The Melbourne Academic Centre
(Royal Melbourne Hospital)
(RMH Departments: Medicine, Surgery, Psychiatry, Radiology, and Obstetrics and Gynaecology RWH)
Faculty of Medicine, Dentistry & Health Sciences, The University of Melbourne

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

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

PROJECTS 2015
Medical Research — Bench to Bedside

Affiliations:
The Royal Melbourne Hospital (Depts of Medicine, Surgery, Psychiatry), The Royal Women’s Hospital, NorthWest Academic Centre (NWAC), The Peter MacCallum Cancer Centre, The Burnet Institute-Centre for Population Health, Melbourne Brain Centre, Florey Neuroscience Institute, Melbourne Neuropsychiatry Centre, Mental Health Research Institute, CSIRO, The Northern Hospital.
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**2014/15 KEY DATES**

**HONOURS ENTRY REQUIREMENTS**

**HONOURS COURSEWORK**

**HOW TO APPLY - HONOURS**

**MASTER OF BIOMEDICAL SCIENCE - COURSEWORK**

**HOW TO APPLY - MBIOMEDSC**

**ENQUIRIES**

**RMH ACADEMIC CENTRE DEPARTMENT LINKS:**
AGEING

1. **Inhale-swallow-exhale: neurotransmitters that prevent food going down the wrong pipes**
   - **Supervisors:** Dr. Tara Bautista, Dr. Mathias Dutschmann, Dr. Davor Stanic
   - **Project Site:** Florey Institute of Neuroscience and Mental Health
   - **Contact:** tara.bautista@florey.edu.au or mathias.dutschmann@florey.edu.au
   **Project description:** Swallowing disorders are common in the elderly and in patients with neurodegenerative diseases such as Parkinson’s and Alzheimer’s diseases. These are linked to an increased risk of aspiration and consequent aspiration pneumonia. Growing evidence points to pathophysiological alterations to the centrally-mediated coordination of swallowing and breathing as an important contributor to the increased risk of aspiration in such conditions. Our research group recently published a pioneering study on the novel use of the *in situ* brainstem rodent preparation for the study of swallowing. This project will characterise the neurotransmitters utilised in the central control of the swallowing reflex and its coordination with breathing, as an important first step in identifying potential drug therapies for treating swallowing disorders. Techniques involved will include immunohistochemistry and retrograde tracing of neuronal pathways using a rodent model.

2. **Characterisation of the Onset and Progression of Tauopathy in the Pontomedullary Brainstem Nuclei of mice undergoing Neurodegeneration**
   - **Supervisors:** Dr Davor Stanic, Dr Tara Bautista 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 mice undergoing neurodegeneration, with particular focus on the NTS, NA and KF. The project also aims to identify the neurochemical profile of neurons in these brainstem regions that are susceptible to tauopathy.

**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.

This project examines whether: a) the rate of stem cell division; b) migration of newly born cells; and c) the positioning and phenotype of newly born cells in the olfactory bulb and dentate gyrus, are altered in an established model of neurodegeneration.

Techniques include: immunohistochemistry, and stereology
3. **Acquired epilepsy in Alzheimer’s disease - also offered as MBiomedSc**

   **Supervisors:** Professor Patrick Kwan, Dr Nigel Jones  
   **Project Sites:** Department of Medicine (RMH), Melbourne Brain Centre at Parkville  
   **Contact:** Professor Patrick Kwan, E: Patrick.kwan@unimelb.edu.au  
   Dr Nigel Jones, E: ncjones@unimelb.edu.au  

**Project description:** People with Alzheimer’s disease (AD) are 10 times more likely to develop epilepsy compared with age-matched controls. Recurrent seizures and their treatment with conventional antiepileptic drugs may exacerbate cognitive decline, yet the pathological basis for the increased risk of epilepsy is largely unknown, and there are no treatments that prevent epilepsy in AD patients. The relationships between the pathological processes of AD and neuronal hyperexcitability are poorly understood. Elucidating the pathomechanisms of epileptogenesis in AD is critical in identifying effective therapeutic strategies to prevent the development of epilepsy in this high risk and vulnerable population.

The novelty of this project lies in its aims to directly address the mechanisms of epileptogenesis in AD through the study of relevant animal models of AD and acquired epilepsy. It will identify the mechanistic processes of epileptogenesis in AD under a coherent hypothesis. The aims will be achieved by subjecting transgenic AD models reflecting the pathological hallmarks to acquired epileptogenesis and treating them novel compounds. The phenotypic changes (epileptogenesis and cognitive/behavioural outcomes) will be correlated with the molecular and cellular changes in these pathways. The findings will identify novel therapeutic approaches to prevent the development of epilepsy in AD patients.

4. **Lifestyle Factors for healthy Ageing – also offered as MBiomedSc**

   **Supervisor:** A/Professor Cassandra Szoeke  
   **Project Site:** Dept of Medicine, UoM, Parkville, Vic 3052.  
   Women’s Healthy Ageing Project (WHAP)  
   **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.

5. **Causes of Depressive Symptoms in Early Ageing – also offered as MBiomedSc**

   **Supervisor:** A/Professor Cassandra Szoeke  
   **Project Site:** Dept of Medicine, UoM, Parkville, Vic 3052.  
   Women’s Healthy Ageing Project (WHAP)  
   **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 in 2012/2013. 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 from this study are:**
1. There is opportunity for publication within one year  
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.
6. **Early detection and prevention of age associated diseases using imaging - ONLY offered as MBiomedSc**

   **Supervisor:** Professor Patricia Desmond, A/Professor Cassandra Szoeke  
   **Project Site:** Dept of Medicine, UoM, Parkville, Vic 3052.  
   **Women’s Healthy Ageing Project (WHAP)**  
   **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 publication.
   - This project will suit a candidate with an interest in neuroimaging.

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

   **Supervisors:** A/Professor Cassandra Szoeke, Professor Meg Morris  
   **Project Site:** Dept of Medicine, UoM, Parkville, Vic 3052.  
   **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 re-known Women’s Healthy Ageing Project (WHAP).

   **Opportunities:-** You will have the opportunity to work with an internationally re-known cohort and research team each with international recognition. (Prof L Dennerstein, Prof D Ames, Dr C Szoeke)
   - The study has data over 20 years already collected.
   - There is opportunity for publication within one year.
   - This project will suit a candidate with interest in media or commercialisation.

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

   **Supervisors:** A/Professor Cassandra Szoeke  
   **Project Site:** Dept of Medicine, UoM, Parkville, Vic, 3052. Women’s Healthy Ageing Project (WHAP).  
   **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.

   **Major benefits from this study are:-**
   - A unique opportunity to work on an Australian dataset with midlife and late-life data collected (data over 20 years).
   - There is opportunity for publication within one year.
   - This project will suit a candidate with interest in commercialisation and ageing.
9. **Nutrient intake and plasma beta-amyloid** - also offered as MBiomedSc

**Supervisors:** A/Professor Cassandra Szoeke  
**Project Site:** Dept of Medicine, UoM, Parkville, Vic, 3052. Women’s Healthy Ageing Project (WHAP).  
**Contact:** A/Professor Cassandra Szoeke T:61 3 8387 2224 F : 61 3 9387 9384 E: cszoeke@unimelb.edu.au

**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.

**Major benefits from this study are:**
- The nutritional data set has already been collected
- The project will suit a candidate with interest in dietary factors and health
- There is opportunity for publication within one year
- This project will suit a candidate with an interest in media or commercialisation and is keen for industry interaction

**You will gain invaluable experience and networking opportunities in groundbreaking research.**

10. **Current definitions of sarcopenia: Associations with indicators of falls and fracture risk in older adults** - also offered as MBiomedSc

**Supervisors:** Dr David Scott, A/Professor Kerrie Sanders  
**Project Site:** NorthWest Academic Centre, Sunshine Hospital, St. Albans  
**Contact:** Dr David Scott T: 8395 8108 E: d.scott@unimelb.edu.au

**Project description:** Sarcopenia describes the age-related decline in skeletal muscle mass and function which leads to disability in older adults. Sarcopenia does not receive adequate attention in clinical settings in part due to a number of conflicting definitions and assessment techniques. This study will investigate whether sarcopenia defined by current definitions is associated with indicators of falls (including balance and walking ability) and fracture (including bone quality measurements using dual-energy X-ray absorptiometry and peripheral quantitative computed tomography) risk in community-dwelling older adults.

11. **The metabolic syndrome and musculoskeletal health in older adults** - also offered as MBiomedSc

**Supervisors:** Dr David Scott, A/Professor Kerrie Sanders  
**Project Site:** NorthWest Academic Centre, Sunshine Hospital, St. Albans  
**Contact:** Dr David Scott T: 8395 8108 E: d.scott@unimelb.edu.au

**Project description:** The metabolic syndrome is a constellation of cardiometabolic disorders including visceral obesity, dyslipidaemia, hyperglycaemia and hypertension. The metabolic syndrome is highly prevalent in older adult populations. In addition to increased risk for cardiovascular disease and type II diabetes, it is likely that the metabolic syndrome contributes to declines in muscle (sarcopenia) and bone (osteoporosis) quality with age. This study will investigate whether older adults with the metabolic syndrome demonstrate poorer muscle and bone quality, determined by advanced imaging techniques, compared to healthy older adults.

**ALCOHOL**

12. **Street drinking in Footscray** - 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:** pauld@burnet.edu.au

**Project Description:** Public alcohol consumption is a major issue in many local communities. The Footscray Central Business District has been identified as a site in the City of Maribyrnong with public drinking issues, with pockets of drinkers identified across different parts of the CBD. This study will involve structured observation of the Footscray CBD along with interviews with in-depth interviews with public drinkers about their experiences of drinking and choices of drinking locations.
perception, current self-management strategies for living with HCV.

In the increased bone remodeling that accompanies OA, bone accrual is associated with early downregulation of Wnt signalling antagonists DKK1 and sclerostin in bone cells. Importantly at later times this bone tissue appears to be osteonecrotic. In healthy bone, osteocytes occupy lacunae within the bone matrix; from this location they can respond to mechanical load by inducing local bone formation, bone resorption and vascularization. In the increased bone remodeling that accompanies OA, bone accrual is associated with early downregulation of Wnt signalling antagonists DKK1 and sclerostin in bone cells. Importantly at later times this bone tissue appears to be osteonecrotic. In healthy bone, osteocytes occupy lacunae within the bone matrix; from this location they can respond to mechanical load by inducing local bone formation, bone resorption and vascularization.

### ARTHRITIS AND INFLAMMATION RESEARCH

13. **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: 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.

14. **Anterior cruciate ligament injury during high risk movements – also offered as MBiomedSc**

   **Supervisors:** A/Prof Peter Pivonka and Dr Hossein Mokhtarzadeh
   **Project Collaborator:** A/Prof Adam Bryant
   **Project Site:** NWAC, Sunshine Hospital, St Albans
   **Contact:** Dr Peter Pivonka; Tel: 8395 8095; E: peter.pivonka@unimelb.edu.au

   **Project Description:** Knee injuries are common in sports. One of the major knee injuries that accounts for about 70% of non-contact injuries occur to the anterior cruciate ligament (ACL). Since human joints are connected to each other via bones, muscles surrounding one joint e.g. ankle joint can affect the loadings on the proximal or distal joint e.g. the knee joint. In addition, the interaction of upper body with the lower limbs may influence the muscle contribution surrounding a particular joint e.g. ankle muscles due to dynamic coupling of a neuromusculoskeletal system.

   We have shown that ankle muscles may load or unload the ACL during landing tasks considering their muscles lines of action. However, it is not clear whether upper body positions would influence the lower limb muscles contributions to the ACL loading during high risk movements. This project aims to evaluate the effect of upper body positions on lower limb muscle recruitment during landing. These assessments will enable us to develop a new training method to reduce the ACL loading during different landing maneuvers. Finally, another neuromusculoskeletal model will be developed to compare the efficacy of the new training method on ACL loading versus traditional ACL injury prevention one. In summary, this project aims to provide insight into the role of upper body positions and lower limb muscles recruitments on knee joint ligaments during landing. A series of complex mathematical model will be used to simulate the landing tasks and to predict individual muscles forces, joint forces and ACL loading. We anticipate identifying ideal training regimes including combined upper-body and lower-body coordination during trainings.

