical consequences result from acute neuronal failure secondary to precipitous decrease in arterial perfusion. Apart from intravenous thrombolytics, mechanical clot retrieval holds promise as an effective means to reopen blocked arteries. However, the success clot retrieval depends partly on clot composition. It is known that clots undergo pathological change from red-cell dominant, then to fibrin dominant and finally to organized fibrin strands. It is thought that clots with organized fibrin are the most resistant to mechanical retrieval. The difficulty is that up till now, there are no reliable methods to judge clot composition prior to mechanical retrieval. In this project, we aim to employ advanced CT angiogram imaging pre-procedure and to correlate the imaging characteristics with histopathological examination of clots. The implication of the findings is that we may be able to more accurately predict the success rate of clot retrieval and to triage patients prior to invasive therapies.

Research plan: Human research ethics committee approval has been obtained. Acute stroke patients eligible for acute clot retrieval will be recruited prospectively into the study. Imaging modalities include plain CT, CT angiogram and CT perfusion (this is part of standard stroke treatment protocol). Clot retrieval will be performed by RMH neurointerventionists. Clot samples will be sent for standard H & E staining and immunohistochemisty for platelet markers. The imaging parameters will be correlated with histopathological examination of clots and the degree of success of clot retrieval and vessel recanalization.

202. STROKE WATCH – a wireless, wearable device for intensive monitoring of motor system fluctuations post acute stroke - *also offered as MBiomedSc*

Supervisors: A/Professor Bernard Yan, Professor Stephen Davis
Project Site: Department of Neurology, Melbourne Brain Centre at Royal Melbourne Hospital

Contact: A/Professor Bernard Yan, Neurointerventionist, Neurovascular Research Group.
T: +61 3 9349 2477 / F: +61 3 9349 4489, Email: bernard.yan@mh.org.au

Project description: Acute stroke is caused by a blockage of one of the arteries in the brain resulting in interrupted blood supply. Brain cells deprived of oxygenated blood die rapidly unless blood supply is restored. The clinical manifestation is acute loss of neurological function e.g. paralysis of arms and legs. A significant proportion of stroke patients demonstrate motor function fluctuations in the immediate post stroke period. Current monitoring processes have high inter-rater and intra-rater disagreements, leading to missed opportunities for therapeutic interventions. The STROKE WATCH is a wireless, wearable device with in-built multi-axis accelerometry system. In our pilot study, STROKE WATCH is able to track the motor fluctuations of chronic stroke patients. In this current study, we aim to investigate the utility of the STROKE WATCH in acute stroke patients and test the hypothesis that STROKE WATCH monitoring is capable to detect motor deterioration, leading to timely intervention and better patient outcomes. This research project has already received hospital ethics approval to operate

OPHTHALMOLOGY

203. Which genes affected in structural renal disease and renal complement diseases? – *also offered as MBiomedSc*

Supervisors: Prof Savige and A/Prof Deb Colville
Project Site: Department of Medicine, Royal Melbourne Hospital
Contact: Prof Savige on 8344 3260 or j.savige@unimelb.edu.au

Project description: The genes for many forms of inherited renal disease are still unknown. We have several families with inherited disease in whom we will try to identify the abnormal genes. This involves carefully characterizing clinical features, collecting DNA, undertaking exomic sequencing, and checking for mutations in candidate genes. Any possible mutation will then be confirmed in other affected family members by DNA sequencing.

Techniques to be used and skills acquired: This project involves patient contact, a small amount of lab work and how to interpret DNA sequence abnormalities.

Feasibility: All the techniques for this project are already available in our laboratory.

204. Small vessel disease as a marker for poorly controlled hypertension – *also offered as MBiomedSc*

Supervisors: Prof Savige, A/Prof Deb Colville
Project Site: Department of Medicine, Royal Melbourne Hospital
Contact: Prof Savige on 8344 3260 or j.savige@unimelb.edu.au

Project description: This project involves taking retinal photographs in patients with hypertension relating any small vessel disease in the retina blood pressure control. This study is to investigate whether retinal photographs might be useful in predicting blood pressure control.

Techniques to be used and skills acquired: This project involves patient contact, poor blood pressure control learning how to take retinal photographs and how to interpret retinal abnormalities.

Feasibility: Many of the medical students who have undertaken similar projects during a research year have achieved a publication from their work study. Nevertheless whenever the small vessels in the heart are affected, small vessels are diseased throughout the body. This includes the vessels in the retina, which are very accessible using a retinal camera and photography. So we propose to examine the retinal small vessels as a model for the coronary arterioles and determine whether renal failure or diabetes means these vessels are diseased and respond less well to medication.

This study involves recruiting patients from the wards with renal failure or diabetes and testing the effect of a tablet that usually dilates small vessels. You will help the patient fill out a questionnaire and also take their blood pressure and retinal photographs, and then review the photographs under the supervision of an ophthalmologist. In addition the retinal photos will be sent to the Centre for Eye Research Australia for the vessel diameters to be measured precisely. The aim of this project is then to determine whether small vessels are less responsive in diabetes and renal failure, and whether medication doses should be increased. The analysis includes univariate and multivariate statistics and backwards linear regression (we will help you with the statistics).

205. Retinal small vessel disease in pregnancy – *also offered as MBiomedSc*

Supervisors: Prof Judy Savige and A/Prof Deb Colville
Project Site: Northern Health
Contact: Prof Judy Savige 8344 3260 or j.savige@unimelb.edu.au

Project description: This study investigates retinal endothelial responsiveness in normal pregnancy and in patients with pregnancy associated hypertension, diabetes and small for gestational age babies. It uses a non-mydriatic retinal camera and the 'flicker' machine/camera

The aim is to understand better these diseases of pregnancy (retinal small vessels resemble the placental small vessels). In addition it may be possible to use retinal small vessel changes to identify those women at risk of pregnancy associated hypertension, diabetes or small for gestational dates babies) and to monitor treatment.