15. **Assessment of cartilage and subchondral bone cross talk in post-traumatic knee OA – also offered as MBiomedSc**

   **Supervisors:** A/Prof Peter Pivonka and Dr Hossein Mokhtarzadeh
   **Project Collaborator:** Dr Nicole Walsh
   **Project Site:** NWAC, Sunshine Hospital, St Albans
   **Contact:** Dr Peter Pivonka; Tel: 8395 8095; E: peter.pivonka@unimelb.edu.au

   **Project Description:** Osteoarthritis (OA) results in local destruction of articular cartilage and abnormal accrual of bone. Patients suffer significant pain, joint dysfunction and reduced mobility. Approximately 12% of OA cases occur secondary to joint injury (post-traumatic OA) and many of these patients are young. Early therapeutic intervention after acute joint injury could prevent or delay the OA onset and/or progression.

   It has been hypothesized that changes in cartilage morphology and biochemical composition during post-traumatic knee injury subsequently leads to changes in subchondral bone. However, some researchers have suggested that the changes in subchondral bone might also provide feedback to enhance cartilage destruction. In order to test these hypotheses we have used a mouse model of post-traumatic knee OA to define the impact of joint injury on bone. Using micro-computed tomography (μCT) techniques we found that surgically-induced knee injury (DMM) results in focal accrual of bone immediately below the affected tibial cartilage (subchondral bone). This bone accrual is associated with early downregulation of Wnt signalling antagonists DKK1 and sclerostin in bone cells. Importantly at later times this bone tissue appears to be osteonecrotic. In healthy bone, osteocytes occupy lacunae within the bone matrix; from this location they respond to mechanical load by inducing local bone formation, bone resorption and vascularization. In the increased...
subchondral bone in DMM-OA, these osteocytes are absent, leaving behind empty lacunae. This osteocyte death suggests a key pathological mechanism that will affect the surrounding bone and may have broader consequences for the health of nearby cartilage. The etiology and impact of this pathology will be explored in this project.

**ARTHRITEIS 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.

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

   **Supervisor:** Dr Andrew Cook  
   **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.

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

   **Supervisor:** Dr Andrew Cook  
   **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.

18. **The role of Interferon Regulatory factors in Arthritis**

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

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

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

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**19. The role of a novel macrophage inflammatory mediator in arthritis**

**Supervisors:** Dr Andrew Cook 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 protein 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

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**20. 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).

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**21. 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 glucocorticoid-controlled genes in inflammatory conditions. Enhancing our understanding of molecular signalling pathways that are governed by glucocorticoids may lead to improved clinical therapies with minimal side effects.

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

22. **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.

23. **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.

24. **Does the use of health and community-based services following an osteoporotic fracture vary by socio-economic status? – also offered as MBiomedSc**

   - **Supervisors:** A/Prof Kerrie Sanders, Dr David Scott
   - **Project Site:** NWAC Sunshine Hospital, St Albans
   - **Contact:** A/Prof Kerrie Sanders T: 8395 8114 E: ksanders@unimelb.edu.au

   **Project Description:** Australia’s healthcare policy aims to provide equal access to healthcare services for all Australians yet this goal is often not met. This project will help identify gaps in access to healthcare post-fracture between adults from a range of socio-economic backgrounds. The data is already collected from participants in the AusCUROS study. The acronym refers to the Australian arm of the International Costs and Utilities Related to Osteoporotic fractures initiated through the International Osteoporosis Foundation. The study is funded through the NHMRC with supplementary funding from Merck Pty Ltd. Over 800 participants with recent fracture and aged at least 50 years old have been recruited from the eight study centres around Australia. Quality of life and healthcare utilisation data has been collected at pre-determined time-points and will be used in this project.

25. **Are there differences in the characteristics of older women who fall at home compared with those who fall outside the home? – also offered as MBiomedSc**

   - **Supervisors:** Dr David Scott and A/Prof Kerrie Sanders
   - **Project Site:** NWAC Sunshine Hospital, St Albans
   - **Contact:** A/Prof Kerrie Sanders T: 8395 8114 E: ksanders@unimelb.edu.au

   **Project Description:** Falls are an important health problem with about 30% of people aged 65 years and older having at least one fall each year. We have previously conducted a large randomised placebo-controlled trial in older women with the primary outcomes of falls and fractures. Falls were ascertained on a self-reported monthly basis for 3 to 5 years with all details of the falls events recorded. The study is now completed and investigators have been ‘unblinded’. The circumstances and characteristics of the 2,512 falls that occurred in the 1,125 participants in the placebo group have been recorded.

   Through database management skills and basic statistical analysis this project involves developing a typical profile of the older woman who falls in their familiar home environment and investigate differences in ‘falls risk behaviour’ between those that have fallen at home and older women who fall outside the home. The results will provide unique Australian data particularly...
relating to the longitudinal 5-year duration of falls ascertainment and the level of detail collected surrounding each fall event. The work could form the basis for new strategies to prevent falls in older persons based on whether they are in familiar environments or not.

26. **Dietary calcium assessment in children: validation of the questionnaire** – also offered as MBiomedSc  
   **Supervisors:** A/Prof Kerrie Sanders and A/Prof Christine Rhodda  
   **Project Site:** NorthWest Academic Centre, Sunshine Hospital, St. Albans  
   **Contact:** A/Prof Kerrie Sanders T: 8395 8114 E: ksanders@unimelb.edu.au  
   **Project description:** As part of a trial on fracture healing and vitamin D status in children we will be assessing dietary calcium intake. This project involves talking to children and their parents and includes assessing dietary intake using two different methods. The work will provide a good insight into clinical research. Results will be immediately available and will be submitted as an abstract to a conference and be included in a publication.

27. **Assessment of changes of spatial heterogeneity of DMB in aging** – also offered as MBiomedSc  
   **Supervisors:** A/Prof Peter Pivonka  
   **Project Collaborators:** Prof John Clement, Prof Peter Ebeling  
   **Project Site:** NWAC, Sunshine Hospital, St Albans  
   **Contact:** Dr Peter Pivonka, Tel: 8395 8095; email: peter.pivonka@unimelb.edu.au  
   **Project Description:** Changes in the degree of mineralization of bone (DMB) have been associated with significant changes in mechanical properties of bone and fracture risk. The commonly accepted view of how DMB effects mechanical properties of bone is that a decrease in remodeling activity due to for example anti-resorptive drugs leads to an increase of DBM and, hence, an increase in mechanical stiffness and strength of bone.  
   Our group has previously assessed the spatial heterogeneity of cortical bone loss and found that bone resorption during aging is not uniform in a cortical bone cross section. Increased bone resorption could be found in areas subjected to lesser mechanical stresses (i.e., around the neutral axis). Currently no reliable data on DMB is available which investigates the spatial variation of DMB in cortical bone cross sections and looking at effects of aging. The aim of this project is to use high-resolution imaging to assess the age-related changes in the distribution of DMB in the femoral midshaft both in male and female bones. Femur bones from the Melbourne Femur Collection (MFC) will be used for this study.

28. **Assessment of local bone adaptation due to mechanical loading in the mouse tibia loading model** – also offered as MBiomedSc  
   **Supervisors:** A/Prof Peter Pivonka and Dr Jonathan Gooi  
   **Project Collaborators:** A/Prof Natalie Sims  
   **Project Site:** NWAC, Sunshine Hospital, St Albans  
   **Contact:** Dr Peter Pivonka, Tel: 8395 8095; email: peter.pivonka@unimelb.edu.au  
   **Project Description:** Bone is a dynamic living tissue which has the ability to respond to changes in its mechanical loading environment. Osteocytes are the bone cells embedded in the bone mineral matrix and are thought to be the mechanosensory cells of bone. Osteocytes “translate” mechanical loading into biomolecular signals leading to bone adaptation responses. In order to better understand bone’s local adaptation responses we will utilise a established murine model, i.e., the mouse tibia loading model. Using a well defined mechanical loading regime in the form of maximum load, frequency, and resting intervals we will characterise the morphological changes of mouse tibia bones due to mechanical loading using in-vivo high resolution microCT imaging. Furthermore, we will identify different cell populations and major regulatory factors involved in bone’s adaptation response using bone histomorphometry and immunohistochemistry.  
   Our group has a strong focus on mechanobiological regulation of musculoskeletal tissues and the different contributions of muscle, bone and cartilage to local adaptation responses. In collaboration with A/Prof N Sims from the St Vincent’s Institute (SVI) we are currently investigating the contribution of muscle tissue to bone response due to mechanical loading.

29. **Investigating the interaction between skeletal muscle and bone** – also offered as MBiomedSc  
   **Supervisors:** Dr Jonathan Gooi  
   **Project Site:** NWAC, Sunshine Hospital, St Albans  
   **Contact:** Dr Jonathan Gooi, Tel: 8395 8104; email: jgooi@unimelb.edu.au  
   **Project Description:** Skeletal muscle has a close functional relationship with bone. Both show major changes during aging and in the same way, sarcopenia and osteoporosis both contribute to frailty. Throughout life, the tissue mass of bone and muscle are intimately connected. Increases in muscle and bone mass result from weight-bearing exercise, while disuse results in the loss of both. For example muscular dystrophies are associated with relatively low bone density and an increased incidence of fractures. Conversely, significant increases in muscle mass, resulting from myostatin deficiency is associated with increases in bone mineral density. Despite these observations pointing to a coupling of bone and muscle mass, the precise mechanisms responsible for synchronizing bone and skeletal mass remains unclear.
A variety of clinical observations have provided support for the hypothesis that skeletal muscle plays an integral role in normal bone formation. It has previously been observed that covering bone fractures with muscle flaps improves fracture healing in cases of traumatic orthopaedic injury, whereas damage to muscle surrounding a bone fracture can delay fracture healing. These observations suggest that skeletal muscle has the capability to act as a local paracrine or endocrine source of osteogenic factors. This has important implications for the field of bone biology as it provides novel therapeutic opportunities for targeting muscle in order to restore the osteoporotic skeleton.

While the ability of skeletal muscle to secrete growth factors and cytokines is well established, the impact of the skeletal muscle secretome on bone is less well understood, with a large number of unanswered questions. For example, how do muscle and bone cells communicate and regulate each other’s functions? Do skeletal muscle secreted products have specific effects on osteoblastic bone formation, osteoclastic bone resorption or osteocytic mechanosensing? Does the skeletal muscle secretome differ based on the type of muscle activity such as concentric and eccentric contraction, disuse or damage? Are these signals dependent on mechanical stimulation and what effects do loading/unloading have? Finally, do bone-derived signals influence skeletal muscle function? These unanswered questions demonstrate the need to critically address the cellular interactions between skeletal muscle and bone. Therefore the aim of this project is to investigate cellular communication between muscle and bone cells.

30. Investigating the role of Vitamin D in cortical bone remodelling– also offered as MBiomedSc

Supervisors: Dr Jonathan Gooi
Project Site: NWAC, Sunshine Hospital, St Albans
Contact: Dr Jonathan Gooi, Tel: 8395 8104; email: jgooi@unimelb.edu.au

Project Description: Osteoporosis (increased risk of fracture) affects 2.2M Australians. Vertebral and hip fractures are the most common, and hip fractures the most devastating. More than 22,000 hip fractures occur in Australia each year; 20-30% of these patients die within 12 months, and 50% of those who survive will be permanently disabled and not regain independence. The cost of treatment exceed expenses for most other medical conditions in the elderly, exceeding >AUD$1.9 billion in direct costs.

Vitamin D has been shown to be an important regulator of calcium and bone homeostasis. Recent work by Lieben et al demonstrates an effect of Vitamin D on periosteal surfaces. Mice deficient in the vitamin D receptor expressed in the intestine displayed a hypomineralisation of cortical bone with a profound decrease in tibial bone mineral density. This data indicates that Vitamin D may have a key role in cortical bone remodelling. These findings raise the possibility of controlling bone formation on cortical bone surfaces resulting in increased bone strength and resistance to fracture. Therefore the aim of this study is to investigate the role of vitamin D in cortical bone remodelling by assessing its role in the normal response to mechanical load.

31. Developing New Therapies for Musculoskeletal Disease – Investigating the Fundamental Mechanisms of Osteocyte Mechanosensing– also offered as MBiomedSc

Supervisors: Dr Jonathan Gooi
Project Site: NWAC, Sunshine Hospital, St Albans
Contact: Dr Jonathan Gooi, Tel: 8395 8104; email: jgooi@unimelb.edu.au

The human skeleton performs a variety of essential roles for our daily health and wellbeing, including protection of vital organs, movement, blood cell production and a reservoir for mineral storage. Throughout our lives our skeleton undergoes continual remodelling to successfully fulfill these roles. However, an imbalance of remodelling can result in severe musculoskeletal diseases, including osteoporosis, which affects millions of people worldwide. Currently, treatments of osteoporosis prevent further bone loss, however are not capable of forming new bone. Thus, there is an urgent need for treatments that can rebuild fragile bones. This project aims to address the fundamental causes of musculoskeletal disease, specifically osteoporosis.

This project will capitalise on my recent development of a novel three dimensional (3D) osteocyte cell culture model which will enable, for the first time, an in depth investigation of osteocyte differentiation and mechanosensing in an in vivo like setting. Therefore, the broad aim of this work is to characterize the fundamental mechanisms by which osteocytes differentiate, contribute to the sensing of mechanical load and to understand their role in the control of osteoclast and osteoblast function and the maintenance of bone strength throughout life. This knowledge will be readily translated into new interventions strategies to improve osteoporosis outcomes and aid in the treatment of musculoskeletal disease.

The specific aims are to:
1) Investigate the mechanisms of osteocyte differentiation
2) Determine how osteocytes perceive mechanical signals
3) Understand the osteocyte response to mechanical stimulation
32. **Measuring bone and muscle health in young women - also offered as MBiomedSc**  
**Supervisors:** Prof John Wark, Prof Suzanne Garland, Ms Alexandra Gorelik, Ms Stefanie Hartley,  
**Project Site:** Department of Medicine, (RMH) Parkville Campus  
**Contact:** E: jdwark@unimelb.edu.au  
**Project description:** The Leonardo mechanograph is an instrument which measures muscle strength and power, and balance. The device has not been previously used in young women. Likewise, peripheral quantitative computed tomography (pQCT), which provides highly-resolved measures of bone density and bone strength, is a method not commonly used in young adults. What are the normative data ranges for Leonardo mechanography and pQCT for young women and how are these measures of muscle and bone health related? This project will focus on establishing the normative data range for these instruments in this population of young women. Subsequently, the relationship between these important measures of muscle and bone health and their determinants can be explored.

33. **A critical analysis of Sunsmart behaviour in young Australian women - also offered as MBiomedSc**  
**Supervisors:** Prof John Wark, Dr George Varigos, Ms Stefanie Hartley, 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.

34. **Recruitment of young women into health research via social networking sites: the impact of advertising and study characteristics – also offered as MBiomedSc.**  
**Supervisors:** Prof John Wark, Dr Shanton Chang, Prof Suzanne Garland, Ms Stefanie Hartley  
**Project site:** Department of Medicine (RMH), Parkville campus  
**Contact:** jdwark@unimelb.edu.au  
**Project description:** The Young Female Health Initiative (YFHI) has successfully recruited young Victorian women aged 16 – 25 years into a range of health-related research projects via Facebook advertising and information conveyed from linked secure study-specific websites. Preliminary analysis suggests differences in the characteristics of participants recruited into these studies. What are the determinants and consequences of these different recruitment patterns? Do such differences impact on the outcomes of these studies? These important questions will be addressed by comparing study populations recruited into several YFHI projects.

35. **Air pollution may impair vitamin D status in young Victorian women - also offered as MBiomedSc**  
**Supervisors:** Prof John Wark, Ms Alexandra Gorelik, Ms Stefanie Hartley,  
**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.

36. **Factors associated with self-perception of body image in young women - also offered as MBiomedSc**  
**Supervisors:** Prof John Wark, Dr Yasmin Jayasinghe, Dr Nicola Reavley, Ms Stefanie Hartley, Prof Suzanne Garland  
**Project Site:** Department of Medicine, (RMH) Parkville Campus  
**Contact:** E: jdwark@unimelb.edu.au  
**Project description:** Disturbances of body image perception are becoming increasingly common in young women and may lead to major health problems. How does young women’s body image perception correlate with objective measures of body mass and composition and what factors are associated with disturbed body image? The student will examine questionnaire data from young women covering body image, and compare this with clinical measurements including BMI, hip and waist measures, and body composition measured using DXA scans. There is scope to examine associations between body image and nutrition, disordered eating, measures of mood and lifestyle behaviours.
37. 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, Ms Stefanie Hartley

Project Site: Department of Medicine, RMH, Parkville Campus

Contact: suzanne.garland@thewomens.org.au; 8345 3670
         jdwark@unimelb.edu.au; 9342 7109
         stefanie.hartley@mcri.edu.au; 8345 3692
         rachel.skinner@health.nsw.gov.au

Project description: Some young people experience considerable anxiety associated with receiving injections and needles¹, such as in blood collection and immunisation. BrightHearts (BHs) is a novel biofeedback² 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.

38. Regulation of Nerve Fibre Growth in Eutopic and Ectopic Endometrium: Links with endometriosis-Associated Pain - also offered as MBiomedSc

Supervisors: Dr Jane Girling and Prof Janet Keast

Project Site: Department of Obstetrics and Gynaecology, Royal Women’s Hospital, Department of Anatomy and Neuroscience, Parkville

Contact: Dr Jane Girling T: 8345 3721 E: jgirling@unimelb.edu.au;
         Prof Janet Keast T: 9035 9759 E: janet.keast@unimelb.edu.au

Project description: Endometriosis affects 8-10% of reproductive-aged women. Women living with endometriosis endure chronic pelvic pain, including severe menstrual pain, pain during sexual intercourse and pain during defecation. The personal and healthcare costs of endometriosis are huge. Various types of nerve fibres are present in endometriotic lesions and are thought to mediate endometriosis-induced pain. There are also distinct patterns of nerve fibres present in the uterus; the distribution of these fibres is abnormal in women with endometriosis.

The overall aim of this research is to elucidate how aberrant uterine innervation leads to endometriosis-induced pain. The overall hypothesis is that endometriosis-associated pain reflects an imbalance of localised neuronal growth factors and chemo-repellents in uterine tissues and endometriotic lesions, resulting in aberrant innervation and nociceptive function. Projects will be available to examine the expression of proteins that are critical for initiating and directing new nerve growth (neurotrophic and guidance factors), and the features of nociceptor nerves in carefully characterised clinical samples (uterus, endometriotic lesions) collected on the basis of presence/absence of endometriosis and specific pain symptoms. Potential techniques for analysis include laser-capture microscopy and quantitative PCR, multi-label fluorescence immunohistochemistry and confocal microscopy. Projects may also be available to examine the mechanisms responsible for abnormal nerve growth and function in endometriotic lesions using a well validated rodent model of endometriosis. This may include visualising individual nociceptor neurons that have innervated endometrial lesions to investigate how they have developed abnormal function.

39. Investigation of genes associated with increased risk of endometriosis

Supervisors: Prof Peter Rogers, Dr Sarah Holdsworth-Carson

Project Site: Department of Obstetrics and Gynaecology, Royal Women’s Hospital

Contact: Prof Peter Rogers (parogers@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 can cause severe pain, and is associated with peritoneal inflammation, fibrosis and adhesions. It has been estimated that 8-10% of women in their reproductive years suffer from endometriosis. 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. In this project, we will develop studies 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.

40. Growth and Development of Uterine Fibroids
   Supervisors: Prof Peter Rogers, Dr Sarah Holdsworth-Carson
   Project Site: Department of Obstetrics and Gynaecology, Royal Women’s Hospital
   Contact: Prof Peter Rogers (parogers@unimelb.edu.au)
   Project description: Uterine fibroids are benign tumours of the smooth muscle of the uterus, with symptoms including heavy menstrual bleeding and pain/pressure symptoms. Fibroids are the most common cause of hysterectomy in women today, with an estimated annual direct healthcare cost in the USA of $2 billion dollars. This project will build on extensive molecular profiling and protein work undertaken on fibroids over several years to investigate the mechanisms associated with fibroid-associated heavy menstrual bleeding, particularly the contribution of uterine natural killer cells to the bleeding process.

BRAIN BIONICS

41. Brain Computer Interface – Evaluation of Implantation and Removability of a Novel Stent Electrode - also offered as MBiomedSc
   Supervisors: Nicholas Opie, Tom Oxley, Sam John
   Project Site: Department of Medicine (RMH)
   Contact: Nicholas Opie Email: nicholas.opie@unimelb.edu.au
   Project description: Our team has developed a minimally invasive brain machine interface that can be inserted over the motor cortex to extract neural information which may be used by a person with paralysis to control an exoskeleton, prosthetic limb or computer.
   Prior to our first-in-man study, we need to demonstrate that devices can be safety removed following acute implantation. Through histological and pathological evaluation in a large animal model, removal risk will be evaluated for a number of devices following acute (12 hour to 3 day) implantation.

42. Brain Computer Interface – Effect of Endothelialisation on Impedance Change of an Endovascular Electrode Array - also offered as MBiomedSc
   Supervisors: Nicholas Opie, Tom Oxley, Sam John
   Project Site: Department of Medicine (RMH)
   Contact: Nicholas Opie Email: nicholas.opie@unimelb.edu.au
   Project description: Our team has developed a minimally invasive brain machine interface that can be inserted over the motor cortex to extract neural information which may be used by a person with paralysis to control an exoskeleton, prosthetic limb or computer.
   Endothelialisation is an ongoing process of intimal remodeling that incorporates the endoluminal electrode array. Recording quality of the electrodes is affected by changes in impedance. This project aims to quantify the relationship between changes in impedance as the electrode array is incorporated into the vessel wall.

43. Brain Computer Interface – Limb Movement Classification - also offered as MBiomedSc
   Supervisors: Sam John, Thomas Oxley, Nick Opie
   Project Site: Royal Melbourne Hospital, The Florey Institute of Neuroscience and Mental Health
   Contact: Sam John Email: sam.john@unimelb.edu.au
   Project description: The aim of this project is to classify signal features relating to limb movement from brain signal recording over the sheep motor cortex using an endovascular brain computer interface. Brain-machine interface systems translate recorded neural signals into command signals for assistive technology. This project will determine if endovascularly recorded brain signals contain sufficient information to isolate limb movement.

44. Brain Computer Interface – Evoked Gamma Oscillation from Motor Cortex Stimulation - also offered as MBiomedSc
   Supervisors: Sam John, Thomas Oxley, Nick Opie
   Project Site: Royal Melbourne Hospital, The Florey Institute of Neuroscience and Mental Health
   Contact: Sam John Email: sam.john@unimelb.edu.au
   Project description: The aim of this project is to evaluate the effect of stimulation amplitude and electrode position on gamma band strength in an ovine cortex. It has been previously shown that there is a clear relationship between evoked gamma oscillations magnitude and electrode position and stimulation amplitude. We use evoked gamma oscillation magnitude to cortical stimulation to investigate the performance of a novel intravascular stimulation device.
45. **Brain Computer Interface - Ideal electrode size and configuration for vascular electroencephalography** - *also offered as MBiomedSc*

Supervisors: Sam John, Thomas Oxley, Nick Opie
Project Site: Royal Melbourne Hospital, The Florey Institute of Neuroscience and Mental Health
Contact: Sam John E: sam.john@unimelb.edu.au

**Project description:** The aim of this project is to compare the performance of an epidural recording array to the endovascular recording array in order to determine the ideal electrode size for an endovascular recording array. Electrocorticography (ECoG) involves recording electrical activity from the cortical surface using either epidural or subdural electrode contacts. We developed a novel endovascular device capable of recording cortical electrical activity through electrodes implanted in the blood vessel. Using somatosensory evoked potentials and resting brain signals we will evaluate the ideal electrode size for an endovascular recording array.