This is a very clinical project with lots of patient contact

PHARMACOGENETICS AND PRECISION MEDICINE

206. Wearable devices for non-invasive, ambulatory seizure monitoring and prediction - ***also offered as MBiomedSc***

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.

207. Stroke and epilepsy a bi-directional relationship? - ***also offered as MBiomedSc***

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.

208. Clinical utility of clinical whole exome sequencing for epilepsy - ***also offered as MBiomedSc***

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.

209. Development of a low cost, point-of-care diagnostic test to prevent abacavir hypersensitivity

Supervisors: Prof Patrick Kwan, Prof Stan Skafidas
Project sites: Department of Medicine (Royal Melbourne Hospital), Centre for Neural Engineering
Contact: Professor Patrick Kwan, Department of Medicine (RMH)
E: patrick.kwan@unimelb.edu.au

Project description: Abacavir is a nucleoside analog reverse transcriptase inhibitor (NRTI) used to treat HIV and AIDS. 5-8% people develop hypersensitivity to abacavir. It has been found that abacavir hypersensitivity is strongly associated with HLA-B*57:01, and pre-therapy HLA testing is recommended by regulatory agencies and all major treatment guidelines. However, conventional testing is laboratory based with long turnaround time and is not accessible or affordable for people living in developing countries where many people with HIV live.

A monoclonal antibody that recognises HLA-B*57:01 has been developed. This project aims to use this antibody to develop a simple, rapid, low cost HLA-B*57:01 test kit.

210. Express ambulatory point-of-care molecular diagnosis - *also offered as MBiomedSc*

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;

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.

211. Immune self-reactivity triggered by carbamazepine-modified HLA-peptide repertoire - *also offered as MBiomedSc*

Supervisors: Professor Patrick Kwan, Dr Nicole Mifsud
Project Site: Department of Medicine (RMH), University of Melbourne, Department of Biochemistry & Molecular Biology, Monash University
Contact: Professor Patrick Kwan, Departments of Medicine and Neurology, E: patrick.kwan@unimelb.edu.au

Project description: Human leukocyte antigens (HLAs) are highly polymorphic proteins that initiate immunity by presenting pathogen-derived peptides to T cells. HLA polymorphisms mostly map to the antigen-binding cleft, thereby diversifying the repertoire of self-derived and pathogen derived peptide antigens selected by different HLA allotypes. Recently, a growing number of immunologically based drug reactions have been found to be strongly associated with specific HLA alleles. In particular, HLA-B*15:02 and HLA-A*31:01 are associated with severe skin reactions caused by certain antiepileptic drugs, but little is known about the underlying mechanisms of these associations. Recent research has demonstrated that direct binding of the drug to the HLA molecule led to changes in the shape and chemistry of the antigen-binding cleft, thereby altering the repertoire of endogenous peptides and driving T-cell activation. This project aims to find out whether this mechanism also applies to the case of the interactions between antiepileptic drugs and these HLA alleles.

212. HLA and its association with skin rashes and drug induced hepatitis: The role of pharmacogenetics to predict anti-epileptic drug side-effect - *also offered as MBiomedSc*

Supervisors: Dr. Marian Todaro, Dr Slave Petrovski, Prof Terence O'Brien, Prof Patrick Kwan
Project Site: The Comprehensive Epilepsy Program, Department of Neurology, The Royal Melbourne Hospital.
Contact: Dr Marian Todaro T: 9342 7500 E: Marian.Todaro@mh.org.au;
Dr Slave Petrovski E: slavep@unimelb.edu.au;
Professor Terence O'Brien T: 8344 5479 E: obrientj@unimelb.edu.au

Project Description: This study aims to investigate the individual responses of patients who developed a rash or drug-induced hepatitis due to an anti-epileptic drug (AED), and link this information to the genetic profile of each patient – in particular that for the human leukocyte antigens (HLA). The results will help to identify genetic markers that could predict when a patient is at risk of having side effects with a particular medication.

Previous experience has shown that individuals vary greatly in their responses to drugs. Although medication is effective and well tolerated in most patients side-effects can necessitate treatment changes. One of the most common, and

potential serious, types of side effects to anti-epileptic drugs is hypersensitivity reactions - including generalised skin rashes, Steven Johnson Syndrome (SJS), and drug-induced hepatitis. It has been shown that genetic factors play an important role in determining an individual's response to medication. Recently, the occurrence of SJS in Asian patients taking carbamazepine has been repeatedly associated with the carriage of a particular HLA antigen, HLA-B*1502. However, this association does not persist in non-Asian populations and HLA associations in other populations, or with other types of AED-induced hypersensitive reactions, have not yet been identified. Understanding why responses vary has the potential to improve the safety and effectiveness of medical treatment for various conditions.

This project will utilize an international unique cohort of more than 400 patients who have been prospectively enrolled and followed following starting treatment with an AED for the first time. The HLA profiles of patients who developed hypersensitivity reactions will be compared with those who took the same drug but did not develop any such reactions. The goal of this research is to eventually allow the choice of medication to be tailored to an individual's specific genetic profile.

Skills to be learned: Human genomics, immunogenetics, bioinformatics, clinical phenotyping, multivariate statistics.