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46. **Unravelling the role of chemokines in central control of the cardiovascular system**

Supervisors: Dr Song Yao
Project Site: Florey Institute of Neuroscience and Mental Health
Contact: Dr Song Yao E: song.yao@florey.edu.au

**Project description:** The brain controls the cardiovascular system via a complex network spanning a number of specialised brain structures. We are particularly interested in an area known as the paraventricular nucleus of the hypothalamus or PVN. While the projections from the PVN to other brain centres that control the heart and blood vessels are well documented, the neurotransmitters and signalling molecules utilised by these projections are less well known. In this project, we will determine the function of a new class of neuromodulators called chemokines. Chemokines are well known for their role in mounting an inflammatory response in the periphery but the recent discovery that chemokines might also act as a signalling molecule within the brain opens up an exciting avenue of research.

This project will investigate the role of a specific chemokine known as CCL2 and its cognate receptor CCR2 in signalling to PVN neurones that project to another vitally important cardiovascular centre called the RVLM. This project will be relatively demanding and involve using a number of different techniques including electrophysiology if time permits. The successful completion of the project will increase our understanding of some of the fundamental mechanisms underpinning central cardiovascular regulation and control.

In this project we will be asking the following questions:

1. What is the distribution pattern of CCL2 and CCR2 within PVN and how many of these cells project to the RVLM.
2. How do PVN neurones react to exogenously applied CCL2?

**Techniques involved:**
*small animal surgery (microinjection of neuronal tracers into the PVN)
*tissue sectioning
*immunohistochemistry (DAB and fluorescence)
*microscopy (light, fluorescence, confocal)
*in vitro electrophysiology (if time permits)

47. **The role of Co in brain injury and disease.**

Supervisors: Dr. Blaine R. Roberts, Dr. Dominic Hare
Project Site: Florey Inst. Neuroscience and Mental Health-Melbourne Brain Centre
Contact: Dr. Blaine R. Roberts blaine.roberts@florey.edu.au

**Project description:** Cobalt is an essential micronutrient that acts as a cofactor in a number of neurologically important metalloproteins and small molecules. We have recently found that there is a perturbation in the levels of cobalt and other biometals following traumatic brain injury (TBI) in humans and a number of acute brain injury animal models. This project will use a metalloproteomic approach to determine the precise cobalt-binding species that is responsible for this alteration in brain cobalt levels following TBI. Specifically, this project will use multidimensional chromatography and a range of mass spectrometry approaches to isolate, characterise and quantify the protein or proteins associated with cobalt dyshomeostasis, and to determine if this effect is due to either disrupted cobalt brining or altered protein expression. Additionally, this project will examine if this perturbation in cobalt levels is reflected in the periphery, and if so, the possibility of a rapid field-test for TBI via cobalt assay.

48. **Targeting Tau phosphorylation to treat and prevent acquired epilepsy, neurodegeneration and neuropsychiatric disease following a brain injury** - *also offered as MBiomedSc*

Supervisors: Dr Sandy Shultz, Professor Terence O’Brien
Project Site: Departments of Medicine, Surgery and Psychiatry, The Royal Melbourne Hospital, University of Melbourne
Contact: Dr Sandy Shultz E: sandy.shultz@unimelb.edu.au
Project Description: This project will advance an entirely novel approach to the treatment of traumatic brain injury, seizures and epileptogenesis, and the associated neurodegenerative changes. This approach involves the inhibition of pathological hyperphosphorylation of the Tau protein via enhancing PP2A activity. Our work to date has demonstrated that treatment with sodium selenate specifically enhances the activity of the Tau protein phosphatase, PP2A leading to inhibition of the pathological hyperphosphorylation of Tau. Strongly supporting a role for pathological Tau in epilepsy we have found that sodium selenate is effective in suppressing induced seizures in a variety of rodent models. The proposed study will extend this line of translational research to establish:

1. That treatment with sodium selenate is effective at inhibiting neurological deficits, epileptogenesis, and neurodegeneration following a model of traumatic brain injury in the rat (fluid percussion brain injury).
2. Treatment with sodium selenate will mitigate the increased tissue expression of total and phospho-tau following a traumatic brain injury, with and without the development of epilepsy.

The outcomes of this project will advance the pre-clinical development of this approach, building on a sound basic science rational and strong preliminary data. Selenate has already been demonstrated to be safe and well tolerated in a 6 month Phase I trial in humans with prostate cancer, meaning a positive result from these studies has the potential to be expediently translated into clinical studies. In addition this project has relevance for epilepsy secondary to sporadic neurodegenerative conditions such as Alzheimer’s disease.

Skills: Small animal handling, neurosurgery (electrode implantations and fluid percussion injury), rat electroencephalography recordings, rat behavioral testing, brain perfusion and fixation, brain histological techniques, drug administration and in-vivo small animal MRI acquisition and analysis.

49. Post traumatic brain injury and epilepsy onset: Imaging the brain to investigate neural circuits and appropriate therapy interventions - also offered as MBiomedSc

Supervisor/s: Dr Sandy Shultz, Professor Terence O’Brien, and Dr Nigel Jones
Project Site: Department of Medicine (RMH), MBC Neurosciences Building Parkville, and the Centre for Molecular Imaging, The Peter MacCallum Cancer Institute
Email Dr Sandy Shultz: sandy.shultz@unimelb.edu.au

Project Description: Closed-head traumatic brain injury (TBI) is a common condition that has dramatic and often long-lasting impacts on the patient and their family. The annual incidence of significant TBI in developed countries has been estimated to be 1/1000.

One of the dramatic and disabling long-term consequences of TBI is the development of post-traumatic epilepsy (PTE), which occurs in up to 25% of patients with moderate to severe injuries. With penetrating brain injuries the incidence is over 50%. Epilepsy is defined as the occurrence of recurrent unprovoked seizures and is a prevalent neurological disorder as it affects up to 3% of the population in a lifetime and 0.5-1% at any one time. PTE often has severe morbidity and is difficult to treat as the seizures that develop are highly refractory complex partial seizures.

There is a lack of information about the mechanisms underlying the late epileptic, neurocognitive and neuropsychiatric changes occurring post-TBI. Neuronal plasticity occurring after TBI may explain the altered neuronal circuitry that, potentially, involves multiple physiological processes including neuronal death, axonal sprouting with formation of aberrant circuitry, neurogenesis and altered circuit connectivity caused by both axonal and dendritic plasticity. The neural changes that occur during the onset and development of PTE are poorly understood so this project has been designed to investigate structural changes that occur in the cortex, hippocampus, and white matter, key structures of the brain neural network circuitry.

Several projects are available that will study TBI in the rat using the fluid percussion injury model. Techniques involved in these projects include small animal MRI and diffusion tensor imaging (DTI), video-EEG monitoring and histological techniques to investigate neural network changes associated with seizure onset after head trauma, and the study of neurocognitive and neurobehavioural testing to study the consequences of TBI. The following projects have been designed to investigate the progressive neurological changes that occur post-TBI. The long-term aim is to investigate potential therapies that may protect the neural circuitry immediately after injury. To date, no effective neuroprotective strategies that have significant, long-term, benefits have been developed to treat TBI and PTE.

Project 1: A study of the neurocognitive and neurobehavioural changes that occur after closed-head traumatic brain injury in the rat (fluid percussion injury);
Project 2: Structural changes in the brain monitored by DTI and MRI after closed-head traumatic brain injury;

These projects will be conducted through the Department of Medicine at the Royal Melbourne Hospital and imaging will be performed at both the Howard Florey Institute and the Centre for Molecular Imaging at the Peter MacCallum Cancer Institute.
50. **Repeated brain concussions – understanding mechanisms and proposing new treatments** - also offered as MBiomedSc

**Supervisors:** Dr. Sandy Shultz, Prof. Terence O’Brien

**Project Site:** Department of Medicine, The Royal Melbourne Hospital, Melbourne Brain Centre, University of Melbourne

**Contact:** Dr. Sandy Shultz   E: sandy.shultz@unimelb.edu.au

**Project description:** Traumatic brain injuries (TBI) are an international health concern and growing socioeconomic problem. To date, no effective pharmaceutical treatment for TBI exists. Concussions, or mild TBI, account for 80% of TBI cases. However, despite the high incidence of concussion, there is a poor understanding of what occurs in the brain following this injury and much debate surrounding the medical management and treatment of concussion. Of particular concern are athletes and soldiers, who are at risk of suffering multiple concussions, as growing evidence indicates that repeated concussions can result in chronic neurological impairments and neurodegenerative disease. As little is known regarding what pathophysiological mechanisms actually contribute to the disease process, there are currently no specific treatment options for concussions and patients are simply instructed to rest until symptoms subside. However, soldiers, athletes, and other high-risk individuals represent a unique population where pre- and/or chronic treatment with neuroprotective compounds is conceivable and should be explored. Considering the limited understanding, high incidence, lack of effective treatment, and increased public concern it is imperative that research is carried out to address the issue of concussion.

Given the limitations associated with studying the pathophysiological mechanisms and novel treatments of TBI in the clinical setting, the use of animal models is beneficial. The lateral fluid percussion injury is the most commonly used and well-validated animal model of TBI, and our lab recently developed a repeated injury schedule that is similar to what might occur in athletes and soldiers. The proposed project will utilize this novel model with the goal of examining the underlying mechanisms and potential treatments of concussion.

**Aim 1** will examine the role of hyperphosphorylated tau in repeated concussion, and its potential treatment with sodium selenate, a potent inhibitor of hyperphosphorylated tau. Our previous work has found sodium selenate to be neuroprotective after severe TBI in rats.

**Aim 2** will examine the role of Nedd4-WW domain-binding protein 5 (Ndfip1), an endogenous neuroprotective protein, in repeated concussion, and the use of a novel cobalt complex treatment to up-regulate Ndfip1. Ndfip1 is up-regulated in surviving neurons post-TBI, and cobalt complexes are capable of increasing Ndfip1 expression in the brain. Therefore, increasing Ndfip1 expression in rats with cobalt complex treatment may reduce neuronal death and improve outcome after repeated concussions.

Both aims will incorporate advanced neuroimaging, behavioural, molecular, and immunohistochemical techniques. Taken together, these projects will provide novel data regarding the underlying mechanisms and potential treatments of concussions, and hold important implications for their management in the clinical setting.

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51. **Using novel immunotherapies to control chronic lymphocytic leukaemia responses**

**Supervisors:** Dr Joanne Davis, Dr Kylie Mason and Dr Rachel Koldej

**Project Site:** Department of Medicine (RMH)

**Contact:** Dr Joanne Davis    E: joanne.davis@mh.org.au

**Project description:** Chronic lymphocytic leukaemia (CLL) is a B cell malignancy that results in profound immunodeficiency, contributing to infection, tumour progression and mortality. Novel immunotherapies are being trialed, including lenalidomide, and agonistic CD40 antibodies, which activate CLL-B cells to promote an anti-tumour immune response. It is unknown if this unique combination of drugs may inadvertently promote survival of CLL-B tumour cells. Therefore in this project you will investigate if pro-survival Bcl-2 family antagonists may render tumour cells sensitive to apoptosis. In collaboration with the Peter MacCallum Cancer Centre, we have collected a unique cohort of CLL patient samples, to test our novel immunotherapeutic drugs and Bcl-2 family antagonists. CLL B cells will be isolated and activated with various combinations of immunotherapies, cultured with NKT cells and tested for their ability to survive and resist apoptosis by upregulation of pro-survival proteins including Bcl-2 and Mcl-1. In addition, the NKT cells will be tested for their ability to kill activated CLL cells and for the secretion of inflammatory cytokines. This study has important implications for clinical trial design for the treatment of CLL patients.

**Skill acquisition:** Sterile tissue culture techniques, magnetic bead cell separation, killing assays, cytometric bead array, western blotting, flow cytometry
52. **Glioma stem cells: biology and molecular targets**  
**Supervisor:** Dr Andrew Morokoff  
**Co-Supervisors:** A/Prof Kate Drummond, Prof Andrew Kaye.  
**Location:** Department of Surgery, Royal Melbourne Hospital  
**Contact:** Dr Andrew Morokoff (morokoff@unimelb.edu.au) T: 9035 8586  
**Project Description:** Gliomas 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 neurosphere 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 transcriptome sequencing. These cell lines and mouse xenograft models utilising bioluminescence will be used to test novel compounds targeting these pathways.

53. **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, St Andrews Place, East Melbourne  
**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.

54. **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, St Andrews Place, East Melbourne  
**Contact:** A/Professor Alex Boussioutas T: +61 03 9656 1287 E: alexb@unimelb.edu.au; 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.
55. **Role of the Tumour Microenvironment in Gastric Cancer**

**Supervisors:** A/Professor Alex Boussioutas. Co-supervisor: Dr Rita Busuttil

**Project Site:** Peter MacCallum Cancer Centre, St Andrews Place, East Melbourne

**Contact:** A/Professor Alex Boussioutas T: +61 03 9656 1287 E: alexb@unimelb.edu.au/H

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.

**Outcomes/Benefits:** Successful completion of the project may provide a model of suppressing peritoneal dissemination of ovarian carcinoma.

**Project Site:** Work will be conducted at the laboratories of the Royal Women’s Hospitals & Department of Obstetrics & Gynaecology, University of Melbourne

**Contact:** Dr Nuzhat Ahmed, Women’s Cancer Research Centre, RWH. T: 8345 3734 E: Nuzhat.Ahmed@thewomens.org.au

56. **Understanding peritoneal metastasis in the context of tumour recurrence in ovarian cancer**

**Supervisors:** Dr Nuzhat Ahmed, Prof Jock Findlay (Women’s Cancer Research Centre, Royal Women’s Hospital & Department of Obstetrics & Gynaecology, University of Melbourne)

**Project Site:** Work will be conducted at the laboratories of the Royal Women’s Hospitals

**Contact:** Dr Nuzhat Ahmed, Women’s Cancer Research Centre, RWH. T: 8345 3734 E: Nuzhat.Ahmed@thewomens.org.au

**Aims/Hypothesis:** Hypotheses-Peritoneal tumour cellular aggregates (PTCs) surviving in ascites undergo epithelial to mesenchymal transition (EMT) in response to chemotherapy treatment. The regulation of EMT-associated molecules in response to drug treatment is crucial for maintaining the survival and invasiveness of PTCs for secondary growth (recurrence); and suppression of ovarian cancer growth in the peritoneum may be achieved by targeting drug induced EMT associated molecules.

**The specific aims** of the project are: (i) to characterize the EMT status in ovarian PTCs isolated from ascites of cancer patients in response to chemotherapy; and (ii) to suppress the growth of PTCs by targeting EMT associated molecules that are up regulated in response to chemotherapy.

**Background/Rationale:** The development of peritoneal metastases is a major clinical issue in the prognosis and management of ovarian cancer. A significant proportion of ovarian cancer cells in peritoneal ascites exist as PTCs with the capacity to metastasize to local organs. The pathology of localized metastasis includes attachment of shed PTCs in the peritoneum onto mesothelial-lined spaces resulting in tumour masses as a secondary growth. In most cases it is difficult to completely eradicate PTCs during debulking surgery. These free floating PTCs survive chemotherapy treatment and are a major source of recurrence which kills 80% of ovarian cancer patients treated with first line of chemotherapy. Hence, a comprehensive understanding of ascites tumour biology and its response to chemotherapy is needed to combat ovarian cancer dissemination/recurrence.

**Outcomes/Benefits:** Understanding the processes of growth/survival and the response of ascites PTCs to chemotherapy is essential for the clinical management of ovarian cancer patients. The project will involve isolating PTCs from ascites of cancer patients and using Western blot, quantitative PCR and immunofluorescence to identify novel proteins of interest. Successful completion of the project may provide a model of suppressing peritoneal dissemination of ovarian carcinoma. This will also provide a platform for a graduate student to understand the basics of clinical research. Results from this project will be published in biochemical/cancer journals and presented at a national or international conference.

Human ethics application (HEC #09/09) has been approved by the Royal Women’s Hospital Human Ethics Committee.

**Project Site:** Work will be conducted at the laboratories of the Royal Women’s Hospitals

**Contact:** Dr Nuzhat Ahmed, Women’s Cancer Research Centre, RWH. T: 8345 3734 E: Nuzhat.Ahmed@thewomens.org.au

57. **Characterization of cross-talk between tumour and stromal cells in inducing metastasis and resistance to chemotherapy in ovarian cancer**

**Supervisors:** Dr Nuzhat Ahmed, Prof Jock Findlay (Women’s Cancer Research Centre, Royal Women’s Hospital & Department of Obstetrics & Gynaecology, University of Melbourne)

**Project Site:** Work will be conducted at the laboratories of the Royal Women’s Hospitals

**Contact:** Dr Nuzhat Ahmed, Women’s Cancer Research Centre, RWH. T: 8345 3734 E: Nuzhat.Ahmed@thewomens.org.au
**Aims/Hypothesis: Hypotheses** - Peritoneal dissemination of ovarian cancer is dictated by the extent of invasiveness in the tumour cells of ascites that survive as peritoneal tumour aggregates (PTCs), and is largely dependent on the biological changes induced by the surrounding stroma. We further hypothesize that identification of cross talk between tumour PTCs and stroma will successfully identify potential molecules involved in the predisposition of the tumour cells to metastasise locally as well as respond to chemotherapy.

**Specific aims:** (i) To determine whether cancer associated fibroblasts (CAFs isolated fresh from ascites) can alter the spheroid forming and invasive ability of ovarian cancer cell lines in vitro; & (ii) to determine if CAFs can alter the response of ovarian cancer cell lines to chemotherapy.

**Background/Rationale:** About 75% of ovarian cancer patients are diagnosed at an advanced-stage as symptoms are non specific and diagnosis delayed until the tumour has metastasized to the surrounding abdominal peritoneum and omentum. This type of peritoneal dissemination is almost unique to ovarian cancer and occurs due to the exfoliation of transformed ovarian surface epithelial cells. In the peritoneal cavity transformed cells disseminate as single cells or PTCs influenced by the flow of peritoneal tumour fluid or ascites. The unique biology of tumour cell exfoliation from the surface of the ovary, survival as single cells or as PTCs in the peritoneum, predisposition to peritoneal organs and innate resistance to chemotherapy suggests that ovarian cancer PTCs possess distinct traits which enables them to self renew and adapt to the changing local environment. In animal models of cancer, normal epithelial cells have been shown to become malignant when surrounded by tumour-derived fibroblasts but not normal fibroblasts. These results signal the need to study the biological alterations induced by stroma on ascites tumours cells of ovarian cancer.

**Outcomes/Benefits:** This proposal represents a novel model of ovarian cancer progression where the inherent traits in ascites PTCs will be compared in the presence and absence of associated stroma. PTCs and stromal cells will be isolated from the ascites of ovarian cancer patients and evaluation of the biological alterations induced by the associated stroma that result in enhancing the metastasising capacity of ascites PTCs will be assessed by biological methods such as Western blot, quantitative PCR and immunofluorescence. The identification of these changes/molecules may lead to the development of novel prognostic indicators.

Human ethics application (HEC#09/09) has been approved by the Royal Women’s Hospital Human Ethics Committee.

58. **Elucidating the role of mesenchymal stem cells in promoting metastasis of ovarian cancer cells**

**Supervisors:** Dr Nuzhat Ahmed (Women’s Cancer Research Centre, RWH), Dr Bill Kalionis (Pregnancy Research Centre, RWH)

**Project Site:** Work will be conducted at the laboratories of the Royal Women’s Hospitals

**Contact:** Dr Nuzhat Ahmed, Women’s Cancer Research Centre, RWH. T: 8345 3734

**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 ovcaosphere 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 ³H-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.

59. **Synchrotron radiotherapy for the treatment of cancer**

**Supervisors:** Prof Peter Rogers, Dr Jeffrey Crosbie, Dr Yuqing Yang

**Project Site:** The Royal Women’s Hospital

**Contact:** Peter Rogers E: parogers@unimelb.edu.au, Jeffrey Crosbie E: jcrosbie@unimelb.edu.au

**Project description:** The synchrotron produces near-parallel X-ray beams that are up to ten billion times more intense than those currently used for radiotherapy in the treatment of cancer. Synchrotron radiation provides novel opportunities
for segmenting the beam into narrow microbeams in order to treat tumours. Normal tissues appear to be resistant to arrays of microbeam radiation (MRT), with survival following doses up to a hundred times greater than with conventional radiation. Conversely, tumours can be readily destroyed using microbeam radiation, although the molecular and cellular mechanisms behind this susceptibility are currently unknown. We offer projects covering all aspects of synchrotron MRT, from physics to biology. The prospective student will gain experience with cutting-edge molecular biology techniques and will utilise the Australian Synchrotron to investigate the mechanisms that underpin the response of normal and tumour cells to microbeam radiation. We also offer projects which have more of a physics and chemistry component to them and which may appeal to some students.

60.  **TGF-signalling and cancer development**  
**Supervisors:** Dr. Hong-Jian Zhu (and 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 TGF 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, sRNA (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**  
**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: chovens@unimelb.edu.au  
**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. Prostate Cancer – what can we learn from its mistakes?
Supervisors: A/Prof Chris Hovens, Dr Michael Clarkson
Project Site: Department of Surgery (RMH), 5th Floor, Clinical Sciences Building
Contact: Dr Michael Clarkson E: michael.clarkson@epworth.org.au

Background/Rationale: “So many roads. So many detours. So many choices. So many mistakes.” Although Sarah Jessica Parker was almost certainly not thinking about cancer when she said this, it none the less applies. One of the first identifiable “mistakes” that occur in Prostate cancer are genomic rearrangements, some of these contribute directly to cancer initiation and progression. There are also rare cases where the cancer genome has become hypermutated. We and others have found that hypermutator forms of prostate cancer have mutation or deletion in genes that are required for DNA mismatch repair, MSH2 or MSH6. In order to better understand the mechanism by which MSH2 becomes mutated and the consequences of this gene inactivation we have obtained prostate cancer samples from patients heterozygous for germline MSH2 and MSH6 defects (Lynch syndrome). These individuals have a 10 fold higher chance of developing Prostate cancer than the general population and a 10 year earlier onset. Since androgen has been shown to direct genomic rearrangements we hypothesise that in Lynch syndrome, the second copy of the MSH2 gene is inactivated by an androgen dependent mechanism. Interestingly, in the five known examples of the hypermutator phenotype, none appear to exhibit the most common genomic rearrangements seen in Prostate cancer. From this, we hypothesise that MSH2 is required for androgen dependent genomic rearrangements.

Project Description: We will conduct complementary experiments to address our two hypotheses at the same time. Lynch syndrome patient material will be characterised in order to define both the type of mutation in MSH2 and whether it contains other androgen dependent genomic rearrangements that are commonly seen in prostate cancer. We will also examine whether androgen dependent rearrangements are able to disrupt the MSH2 gene and if MSH2 is required for androgen dependent rearrangements.