213. Pharmacogenetics: do mutations in CYP 2C19 alter the clinical effectiveness of clopidogrel in patients with cerebrovascular disease? - *also offered as MBiomedSc*

Supervisors: A/Professor Bernard Yan, A/Professor Peter Mitchell, A/Professor Richard Dowling
Location: Department of Neurology & Department of Radiology, Royal Melbourne Hospital
Contact: A/Professor Bernard Yan, Neurointerventionist, Neurovascular Research Group, Department of Neurology, Royal Melbourne Hospital,
T: +61 3 9349 2477 / F: +61 3 9349 4489, Email: bernard.yan@mh.org.au

Project Description: Stroke is the third leading cause of death in Australia. The prevention of recurrent strokes is an important strategy to improve health and reduce medical costs. Globally, anti-platelet agents (aspirin, clopidogrel, prasurgrel etc) are the first-line treatment to prevent further ischaemic events (i.e. strokes). Anti-platelets work by inhibiting platelet aggregation with consequent reduced risk of artery blockages. However, up to 30% of patients are "resistant" to clopidogrel treatment. Of note, activity of clopidogrel is critically dependent on its conversion from the pro-drug to its active form by a member of the P 450 family of enzymes (CYP 2C19). A genetic mutation, e.g. CYP 2C19*2, predicts lower levels of the active form clopidogrel leading to failure of platelet inhibition. We hypothesize that patients with genetic mutations of CYP 2C19 (e.g. CYP2C19*2) will demonstrate clopidogrel failure and increased risk of stroke. The results will have the potential to change clinical practice in the prescription of clopidogrel.

Research Plan: Our project is part of a large pharmacogenenomics project led by Professor Patrick Kwan's research group. Our research arm focuses on CYP 2C19 genetic mutation and its clinical consequences. Human ethics committee approval has been obtained to test anti-platelet resistance. Inclusions criteria: patients previously exposed to clopidgrel or with plans to start clopidogrel (e.g. aneurysm coiling, pipeline flow diversion device implantation etc). Methods: all patients will be tested for CYP2C19 genetic status by PCR and a novel DNA amplification technique. The patients will be followed clinically and by neuroimaging to identify recurrent cerebral ischaemic events.

214. A Pharmacogenomics study of the teratogenicity valproate based on the prospective Australian Register for Anti-epileptic Drugs in Pregnancy - *also offered as* MBiomedSc

Supervisors: Professor Terence O'Brien, Professor Frank Vajda and Dr Slave Petrovski - Epilepsy and Neuropharmacology Group, The Department of Medicine: The Royal Melbourne Hospital.
Project Site: The Department of Medicine (RMH)
Contacts: Terence O'Brien T: 8344 5479 E: obrientj@unimelb.edu.au;
Frank Vajda E: vajda@netspace.net.au; Slave Petrovski E: slavep@unimelb.edu.au

Project Description: It is long been recognised that women with epilepsy who become pregnant while taking an anti-epileptic drug (AED) have an increased risk of having a foetus or infant with a birth defect (BD). This is particular high for valproate. Despite the increased risk associated with taking AED in pregnancy, most women with epilepsy who become pregnant, or plan to do so in the near future, cannot simply cease the drugs because of the risk to the health and safety of the mother and child of uncontrolled seizures. The development of methods that would allow the prediction that a specific drug would be associated with a higher risk of a birth defect in a particular woman would be of great potential benefit. There is evidence from family and twin studies that genetic factors may play a role in determining predisposing an individual to having a child with an AED associated birth defect. The Australian Register of Anti-epileptic Drugs in Pregnancy has been established in an attempt to obtain more accurate information about the risks of specific AEDs. This is a prospective, voluntary, telephone interview based study that enrols pregnant women with epilepsy, prior to the outcome of the pregnancy being known, and follows the outcomes of their pregnancies. The study has been running since July 1999, and to date has enrolled more than 1600 pregnant women.

This study will attempt to identify genetic markers that predict the risk of valproate-induced birth defects. Participants will be identified through the Australian Registry of Anti-epileptic drugs in pregnancy. Women with epilepsy who were

taking an AED in the first trimester, and their partners, will be offered enrollment. Two types of genetic tests will be performed:

- A *case-control genetic association* studies comparing genetic information from mothers and infants taking a valproate AED during the first trimester with those who were taking the same valproate but did not have a child with a birth defect
- A transmission disequilibrium test (TDT), design will be also be employed. This test looks for significant disequilibrium in the transmission of the allele of interest in the patient with a characteristic of interest. It therefore eliminates any potential sources of bias between the affected patients and non-affected controls, which may occur in case-control association studies. Blood for genetic analysis would be taken from the mother, father and child.

215. Pharmacogenomics in IBD - *also offered as MBiomedSc*

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 guage 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

216. Health and the housing interface; the health impacts of precarious housing amongst refugees in Melbourne

Supervisors: Dr Kudzai Kanhutu, Professor Beverley Ann Biggs, Dr Joanne Gardiner,
Project Site: Doherty Institute/Royal Melbourne Hospital International and Immigrant Health Group
Cohealth community health service
Contact: Dr Kudzai Kanhutu Email: kudzai.kanhutu@mh.org.au

Project description: Victoria currently receives one third of the national refugee intake. In addition 80% of immigrants come from low and middle income countries some of whom are from refugee-like backgrounds.

Refugees and asylum seekers encounter a number of barriers to accessing suitable housing.
Precarious housing can be defined across a number of dimensions.

1. Unaffordable housing; high housing costs in proportion to income,
2. Unsuitable housing; overcrowded and/or poor dwelling condition and/or unsafe and/or poorly located.
3. Insecure housing; insecure tenure type and subject to forced moves.

The negative impact of precarious housing on mental and general health and is well documented in the literature.

Currently, little is known about the frequency of precarious housing in Australian hospital and primary care based patients and the co-occurrence of underlying medical comorbidities.

We intend to perform a prospective study of our outpatient and primary care clinics to establish baseline figures on the prevalence of precarious housing in our cohort of patients from refugee and asylum seeker backgrounds. Survey questionnaires relating to refugee clients perceptions of the impact of housing on their health will provide much needed qualitative data. In addition, participants with a lived experience of precarious housing will also be interviewed regarding what supports could enable them to achieve greater housing security.
The combination of quantitative and qualitative data sets will help to pave the way to developing client focused housing policy and interventions for affected refugee clients.

Skills/techniques acquired:

1. Systematic review – literature search, data synthesis and report writing.
2. Qualitative research methodology – survey writing, data collection and data synthesis.
3. Journal writing for peer review publication.
4. Abstract writing and presentation techniques for conference settings.

Additional career benefits:
The successful applicant will have the opportunity to present their research findings to the Victorian Refugee Health Network, the Department of Health and Human Services as well as representatives from the Federal Government's Department of Immigration and Border Protection.

217. Life-long Exposures for Healthy Ageing – *also offered as MBiomedSc*

Supervisor: A/Profesor Cassandra Szoeke
Project Site: Healthy Ageing Program, Dept of Medicine, Centre for Medical Research, Royal Melbourne Hospital.
Contact: A/Professor Cassandra Szoeke T: 61 3 8344 1835 E: cszoeke@unimelb.edu.au

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 cognitive performance and health.

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. As well as an opportunity for publication.

218. Iron and Fatigue – *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Dept of Medicine, Centre for Medical Research, Royal Melbourne Hospital.
Contact: A/Professor Cassandra Szoeke T:61 3 8344 1835 E: csoeke@unimelb.edu.au

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 commercialisation

219. Vitamin D deficiency and balance - *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke, Professor Meg Morris
Project Site: Healthy Ageing Program, Dept of Medicine, Centre for Medical Research, Royal Melbourne Hospital.
Contact: A/Professor Cassandra Szoeke T: 61 3 8344 1835 E: cszoeke@unimelb.edu.au

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 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 data over 20 years already collected. 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.

220. Sexting, porn, and Tinder. An investigation of education and health promotion needs and evidence

Supervisors: Dr Megan Lim
Project Site: Burnet Institute
Contact: E: lim@burnet.edu.au

Project description: Access to new technologies could present novel risks to young people's sexual health. The emerging popularity of sexting, online pornography use, and dating apps has been linked in some studies to sexual risk behaviours

(e.g. not using condoms). There is very little known about how to educate young people about these topics. Many previous programs have taken a fear-based approach which tends to exaggerate the risks of these behaviours and promote abstinence as the only option. This project will investigate previous campaigns, survey the opinions and needs of young people, schools, parents, and health promotion practitioners, and provide recommendations for future campaigns. A mixed methods approach will involve content analysis and review of existing health promotion, online surveys, interviews, and focus group discussions.

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

Supervisors: Dr Megan Lim
Project Site: Burnet Institute
Contact: E: lim@burnet.edu.au

Project description: Sexually transmitted infections (STI) are on the rise among young Victorians. Since 2005, we have surveyed over 9,000 people aged between 16 and 29 years of age at Melbourne's Big Day Out about sexual risk behaviour and drug use. From 2015, we have moved the survey to an online form. Questions have covered participant's sexual histories, condom use, knowledge and perceptions of STIs, and STI testing histories. We ask about alcohol and other drug use, and other risks and behaviours such as gambling, diet and exercise, contact with police, mental health, and smoking. There is also a series of questions concerning media use, e.g. pornography, sexting, social media and smartphones, online gambling. The student project could focus on one of these issues or a range of themes. These findings, in the context of current public health measures, will be used to advise on the design of future sexual health promotion campaigns.

In this project the student will use the data collected to investigate patterns of sexual risk behaviours, knowledge, and attitudes. This will involve quantitative analysis of the relationship between variables such as condom use, number of sexual partners, drug and alcohol use, and perceptions of risk. The project could also involve in-depth qualitative data collection via focus group discussions or interviews.

222. Taking a punt: Exploring gambling attitudes and behaviours among a sample of young Victorians.

Supervisors: Dr Rebecca Jenkinson and Dr Megan Lim
Project Site: Burnet Institute
Contact: E: rebeccaj@burnet.edu.au

Project description: The gambling environment in Australia has changed markedly over recent years and young people are a high-risk group for experiencing gambling-related harm. While estimates of gambling prevalence among young people vary considerably, there is consensus that gambling participation is increasing among young people and that youth problem gambling rates are around 2-3 times those of adults. With increasing exposure to gambling promotion and greater opportunities to gamble, the 'normalisation' of gambling among young people is likely to continue. In order to respond to increasing concern around these issues and inform future research and policy responses, this project will explore young people's gambling behaviours and experience of negative consequences in more detail, especially with regard to participation in higher risk activities such as sports betting and pokies.

In this project the student could employ a mixed-methods approach to explore gambling attitudes, behaviours and experience of negative consequences among young people (aged 15-29 years) in Victoria. Quantitative data collected as part of the Burnet's online survey of young people's health behaviours could be utilised. In addition to gambling, this annual, cross-sectional survey explores young people's alcohol and other drug use, sexual health and behaviour, experiences of mental health problems, and social media use. The student project could also involve in-depth qualitative data collection via focus group discussions or interviews.