63. Integrated Genomics of Bladder Cancer
Supervisors: A/Prof Chris Hovens and Dr Niall Corcoran
Project Site: Department of Surgery (RMH), 5th Floor, Clinical Sciences Building and Prostate Cancer Epworth Hospital, Richmond
Contact: A/Prof Chris Hovens T: 9342 7703/4 E: chovens@unimelb.edu.au

Project description: With over 2000 patients diagnosed with Bladder Cancer (BC) each year and a significant amount of them having recurrent and progressive disease despite optimum therapy, BC is a very serious cancer. Currently our research team is investigating how bladder cancer progresses at a molecular level using genomic approaches. We have access to human tissue, plasma and urine 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 probe deeper into our analyses of the genomics of bladder cancers. We have identified a number of candidate markers that are altered across various stages of bladder cancer. 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 tumour 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 an excellent track record of publications, 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.

64. STAT3-mediates Resistance to EGFR targeted therapy in Cancer
Supervisors: Dr Rodney Luwor
Location: Dept of Surgery, Royal Melbourne Hospital
Contact: 9342-7703, Email: rlguwor@unimelb.edu.au

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. Furthermore, this project has the scope to evolve into a PhD project starting in 2016/17 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.

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

Supervisors: Dr Rodney Luwor and Dr Stanley Stylli
Location: Dept of Surgery, Level 5, Clinical Sciences Building, Royal Melbourne Hospital
Contact: Dr Rodney Luwor; T: 9342-7703, E: rluwor@unimelb.edu.au or Dr Stan Stylli; T: 9342-7703, E: stanley.stylli@mh.org.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 potential molecular candidates in mediating resistance to current therapy. Both these project directions will utilise 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 2016/17 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.

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

Supervisors: Dr Stanley Stylli and Dr Rodney Luwor
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 or Dr Rodney Luwor; T: 8344 3027, E: rluwor@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. The role of the Eph/Ephrin signaling system in the progression of colon cancer - also offered as MBSc

Supervisors: Dr Paul Senior & Professor Steven Chan
Project Site: North-West Academic Centre, WCHRE Building Sunshine Hospital, St Albans.
Contact: Dr. Paul Senior T: 83958228 E: psenior@unimelb.edu.au

Project Description: The Eph/Ephrin family of receptors and ligands are major regulators of development and are coming to be recognised as important in tissue homeostasis including in the normal colonic epithelium. Loss of expression of several Eph receptors and increased expression of others are linked to poor prognosis in colon cancer. We are interested in understanding the mechanisms by which these receptors influence invasion and metastatic spread in colon cancer. The project involves modulating the expression of Eph receptors in colon cancer cell lines using both over-expression and gene knock down methods. Then utilising these cells to study the effects on invasion, cell migration and receptor ligand interaction using in vitro models together with in vivo experiments using models of metastatic spread.

Acquired skills will include small animal handling, surgery, fluorescent microscopy, cell culture, QPCR, protein & DNA electrophoresis Western blotting.

68. Molecular biomarkers for Human Papillomavirus-related cancer progression

Supervisors: A/Professor Sepehr Tabrizi, Dr Alyssa Cornall, Professor Suzanne Garland
Project Site: Women's Centre for Infectious Diseases (RWH), Bio21 Institute
Contact: A/Prof Sepehr Tabrizi: sepehr.tabrizi@thewomens.org.au;
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.

69. Effect of probiotic supplementation on long term colonization of probiotic strains in preterm infants

Supervisors: A/Professor Sepehr Tabrizi, Dr Jimmy Twin and Professor Suzanne Garland
Project Site: Women's Centre for Infectious Diseases (RWH), Bio21 Institute
Contact: A/Prof Sepehr Tabrizi: sepehr.tabrizi@thewomens.org.au;
Dr. Jimmy Twin: Jimmy.twin@mcri.edu.au

Project description: Probiotics are live microorganisms, which when administered in adequate amounts confer health benefits on the host. Amongst numerous bacteriocidal and nutritional roles, they may also favourably modulate host immune responses in local and remote tissues. The commensal bacteria of the gastrointestinal tract play a key role in the development of healthy immune responses. Healthy term infants acquire these commensal organisms rapidly after birth. However, colonisation in preterm infants is adversely affected by delivery mode, antibiotic treatment and the intensive care environment. Altered microbiota composition may lead to increased colonisation with pathogenic bacteria, poor immune development and susceptibility to sepsis in the preterm infant.

This project focuses on the examination of faecal samples of infants, with and without the influence of oral probiotics over the course of their hospital stay and after discharge. Faecal Samples have been obtained from the Victorian participants from the world’s largest large multi-centre, randomised, double blinded, placebo controlled trial investigating supplementing preterm infants born at < 32 weeks’ gestation and weighing < 1500 g; the Proprems study. The primary outcome measure for this study was late onset sepsis: there were multiple secondary outcomes. In this new study we plan to measure the impact of probiotics on colonization of probiotic strains after discharge using qPCR.

70. Human Papillomavirus (HPV) Genotype Surveillance

Supervisors: Dr Alyssa Cornall, A/Professor Sepehr Tabrizi, A/Professor Jane Hocking, Professor Suzanne Garland, Dr Dorothy Michalek
Project Site: Department of Microbiology and Infectious Diseases, RWH, Parkville Campus
Contact: Dr Alyssa Cornall: alyssa.cornall@mcri.edu.au
A/Prof Sepehr Tabrizi: sepehr.tabrizi@thewomens.org.au
Dr Dorothy Machalek: Dorothy.machalek@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 determine vaccine effectiveness, i.e. measuring the impact in a real world situation. This project will involve genotype testing of clinical surveillance samples. Self-collected genital samples of participants recruited from general practice clinics, including both men and women aged between 18 and 35 years old, will be tested for HPV genotypes. Data from women will help evaluate the direct effect of the vaccine on vaccinated populations, while data from men (most of whom will not have been vaccinated) will provide valuable baseline data of 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 analysis.

71. **Comparison of self-collected versus clinician-collected samples for Human Papillomavirus (HPV) Genotype Surveillance**

*Supervisors:* Dr Alyssa Cornall, A/Professor Sepehr Tabrizi, Professor Suzanne Garland, Dr Dorothy Machalek

*Project Site:* Department of Microbiology and Infectious Diseases, RWH, Parkville Campus

*Contact:* Dr Alyssa Cornall: alyssa.cornall@mcri.edu.au
A/Prof Sepehr Tabrizi: sepehr.tabrizi@thewomens.org.au
Dr Dorothy Machalek: dorothy.machalek@mcri.edu.au

*Project description:* Human Papillomavirus (HPV) is the causative agent for cervical and other anogenital cancers, and 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, the Medical Services Advisory Committee (MSAC) has recommended that cervical cancer screening be changed from 2016 to more sensitive HPV DNA assays, and has suggested that self-sampled specimens might be introduced. This project will involve evaluation of self-collected samples from Australian women. Self-collected and clinician-collected genital samples of women, aged between 18 and 35 years and recruited from family planning clinics, will be tested for HPV genotypes. In addition to evaluating the quality of self-collected samples, this data will help evaluate the effect of the vaccine on vaccinated women by comparing it with baseline HPV prevalence data. This project will involve sample logging and processing, DNA extraction, quality control testing, PCR and genotyping, data management and epidemiological data analysis.

72. **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.

**CANCER – FERTILITY PRESERVATION**

73. **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 beneficence 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.

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### CARDIOLOGY

**74. Evaluation of regional dysfunction of the aged heart post ischemia/reperfusion injury**

*Supervisors:* Xiao-Jun Du, Helen Kiriazis  
*Project Site:* Experimental Cardiology Lab, Baker IDI Heart and Diabetes Institute  
*Contact:* Xiao-Jun Du, E: xiao-jun.du@bakeridi.edu.au T: +61 03 8532 1267

**Project description:** The prevalence of ischemic heart disease increases with age. Moreover, there is a loss of cardioprotection and reduced tolerance to ischemic injury with ageing, leading to more severe cardiac dysfunction. Age-dependent accumulation of collagen in the heart leads to progressive increase in ventricular stiffness and impaired function. Understanding the functional impact of fibrosis in the ageing heart following cardiac ischemia is critical in order to design new therapies. This project will use sophisticated echocardiography (echo) techniques and VevoStrain software, to examine the effects of ischemic duration on regional cardiac dysfunction following ischemia/reperfusion injury in young and aged mice.

Blocked coronary vessels lead to myocardial infarction. In the clinic, these vessels are unblocked allowing reperfusion of the ischemic-damaged heart muscle. We can mimic this condition in mice by inducing ischemia/reperfusion injury. Briefly, the left coronary artery will be tied inducing an ischemic area involving \( \sim 40\% \) of the left ventricle (LV). At specific time-points, this occlusion of the artery will be removed to re-establish blood flow, a process called reperfusion. Mice at 3 (young) and 10-12 (aged) months of age will be studied with 3 ischemic durations tested (60, 120 and 240 min). Echocardiography and VevoStrain analysis will be performed at 0 (baseline), 1, 2, 3 and 4 weeks post surgery to assess changes in regional LV wall motion. Echo findings will be related to cardiac histological examination.

The top echocardiography (echo) image shows tracking of two points on the wall of the LV of a normal mouse (arrows point to a blue and red dot on the wall), with the corresponding blue and red velocity traces of these points against time. In a normal heart, movement of different parts of the wall are synchronised, as shown here.

The bottom panel shows a mouse heart after myocardial infarction (MI). It is clear that the wall motion is not synchronised in this animal. In fact, the red line is flat indicating that this part of the heart wall has been severely damaged by MI and is hardly moving.

[Images from FUJIFILM VisualSonics, Inc.]

This project is suitable for honour students and related methods, skills and technologies include:

- echocardiography
- speckle-tracking based strain analysis
- quantitative histology
- RT-PCR for gene expression

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75. **Antioxidant therapy of fibrotic cardiomyopathy to limit arrhythmogenesis**

**Supervisors:** A/Prof Xiao-Jun Du, Dr Helen Kiriazis, My-Nhan Nguyen

**Project Site:** Experimental Cardiology Lab, Baker IDI Heart and Diabetes Institute

**Contact:** Xiao-Jun Du, E: xiao-jun.du@bakeridi.edu.au T: +61 03 8532 1267

**Project description:** Heart failure is the leading cause of cardiac fatality and a major challenge to modern cardiology. Clinical studies show that about 50% of deaths of heart failure patients are due to arrhythmic sudden death [1]. A failing heart shows significant histopathology including fibrosis, cardiomyocyte hypertrophy and cardiomyocyte apoptosis. Among these, interstitial fibrosis is regarded as a pivotal factor for arrhythmic development [2]. Our previous study on a transgenic (TG) mouse strain revealed development of cardiomyopathy and premature death [3]. Myocardial fibrosis is the most prominent histopathology in this model [2,3]. We recently demonstrated enhanced oxidative stress in the TG mouse heart leading to fibrosis, cardiomyocyte hypertrophy/apoptosis and inflammation [4], and treatment with the antioxidant N-acetylcysteine (NAC) reduced fibrosis and myocyte death and improved cardiac function [4]. These findings support the view that increased oxidative stress in a failing heart is a pivotal molecular mechanism of histopathology, particularly fibrosis [5].

We very recently observed frequent onset of ventricular tachy-arrhythmias in the TG mice (our unpublished data). This TG strain represents an ideal model for pre-clinical therapeutic testing. This project will extend our previous study [4] to test if antioxidant therapy is able to reduce the severity of arrhythmias. TG mice will receive treatment with NAC (0.5 mg/kg/day) for one month. During the treatment period, animals will be studied by echocardiography to determine cardiac function and by telemetry technique to monitor development of ventricular arrhythmias. Another group of TG mice will be similarly studied for comparison. At the end of the treatment period, changes in cardiac fibrosis and degree of cardiac dilatation will be related to ventricular arrhythmias.