223. Alcohol advertising on public transport: level of exposure among children and young people

Supervisors: Dr Megan Lim and Dr Nick Scott
Project Site: Burnet Institute
Contact: E: megan.lim@burnet.edu.au

Project description: Alcohol advertising is associated with increased alcohol consumption, particularly among young people. Current regulations attempt to limit exposure of alcohol marketing to children, however, no restrictions are in place regarding advertising on public transport.

This project will include an audit of alcohol advertising on public transport. Basic modelling will be conducted using publically available public transport usage data. The project will result in a policy document advising on the potential level of exposure of children to these advertisements.

224. Trends in STI testing and positivity in priority populations in Australia

Supervisors: Carol El Hayek
Project Site: Burnet Institute
Contact: E: carol.el-hayek@burnet.edu.au

Project description: In the last decade, communicable disease notification systems have seen a dramatic increase in the number of notifications for chlamydia and several other STIs. Higher prevalence is commonly seen in populations that have higher sexual risk practices (such as men who have sex with men, Aboriginal and Torres Strait Islander People, Sex Workers). It is important to monitor rates of STI testing and positivity in these priority populations, as well as the general population, in order to identify emerging patterns and trends in STI epidemiology.

The Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of Sexually Transmitted Infections and Blood Borne Viruses (ACCESS) project is a sentinel surveillance system that monitors STI testing and positivity in a range of priority populations. This project will use existing data collected in the ACCESS project to explore STI testing and positivity in priority population and identify factors which are associated with both testing and positivity.

This project will involve quantitative data analysis of data collected through the ACCESS project. Data analysis will involve analysis of data collected through either laboratories or general practices and family planning clinics, and supplemented with behavioural data collected in the Victorian Primary Care Network for Sentinel Surveillance of STIs. Data analysis will involve calculation of testing and positivity rates for a range of STIs and factors associated with these (such as age, gender and other relevant characteristics) in priority populations (including men who have sex with men, Aboriginal and Torres Strait Islander People, Sex Workers).

225. Understanding risky single occasion drinking and links to harms in a cohort of young Melburnians – *also offered as* MBiomedSc

Supervisor: Paul Dietze, Michael Livingston, Sarah Callinan
Project Site: Burnet Institute
Contact: E: paul.dietz@burnet.edu.au Telephone: 9282 2134

Project description: Young Australians frequently engage in Risky single occasion drinking (RSOD). This drinking pattern is associated with a variety of harms including increased risk of accidents, exposure to violence and risky sex. Most research on RSOD has focused on normative drinking behaviours within the past year rather than on the specific circumstances of RSOD.The aim of this study is to examine specific occasions of RSOD by young people to understand the specifics of drinking contexts and links to harms.

The proposed study involves analysis of quantitative data collected through the Young Risky Drinkers (YRD) study. The YRD is a representative sample of 802 young high-risk drinkers recruited across metropolitan Melbourne using Computer Assisted Telephone Interviewing (CATI) during 2012. Specific questions were asked about their most recent episode of high risk drinking. The cohort is being followed up in 2013 with a similar questionnaire. Analysis will be undertaken to characterize risky drinking occasions and use findings from these analyses at baseline to examine whether these predict subsequent experiences of harm. Findings from the project will present a unique picture of RSOD.

226. Modeling the syphilis epidemic in Victoria – *also offered as MBiomedSc*

Supervisor: Ms Carol El Hayek, Dr Nick Scott
Project Site: Burnet Institute
Contact: E: carol.el-hayek@burnet.edu.au Telephone: 8506 2303

Project description In Victoria 80% of infectious syphilis cases are in men who have sex with men (MSM). Mathematical modeling of syphilis transmission in Australian MSM suggests an effective way to reduce syphilis is to increase the frequency of testing and treatment of MSM.

In recent years, we have seen a sustained increase in routine syphilis testing among MSM at high caseload clinics alongside a decline in infectious syphilis incidence.

How much testing needs to occur in Victoria's MSM community to eradicate infectious syphilis?
This project will involve the design of a syphilis transmission schema and model for mathematically predicting infection rates. Running the model will require defining input parameters which should be based on an extensive literature review.

227. Low income as a barrier to opioid substitution therapy - *also offered as MBiomedSc*

Supervisor: Dr Peter Higgs, Co-Head, Alcohol & Other Drug Research, Centre for Population Health, Burnet Institute
Project site: Burnet Institute
Email: peterh@burnet.edu.au

Project description: People who inject drugs (PWID) often report low levels of income, with many reporting weekly incomes of less than $250. PWID on opioid substation therapy (OST) commonly describe an adverse impact from pharmacy dispensing fees for accessing OST. These fees are typically around $5 per dose, or $35 per week – for many a significant proportion of weekly income, especially after necessary expenditures (rent, food, etc.) are deducted.

This project would involve analysis of data from the Suboxone (a national year-long examination of a particular OST formulation, with a number of cross-sectional arms investigating the health domains of PWID and practices of prescribing pharmacists) and MIX studies (a Melbourne-based prospective cohort study running since 2008 with over 700 PWID as

participants), examining the dispensing practice/cost for differing pharmacies, and personal in-depth interviews with PWID to further illicit the impact of dispensing costs and the extent that low income is a barrier to substitution therapy

PREGNANCY RESEARCH

228. Investigating matrix metalloproteinases and their inhibitors as biomarkers of preterm labour - *also offered as MBiomedSc*

Supervisors: Dr Harry Georgiou
Project Site: Mercy Hospital for Women and/or Royal Women's Hospital
Contact: Dr Harry Georgiou; E: harrymg@unimelb.edu.au T:8345 3708

Project description: Currently, there are no biomarkers that can accurately predict if and when preterm labour will occur. This study will investigate MMPs and TIMPs in the vaginal fluid of women with symptoms of preterm labour ('threatened preterm labour') and to correlate this with cervical and fetal fibronectin status.

229. Stem cells and their Potential to Treat Clinically Important Disorders of Pregnancy - *also offered as MBiomedSc*

Supervisors: Dr Bill Kalionis
Project Site: Pregnancy Research Centre, Royal Women's Hospital
Contact: Dr Bill Kalionis T: 8345 3748 E: bill.kalionis@thewomens.org.au

Project Description: We are interested in the potential for manipulating gene expression in decidual mesenchymal stem cells as for the treatment for clinically important pregnancy disorders such as preeclampsia.
The latter stages of preeclampsia are characterised by an environment of high oxidative stress in the decidua. We have shown that decidual MSCs are abnormal in their response to oxidative stress in preeclampsia. The aim of the project is to use human cell culture models to test strategies for restoring normal oxidative stress response to abnormal, preeclampsia-affected decidual MSCs (PE-DMSCs). For example, we have shown that aldehyde dehydrogenase expression, which is required for MSCs to resist oxidative stress, is abnormally low in PE-DMSCs. We will increase expression of aldehyde dehydrogenase in PE-DMSCs using plasmid-based expression vectors and test whether resistance to oxidative stress in PE-DMSCs is restored.

Techniques: stem cell preparation and characterisation by immunocytochemistry and FACS, RNA/DNA extraction methods, real-time PCR, siRNA and gene overexpression analysis and immunohistochemistry. Functional analyses will include proliferation, migration and differentiation assays.

230. Stem Cell Microvesicle Repair of the Damaged Endothelium in Preeclampsia. - *also offered as MBiomedSc*

Supervisors: Dr Bill Kalionis
Project Site: Pregnancy Research Centre, Royal Women's Hospital
Contact: Dr Bill Kalionis T: 8345 3748 E: bill.kalionis@thewomens.org.au

Project Description: Preeclampsia is the most significant clinical disorder of pregnancy, affecting 5% of all pregnancies. Preeclampsia is a significant cause of maternal morbidity as well as fetal morbidity and mortality. Currently, there are no early diagnostic tests or effective treatments for preeclampsia. We are interested in the potential for subcellular microvesicles shed from mesenchymal stem cells to treat the symptoms of preeclampsia.
In preeclampsia, the endothelial cells lining the vessel walls become damaged. Systemic vascular damage contributes significantly to the symptoms of preeclampsia. Microvesicles shed from stem cells contain a variety of beneficial growth factors, cytokines and microRNAs that can be delivered to damaged cells, which prevent cell apoptosis, promote cell proliferation and differentiation, and thereby assist cells in recovering from damage. The aim of the project is to identify the growth factors, cytokines and microRNAs produced by microvesicles derived from placental mesenchymal stem cells.

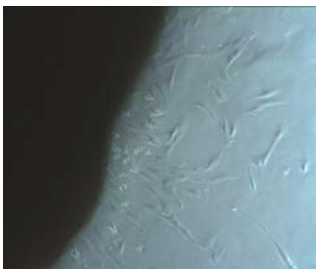
Techniques: Stem cell preparation and characterisation by immunocytochemistry, flow cytometry and differentiation assays, microvesicle preparation from stem cells, ultracentrifugation, microvesicle characterisation and fluorescence labelling, screening assays for microRNA, growth factors and cytokines.

231. How do hormones work: investigating new steroid receptors

Supervisors: Dr. Penelope Sheehan
Project Site: Pregnancy Research Centre, Royal Women's Hospital
Contact: Dr Penelope Sheehan E: penny.sheehan@thewomens.org.au

Project Description: Progesterone is known to be a key hormone in human pregnancy and is particularly thought to play a role in maintaining myometrial quiescence throughout gestation, allowing the fetus to grow. Antiprogestins, such as mifepristone (RU 486), are known to contribute to parturition[1]. Yet, in humans, maternal serum progesterone concentrations do not significantly decrease at labour onset[2], suggesting a change at the receptor level. However detailed knowledge of intracellular and molecular mechanisms are unknown. We have identified two new receptors capable of binding progesterone which may help improve our understanding of progesterone action. The pregnane X receptor (PXR)

is a nuclear receptor which is able to regulate gene transcription. The endogenous ligand with the highest affinity for the PXR is the progesterone metabolite, 5βDHP. Progesterone receptor membrane components 1 and 2 (PGRMC1, PGRMC2) are also putative progesterone receptors. Detailed study of the pathways affected by these receptors using myometrial explant cultures and gene silencing techniques may provide new therapeutic targets for treatment of preterm birth and also for induction of labour in postdates pregnancy.



This project will build on previous Pregnancy Research Centre findings identifying changes in expression of these two new receptors in association with human labour at term in myometrium. The methodologies are established within our laboratories at The Royal Women's Hospital. ***Techniques:*** Tissue culture, siRNA gene silencing, Real-time RT-PCR, western immunoblotting, microarray.

Image: Day 11 explant with myometrial cells growing into the culture medium ready for experiment

232. Can dietary phytophenols prevent the development of diabetes in pregnancy? - *also offered as MBiomedSc*

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 phytophenols 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 phytophenols can prevent the development of GDM.

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

233. Can dietary phytophenols stop preterm birth? - *also offered as MBiomedSc*

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

234. Testing novel therapeutics in a novel mouse model of preeclampsia - *also offered as MBiomedSc*

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.

235. Understanding the pathophysiology of preeclampsia - *also offered as MBiomedSc*

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.