This project is suitable for students for honorary degree and the related methods, skills and technologies include:

- Echocardiography for cardiac functional assessment
- Telemetry recording of electrocardiogram for determination of arrhythmias
- Biochemical assays and quantitative histology
- Drug administration, animal monitoring

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

**Supervisors:** Professor Judy Savige and A/Prof Deb Colville

**Project Site:** NWAC, Northern Hospital, Epping.

**Contact:** Professor Judy 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.

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**CLINICAL RESEARCH**

77. **Hospital-acquired electrolyte disorders – also offered as MBiomedSc**

**Supervisors:** A/Prof Terri Jackson, Dr Anastasia Hutchinson, Prof Peter Brooks, Ms Karen Barclay

**Project Site:** Northern Clinical Research Centre (NCRC), The Northern Hospital, Epping

**Contact:** Dr. Terri Jackson T: 044 872 7240 E: terri.jackson@unimelb.edu.au

**Project Description:** Routine hospital diagnosis data in Australia includes ‘condition onset’ (timing) markers that distinguish co-morbidities (diagnoses documented as present on admission) from hospital-acquired diagnoses. This
project uses a one-year sample of the Victorian Admitted Episodes Database to investigate the correlates of hospital-acquired electrolyte disorders arising from active treatment rather than dehydration. These range from minor biochemical imbalances to major multi-organ disorders. They have been found to be the most costly single complication in hospital data from both Canada and Australia. A better understanding of the factors affecting their clinical course will assist in efforts to reduce incidence.

The specific aims of this project are:
• To identify the patient characteristics and diagnoses most frequently associated with hospital-acquired electrolyte disorders
• To describe patterns of multiple complications causing or arising from electrolyte imbalances
• To estimate the health care implications of these disorders, including incremental additional days of stay, days of ICU care, in-hospital death
• To review the literature on approaches to fluid and electrolyte management to support reduction in the rates of these disorders.

Skills: The project will enable the student to gain skills in: secondary analysis of large hospital data sets (including data validation and cleaning), data linkage, descriptive statistics and multivariate logistic regression. The student will develop an understanding of key concepts in clinical medicine.

78. Are readmissions to The Northern Hospital related to hospital acquired diagnoses in a previous admission? - also offered as MBiomedSc
Supervisors: Dr Terri Jackson, Dr Anastasia Hutchinson, Prof Peter Brooks
Project Site: Northern Clinical Research Centre (NCRC), The Northern Hospital, Epping
Contact: Dr. Terri Jackson T: 044 872 7240 E: terri.jackson@nh.org.au

Project Description: Routine hospital demographic and diagnosis data are used in many health care systems to investigate and improve inpatient care. Diagnosis data in Australia includes ‘condition onset’ (timing) markers that distinguish comorbidities (diagnoses documented as present on admission) from hospital-acquired diagnoses. A body of research has demonstrated that such markers allow for identification of the range of complications and adverse events that compromise patient outcomes. This project seeks to use information on hospital-acquired diagnoses to quantify the proportion of readmissions to The Northern Hospital that are attributable to conditions that arose during a previous hospitalisation.

The specific aims of this project are:
• To estimate the proportion of readmissions associated with a previous hospital-acquired diagnosis and attributable additional days of stay;
• To use multivariate analysis to identify the contributions of demographic characteristics, principal diagnosis, and hospital-acquired diagnoses to the probability of readmission;
• To use the Classification of Hospital Acquired Diagnoses (CHADx) to characterise the major contributors to readmission rates and days of stay at The Northern Hospital.

Skills: The skills expected to be learnt from this project include: secondary analysis of large hospital data sets (including data validation and cleaning), data linkage, descriptive statistics and multivariate logistic regression.

CLINICAL RESEARCH – SURGICAL

Projects would suit a motivated individual interested in making a difference at a clinical level. The successful applicant would have a unique opportunity to be involved in a dynamic surgical setting with a gentle introduction into the World of Surgery and the importance of process and governance in clinical practice. The student would perform a comprehensive literature review, collect and analyse data and prepare and submit a manuscript to a peer-reviewed journal.

79. Documentation of pre-operative decision-making in surgery
Supervisors: Ms Karen Barclay
Project Site: The Northern Hospital, Epping
Contact: Ms Karen Barclay, karen.barclay@nh.org.au

Project description: Documentation is critical in clinical practice. Observation has shown when emergency decisions are made, the documentation of decisions to operate may be sub-optimal. This has consequences for subsequent assessment and also potentially raises medico-legal consequences. The aim of the study is to assess the flow of documentation around operative decision-making in an emergency setting, identify factors which may contribute and suggest possible ways for improvement.
80. The use of computerised tomography for the assessment of emergency surgical patients
Supervisors: Ms Karen Barclay
Project Site: The Northern Hospital, Epping
Contact: Ms Karen Barclay karen.barclay@nh.org.au
Project description: The widespread availability of Computed Tomography (CT) and a change in clinical thinking results in large numbers of procedures being performed. At times, scans are requested by junior colleagues without discussion with a more senior individual. This may lead to the incorrect procedure being performed and a repeat procedure being required. There is a cost to this in terms of resource utilization, radiation exposure and time to diagnosis. In addition, the use of intravenous contrast in acutely unwell patients may worsen impaired renal function or prolong time for renal recovery. The current study looks at practice for requesting CT scans on emergency patients. The aim is to evaluate current practice, assess if there are areas of inefficiency and suggest ways in which practice could be optimised.

81. A scoring system for the assessment of process in rectal cancer management
Supervisors: Ms Karen Barclay
Project Site: The Northern Hospital, Epping
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.

82. Detecting a genetic pre-disposition to colorectal cancer in routine practice.
Supervisors: Ms Karen Barclay
Project Site: The Northern Hospital, Epping
Contact: Ms Karen Barclay karen.barclay@nh.org.au
Project description: Genetic pre-disposition to Colorectal Cancer accounts for 10-15% of cases, with 5% associated with known syndromes like Lynch syndrome (previously HNPCC) or Familial Adenomatous Polyposis (FAP). A complete family history and further testing of appropriate tumours following resection is a good starting point for detection. For those in whom susceptibility is noted, referral to a genetics clinic is appropriate. Full assessment may lead to family members being diagnosed earlier or reassured there is no risk above the average population. In routine clinical practice, full assessment of familial risk in patients with CRC may or may not happen. The current study will assess the familial risk of patients who have undergone resection for CRC based on pathology and documented family history, and how the risk was managed. The aim of the study is to establish the completeness of assessment for familial predisposition, potential barriers to assessment and to propose methods to improve detection rates, if appropriate.

83. Computerised tomography reporting and surgical findings – do they match?
Supervisors: Ms Karen Barclay
Project Site: The Northern Hospital, Epping
Contact: Ms Karen Barclay karen.barclay@nh.org.au
Project description: The widespread availability of Computed Tomography (CT) and a change in clinical thinking results in large numbers of procedures being performed. At times, the CT reporting may over or underestimate pathology and this may influence decisions about the timing of surgical intervention. The correlation between CT reports and surgical findings at our institution is unknown. The student would obtain a list of patients who underwent major abdominal emergency surgery who had a CT scan within a few days of the operation. The computerized clinical records would be searched to correlate CT and surgical findings. Clinical factors which may influence surgical decision-making will also be assessed.

84. The presentation of colorectal cancer in the era of screening
Supervisors: Ms Karen Barclay
Project Site: The Northern Hospital, Epping
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.
85. Can Alvimopan be used to reduce post-operative nausea and vomiting in surgical patients?

**Supervisors:** Ms Karen Barclay

**Project Site:** The Northern Hospital, Epping

**Contact:** Ms Karen Barclay karen.barclay@nh.org.au

**Project description:** Post-operative nausea and vomiting (PONV) have significant consequences including patient discomfort, electrolyte and fluid imbalances and increased length of stay. Although methods such as epidurals and avoidance of non-opioid analgesia have been shown to reduce the incidence of PONV, in some situations (eg emergency patients), this may not be practical. Alvimopan antagonises the peripheral effects of morphine and has been shown to be safe. It has not been used in the surgical setting in Australia. This study would pilot the introduction of Alvimopan in this setting.

86. Do guidelines influence practitioners, and if not, why not?

**Supervisors:** Ms Karen Barclay

**Project Site:** The Northern Hospital, Epping

**Contact:** Ms Karen Barclay karen.barclay@nh.org.au

**Project description:** Guidelines for management following the removal of adenomatous polyps have been present for many years, with the recent publication of simple algorithms to support the initial work. It is unclear whether clinicians are aware of the guidelines or algorithms and whether they influence practice. This study aims to survey the practice of clinicians to establish their level of engagement in this area and identify possible ways this could be improved.

87. Complications of surgical implants in hospital care – also offered as MBiomedSc

**Supervisors:** A/Prof Terri Jackson, Dr Anastasia Hutchinson, Prof Peter Brooks, Ms Wanda Stelmach, Ms Karen Barclay

**Project Site:** Northern Clinical Research Centre (NCRC), The Northern Hospital, Epping

**Contact:** Dr. Terri Jackson T: 044 872 7240 E: terri.jackson@unimelb.edu.au

**Project Description:** Routine computerised diagnosis data from Australian hospitals includes ‘condition onset’ (timing) markers that distinguish co-morbidities (diagnoses documented as present on admission) from hospital-acquired diagnoses. These computerised patient-level records also document all surgical procedures undertaken during an admission. This project investigates the correlates of complications of surgical implants, in particular cardiac and vascular implants, using a one-year sample of de-identified patient level data from all Victorian acute care hospitals (the VAED). Complications of surgical implants have been found to be both frequent and costly in a range of hospitals and health care systems, and this study will help to target these by understanding their impact on patient care and to develop strategies for reducing their incidence.

**The specific aims of this project are:**
- To identify those implants most frequently associated with post-operative complications
- To describe patterns of multiple complications associated with surgical implants
- To estimate the incremental additional days of stay associated with complications of surgical implants
- To estimate the extent to which these are associated with ICU admission and inter-hospital transfers
- To identify the patient groups and procedure types most vulnerable to these complications
- To review the literature on approaches to reduce the rates of these complications.

**Skills:** The project will enable the student to gain skills in: secondary analysis of large hospital data sets (including data validation and cleaning), data linkage, descriptive statistics and multivariate linear and logistic regression. The student will develop an understanding of key concepts in clinical medicine.

**COLORECTAL MEDICINE AND GENETICS**

88. Bioinformatics in colorectal cancer genetics and prevention - also offered as MBiomedSc

**Supervisor:** Professor Finlay Macrae, Head, Colorectal Medicine and Genetics

**Project Site:** Royal Melbourne Hospital, Parkville

**Contact:** Tel: +61 3 9347 0788 Email: finlay.macrae@mh.org.au

**Project Description:** The Department manages a large registry of people at high risk of colorectal cancer, principally based on family history. The surveillance histories of 3000 registrants have been documented and related to their assessed level of risk. This database is now linked through the Australian BioGrid database initiative with the familial cancer database. Advanced front end enquiry facilities have been developed by BioGrid allowing data linkage and searching to be done with facility, and results displayed. A collaboration with the eHealth division of the CSIRO p-Health flagship furthers enhances our capacity to explore this dataset, including through after merging with a similar dataset housed at Flinders University. The project is now poised to deliver important information on differential surveillance outcomes across a range of familial and personal risk groups. Examples of hypotheses being explored locally are: What is the risk to children whose both parents have colorectal cancer? What is the yield of faecal occult blood testing done between scheduled...
colonoscopies in high risk patients? What are the molecular characteristics of cancers and advanced adenomas occurring during surveillance? Do patients with serrated adenomas have high risk for metachronous advanced adenomas and cancers? What are the surveillance outcomes from mismatch repair gene carriers, by gene type and mutation location?