236. Understanding changes in haemostasis during pregnancy and pregnancy complications – *also offered as MBiomedSc*

Supervisors: A/Prof Joanne Said and Dr Briony Cutts
Project Site: Melbourne Medical School, Sunshine Hospital, St Albans.
Contact: E: jsaid@unimelb.edu.au or briony.cutts@thewomens.org.au

Project description: Haemostasis in humans represents a complex balance between prothrombotic and anticoagulant proteins. During pregnancy, this balance is shifted in favour of a prothrombotic state such that pregnant women have an increased risk of developing deep vein thrombosis. This disturbance in coagulation is even more pronounced in a range of pregnancy complications. The aim of this study is to investigate the changes that occur during pregnancy, and in various adverse pregnancy conditions, using the calibrated automated thrombinoscope. This modern technology allows a global assessment of haemostasis rather than investigating individual factors. The project will be conducted in the brand new laboratories at the Centre for Health Research and Education based at Sunshine Hospital. Sunshine Hospital is the second largest maternity unit in Victoria and thus there is an ample population of pregnant women available to participate in this study. Techniques: Recruitment of patients, sample collection, thrombin generation assays.

PSYCHIATRY

237. Causes of Depressive Symptoms in Early Ageing – *also offered as MBiomedSc*

Supervisor: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Dept of Medicine, Centre for Medical Research, Royal Melbourne Hospital, UoM, Parkville, Vic 3052.
Contact: A/Professor Cassandra Szoeke T: 61 3 8344 1835 E: cszoeke@unimelb.edu.au

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

238. Alcohol use and effects on mood in elderly women – *also offered as MBiomedSc*

Supervisors: A/Professor Cassandra Szoeke
Project Site: Healthy Ageing Program, Dept of Medicine, Centre for Medical Research, Royal Melbourne Hospital, UoM, Parkville, Vic 3052.
Contact: A/Professor Cassandra Szoeke T:61 3 8344 1835 E: cszoeke@unimelb.edu.au

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.

SPINAL CORD INJURY

239. Acute management of traumatic central cord syndrome

Supervisors: Dr Peter Batchelor, Dr Camila Battistuzzo
Project Site: Department of Medicine (RMH)
Contact: Dr Peter Batchelor: peter.batch@unimelb.edu.au
Dr Camila Battistuzzo: camilab@unimelb.edu.au

Project description: Acute traumatic central cord syndrome (TCCS) is the most common type of incomplete cervical spinal cord injury. TCCS is usually the result of a hyperextension injury in a patient with pre-existing narrowing of the spinal canal and can result in paralysis and permanent functional deficits. At present there is no standardized treatment for this condition, although early surgery to relieve spinal cord compression may improve neurological recovery. The aim of this project is to map the process of care of people with TCCS to determine the timing of spinal decompression surgery and factors that influence surgical decisions.

This project is part of the Immediate Cooling and Emergency Decompression (ICED) trial. You will have access to our database and opportunity to work with our national and international collaborators. We have already obtained Human Ethics Committee approval. There is opportunity for publication within one year. This project would suit a candidate with an interest in trauma, spinal surgery and acute medicine.

HONOURS AT RMH

Enrolling Department: MEDICINE RMH

For further information please visit our website: http://honoursrmh.unimelb.edu.au/

Visit the website for details on HOW TO APPLY**:** http://sc.mdhs.unimelb.edu.au/how-apply

ENQUIRIES

RMH Honours Coordinator:	Dr Chris French	E: frenchc@unimelb.edu.au
RMH Honours Administrator:	Mary Ljubanovic	E: mlju@unimelb.edu.au T: 61 3 8344 5479

2016/17 KEY DATES

Aug-November 2016:	Contact potential supervisors to discuss Honours projects	(Step 1)
29 August 2016:	Open date to register online application	
5 September 2016:	Open date to lodge project preferences through HATS - *tbc*	
11 November 2016:	Closing date to register online application - *tbc*	(Step 2)
26 November 2015:	Closing date to lodge project preferences through HATS - tbc	(Step 3)
3rd wk December 2016:	First round of offer letters from 18 December sent to students	
6 January 2017:	Closing date for acceptance/rejection by students of First Round offers	
9 January 2017:	Second round of selection and mailing of offer letters begins	
27 January 2017:	Deadline for Late Applications	
13 February 2017:	RMH Honours 2017 Program commences / RMH Student Orientation.	

HONOURS ENTRY REQUIREMENTS

To be eligible to enter the Bachelor of Biomedicine (Honours) or the Bachelor of Science (Honours), applicants must satisfy both:

- the Faculty of Medicine, Dentistry and Health Sciences or Faculty of Science entry requirements;
- and the requirements of the department offering the Honours program.

Please note: The minimum entry requirement is 65 (Weighted Average Mark).

HONOURS COURSEWORK

BIOM40001 – SEMESTER 1: Introduction to Biomedical Research (12.5%)

This core subject contributes 12.5% to the total mark of the Honours year and is administered through the Faculty of Medicine, Dentistry & Health Sciences.

Structure: Series of 10 x 2 hr tutorials to introduce students to processes and strategies at the core of modern biomedical research.

Assessment: *Semester 1: 2 written reports (each not exceeding 3000 words).*

For further details on course work please see the RMH Academic Centre Honours Program Course Structure website: http://honoursrmh.unimelb.edu.au/Applications/CourseDetails.html

MEDI40004 – SEMESTER 1: Advanced Coursework (12.5%)

This subject contributes 12.5% to the total mark of the Honours year.

Structure:	Semester 1:	Attend Seminars in Translational Medicine - thematic topics of approximately 20 lectures (1 hour each).
	Semester 1 & 2:	Attend Weekly Research Seminars. Attendance is compulsory from March to October but not assessed.
Assessment:	*Semester 1:*	*Multiple Choice Question examination covering examinable topics from the Seminars in Translational Medicine.*

MEDI40003 & MEDI40012 – SEMESTER 1 & 2: Research Project (75%)

The written thesis together with an Oral Presentation constitutes the Research Project for Semester 1 & 2 and contributes 75% to the total mark of the Honours Year.

Structure: Research Project (Thesis)

Assessment: *Semester 1:* *Oral Presentation on project outline. Feedback only - not assessed.*
Semester 2: *a) Written research report (thesis) to be submitted. 80%*
b) Formal thesis oral presentation

HOW TO APPLY - HONOURS

Course Codes:
Bachelor of Biomedicine (Honours) – **BH-BMED**
Bachelor of Science (Honours) – **BH-SCI**

How to Apply link: http://sc.mdhs.unimelb.edu.au/how-apply

2016 APPLICATIONS

If you wish to be considered for Honours in 2017, and you would like to undertake your project and coursework with Department of Medicine at RMH, The University of Melbourne (enrolling unit: Department of Medicine (RMH)), you will need to carry out a **THREE STEP PROCESS:**

STEP 1: Contact Potential Supervisor

You will need to decide which Department or Institute(s), Supervisor(s) and Project(s) that you wish to apply for. To do this, **you must speak to potential supervisors.** Please see our Honours project book and Department of Medicine (RMH) website to review our projects available for 2017.
http://honoursrmh.unimelb.edu.au/

STEP 2: Lodge an online application

How to Apply link: http://sc.mdhs.unimelb.edu.au/how-apply

STEP 3: Honours Application and Tracking System (HATS)

Once you have contacted the potential research supervisors (Step 1) and submitted your online application (Step 2), you will be issued with a password for the Honours Application and Tracking System (HATS). This system allows you to submit up to ten (10) research project preferences online.

HATS usernames/passwords are issued once a week (usually on a Monday) to applicants whose applications are submitted properly in the previous week.

Please note that HATS is ONLY available to On-Time applicants for Start Year entry.

It is the responsibility of applicants to ensure their contact details and mailing address are correct and up to date, as offer packs will be sent to the address provided in the original course application, unless other arrangements have been made in advance.

Students who meet the minimum entry requirements for entry to MDHS Honours but do not receive an offer in Round 1 will be considered for a place in Round 2, along with Late Applicants.

Students who do not meet the entry requirements or are not successful in obtaining a place in the course will be advised in writing by the end of January.

For further information on How to Apply see website link: http://sc.mdhs.unimelb.edu.au/how-apply

MASTER OF BIOMEDICAL SCIENCE

The Master Biomedical Science is one of the research training streams of the Master of Science. The research training streams give students the opportunity to undertake a substantive research project in a field of choice as well as a broad range of coursework subjects including a professional tools component, as a pathway to PhD study or to the workforce. The MBiomedSc is a two year course that can be taken in place of Honours.

Students must complete 200 points comprising of:

Major Research Project	(Literature Review, Thesis, & Ora Presentations)	125 points
Core Discipline subject	(Introduction to Biomedical Research BIOM40001)	12.5
Discipline Subjects		37.5 points
Professional Skills		25 points

MAJOR RESEARCH PROJECT: 125 points.

- A literature review of up to 6,000 words. Due end of 2nd semester Year 1. *Assessment hurdle – marked* satisfactory/unsatisfactory.
- Two 20 minute oral presentations.
  Due end of 2nd semester Year 1 and final semester Year 2.
- Major research report of up to 20,000 words. Due end of final semester Year 2.
  As this project is a larger body of research work than an Honours research project (75pts) the expectation about the extent of work undertaken is adjusted and more research output is expected to be achieved. More supervisor input is required but this is over the 2 year duration.

Available Projects: For MBiomedSc projects available with the Royal Melbourne Hospital please see projects listed as available for MBiomedSc in the 2017 Honours / Master of Biomedical Science Project List Handbook: *For further details on the project please contact the supervisor listed in the handbook.*

HOW TO APPLY - MBIOMEDSC

Course Code MC-BMEDSC

1. Applications for the Master of Biomedical Science are made directly via the University online application system. Late applications can be considered for admission (but may not be eligible for competitive fee places or bursaries).
2. Talk with academic staff offering projects you are interested in. Find out what is involved. Talk to the students in the labs. Talk with the Department Masters Coordinator if you have questions about the overall course structure.
3. When you are ready to make a formal application, lodge an online – see links below on how to apply:
   http://mdhs-study.unimelb.edu.au/degrees/master-of-biomedical-science/overview

You will be required to nominate a Department, Supervisor and Project, and have your prospective supervisor provide you with evidence (ie a letter or email) of their potential willingness to supervise your project. You will be required to submit this information as part of your course application.

ENQUIRIES

School of Biomedicine E: biomedsci-gradstudent@unimelb.edu.au

RMH/RWH DEPARTMENT LINKS

Department of Medicine (Royal Melbourne Hospital)	http://www.medrmhwh.unimelb.edu.au/
Department of Surgery (Royal Melbourne Hospital)	http://www.surgeryrmh.unimelb.edu.au/
Department of Psychiatry (Royal Melbourne Hospital)	http://www.psychiatry.unimelb.edu.au/
Department of Radiology (Royal Melbourne Hospital)	http://www.melbourne-radiology.org/Staff.html
Obstetrics & Gynaecology (Royal Women's Hospital)	http://www.obsgyn.unimelb.edu.au/