89. **The Human Variome Project (HVP) and familial bowel cancer - also offered as MBiomedSc**

**Supervisors:** Professor Finlay Macrae, Head, Colorectal Medicine and Genetics, Professor Richard Cotton, Director, Genomic Disorders Research Institute, University of Melbourne

**Project Site:** Dept of Colorectal Medicine and Genetics, RMH; or GDRC, Alan Gilbert Building, Uni of Melb.

**Contact:** Tel: 61 3 9347 0788 E: Finlay.macrae@mh.org.au

**Project Description:** This important project forms a component of the HVP, which aims to document all DNA variants across all genes in man. The International Society for Gastrointestinal Hereditary Tumours is well advanced in formulating processes for the vision, with committees of experts worldwide working on different aspects. A range of Honours and higher degree opportunities are available within the HVP and InSIGHT’s engagement with the HVP. Its aims to position itself as a lead locus for the HVP.

90. **Biogrid and IBD data basing - also offered as MBiomedSc**

**Supervisor:** Professor Finlay Macrae, Head, Colorectal Medicine and Genetics

**Project Site:** Royal Melbourne Hospital, Parkville

**Contact:** Tel: +61 3 9347 0788 Email: finlay.macrae@mh.org.au

**Project Description:** The development of a common database for recording clinical management and outcomes for IBD clinics in Melbourne is being coordinated through the Department of Colorectal Medicine and Genetics. This project will bring students into close contact with the management of IBD, and working alongside a dedicated team of doctors and nurses focusing on IBD. The project will lead to linkage with other similar databases through the Australian BioGrid. [http://www.biogrid.org.au](http://www.biogrid.org.au)

91. **Capsule Colonoscopy as a Screen for Colorectal Cancer - also offered as MBiomedSc**

**Supervisor:** Professor Finlay Macrae, Head, Colorectal Medicine and Genetics, Dr Francesco Amico E: Francesco.Amico@mh.org.au

**Project Site:** Royal Melbourne Hospital, Parkville

**Contact:** Tel: +61 3 9347 0788 Email: finlay.macrae@mh.org.au

**Project Description:** Capsule Colonoscopy is being introduced into Australia late in 2010. After ingestion of the device, the colon is visualized through a wireless capsule CCD device which transmits images to a receiver worn by the patient. The Department will be the Australian lead in the first two Capsule Colonoscopy projects. One is testing its capability on comparison with colonoscopy in an average risk population, and the other will tests its capacity in clinical scenarios where colonoscopy is relatively contraindicated o has failed. Assistance in performing the procedures and documenting the results of the project will be the core of this project.

92. **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 & BMP1A, 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.

93. **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:** Professor 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).

94. **Dietary prevention of adenomas in familial adenomatous polyposis - also offered as MBiomedSc**

**Supervisor:** Professor Finlay Macrae, Head, Dr Suresh Sivanesan

**Project Site:** Royal Melbourne Hospital, Royal Brisbane, Royal Adelaide and Sir Charles Gardiner Hospitals

**Contact:** Tel: +61 3 9347 0788  E: finlay.macrae@mh.org.au

**Project Description:** This is a randomised controlled trial of a new resistant starch preparation capable of releasing large quantities of butyrate for chemoprevention in the colon. The trial will measure adenoma formation of FAP patients through their regular surveillance, comparing activity with placebo study agents. In partnership with CSIRO.

**ELECTROPHYSIOLOGY**

95. **Linking dementia and olfaction: nothing to sniff at**

**Supervisors:** Dr. Tara Bautista, Dr. Mathias Dutschmann

**Project Site:** Florey Institute of Neuroscience and Mental Health

**Contact:** tara.bautista@florey.edu.au or mathias.dutschmann@florey.edu.au

**Project description:** Dementia is the single greatest cause of disability in Australians over 65 years old. Recent data suggests that dementia-causing neuropathology starts within the brainstem, where it may subtly affect vital autonomic functions - much earlier than the onset of cognitive deficits. Olfaction is impaired during the early stages of dementia-related diseases. Olfaction is strongly linked to sniffing, an exploratory behaviour that utilises respiratory motor outputs that are normally controlled by brainstem neuronal circuits. Before we can understand how dementia-causing neuropathology affects sniffing and therefore olfaction, it is important to understand the basic neural circuitry that elaborates sniffing.

In this project, the aim is to elicit and characterise sniffing and other upper airway behaviours in the in situ preparation of rodents, a premier tool for studying central respiratory control. Techniques involved will include electrophysiology (nerve recordings) and immunohistochemistry

96. **Waiting to exhale: role of somatostatin in the central control of respiratory motor patterning**

**Supervisors:** Dr. Tara Bautista, Dr. Mathias Dutschmann, Dr. Davor Stanic

**Project Site:** Florey Institute of Neuroscience and Mental Health

**Contact:** tara.bautista@florey.edu.au or mathias.dutschmann@florey.edu.au

**Project description:** The motor act of breathing, or respiration, is a vital function that occurs more or less continuously throughout life. Previous research on the central control of respiration has primarily focused on elucidating the brainstem areas/mechanisms that are necessary and sufficient to generate respiratory rhythm. On the other hand, the equally important central mechanisms that shape and regulate respiratory motor patterning (depth of breathing, timing of inspiration/expiration, coordination of all respiratory motor outputs etc.) have received much less attention.

This project aims to identify brainstem sources of the neuropeptide somatostatin, which when injected into brainstem respiratory centres causes dramatic alterations in respiratory motor patterning, particularly of expiratory timing. Techniques involved will include immunohistochemistry and electrophysiology (nerve recordings) in the in situ preparation of rodents

97. **Investigating the mechanism of action of antipsychotic drugs 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; Prof Anthony Hannan E: anthony.hannan@unimelb.edu.au; Prof Terence O’Brien E: obrientj@unimelb.edu.au

**Aim of Project:** Studying neuronal activity in brain regions regulating aggression in the NL3 mouse model of Autism. Specifically, the project will investigate:
i. Changes in excitatory/inhibitory activity, and
ii. effects of antipsychotic drugs on network activity in brain slices.

Autism Spectrum Disorder (ASD) is a prevalent neurological disorder characterised by impairments in social interactions, communication, and repetitive behaviour. Aggressive behaviour is reported in 49-68% of ASD patients. Atypical antipsychotics such as risperidone are prescribed for children with ASD demonstrating aggressive behaviours. However, side effects are common and treatments are not effective for all patients. The mechanisms of action of risperidone are not well characterised.

NL3 mice express a mutation in the Neuroligin-3 gene identified in two brothers with autism. These mice show a robust aggressive phenotype which is reversed with risperidone treatment. To determine how risperidone affects neuronal activity, this project will examine the neurophysiology of specific brain regions involved in the neurobiology of aggression: i) the prefrontal cortex, ii) ventromedial hypothalamus (VMH), iii) basolateral amygdala, and iv) the periaqueductal 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.

98. 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.

99. 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
Website: http://sites.google.com/a/hfbg1.net/crf_lab/

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.

100. 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
Website: http://sites.google.com/a/hfbg1.net/crf_lab/

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.
ENDOCRINOLOGY, DIABETES & BONE DENSITY

101. Assessment of the effect of ankle arthrodesis on muscle and bone function using an integrated experimental and computational approach– also offered as MBiomedSc

Supervisors: A/Prof Christine Rodda and A/Prof Peter Pivonka
Project Collaborators: A/Prof Peter Lee
Project Site: NWAC, Sunshine Hospital, St Albans
Contact: Dr Christine Rodda, Tel: 8395 8161; email: christine.rodda@unimelb.edu.au

Project description: Ankle arthrodesis is the fusion of the ankle joint in patients with severe ankle arthritis that leads to a significant reduction in joint flexibility and stability. While this orthopaedic surgical procedure is very effective for pain relief and joint stability only a limited amount of data is available on the functional outcomes of this procedure on muscle and bone. Some of the observed intermediate and long-term effects are reduction of muscle strength (e.g., calf muscle) and stress fractures in the tibia and fibula. In order to address this problem we will apply an integrated experimental and computational approach to quantitatively assess the functional outcomes of ankle arthrodesis on muscle and bone. We plan to recruit 30 adult patients who have undergone ankle fusion at least 2 years previously, from a single orthopaedic surgeon. In order to assess muscle function we will use gait analyses and metatarsal pressure analyses. To assess bone changes we will collect regional DEXA (dual energy X-ray absorptiometry) bone density and peripheral QCT (quantified computerised tomography) measurements of the affected tibia and compare these with the control group. Calf muscle bulk on affected and unaffected sides will also be assessed using pQCT. Data from the gait analyses will be used for a musculoskeletal model of the lower limb (using OpenSim i.e. an open source software to simulate dynamic human movement developed in Stanford University) in order to quantify muscle strength and muscle activation patterns. Using the obtained muscle forces together with the bone material properties (from pQCT) we can calculate the mechanical stress distribution in the tibia. The magnitude of stresses together with the frequency of loading will serve as an indicator of the risk of stress fracture. Findings from this study will enable us to anticipate and inform the intermediate and long-term local musculoskeletal sequelae of ankle arthrodesis, and form the basis for future intervention studies.

EPILEPSY AND NEUROPHARMACOLOGY

102. Fracture Risk in Epilepsy – Investigating Actions of Anti-epileptic Medications on Osteoblast Ion Channels – ONLY available for MBiomedSc

Supervisors: Dr. Sandra Petty, Dr. Carol Milligan and A/Prof. Steven Petrou
Project Site: The Florey Institute of Neuroscience & Mental Health, Division of Epilepsy, Kenneth Myer Building
Contact: Steve Petrou spetrou@unimelb.edu.au; pettys@unimelb.edu.au
Phone: +61 3 8344 1957

Project description: Patients with epilepsy have at least double risk of fractures. The underlying mechanisms for this increase in fracture risk require further investigation, in particular whether there is a side effect of anti-epileptic medication (AEM) which may alter signaling in bone. Most AEMs act directly or indirectly upon ion channels for their anti-convulsant effect. Ion channels are also present in types of bone cells, and therefore these channels may be modulated by AEMs. In this MSc project, the student will undertake laboratory research using techniques including performing mouse primary calvarial osteoblast digests, immunohistochemistry, PCR and patch clamping on the Patchliner System to examine for presence of ion channels and action of AEMs upon these channel in osteoblasts.

103. 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.
104. 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.

105. Modelling Epilepsy and Epilepsy Drug Effects–Computational Neuroscience Project
Supervisor: Dr Chris French
Project Site: Department of Medicine, MBC Neurosciences Building, Parkville
Contact: Chris French 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.

106. 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 student will be involved in recruiting and following up eligible patients. Basic knowledge and skills in biostatistics is preferred

107. 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.
108. Development and validation of clinical assessment tools for population genetic studies of epilepsy in rural China
- also offered as MBiomedSc
Supervisor: Professor Patrick Kwan
Project Site: Department of Medicine (RMH)
Contact: Professor Patrick Kwan, Departments of Medicine and Neurology,
E: patrick.kwan@unimelb.edu.au

Project description: Affecting up to 1% of the population, epilepsy is the most common chronic neurological disorder. Twin and family studies suggest that epilepsy is highly heritable but its genetic architecture in most patients remains unknown. Using a genome-wide association study (GWAS) approach that compared the frequencies of over 400,000 common single nucleotide polymorphisms (SNPs) across the genome between cases and controls, we have identified potential SNPs predisposing to epilepsy in Han Chinese in Hong Kong. These SNPs will be tested in an additional 2000 epilepsy patients recruited in rural China.

This honours project will analyse the clinical and genetics data to determine the validity of the phenotyping, and to identify significant SNPs associated with epilepsy in this largest Han Chinese cohort ever studied. The project is suitable for students with background in mathematics/statistical genetics/bioinformatics.

109. Investigations into the role of neuropeptide y in a genetic rat model of absence epilepsy - also offered as MBiomedSc
Supervisor: Dr Kim Powell, Prof Terence J O'Brien, Prof Margaret Morris
Project Site: Department of Medicine and Department of Pharmacology, University of New South Wales.
Contact: Dr Kim Powell T: 9035 6394 E: kpowell@unimelb.edu.au
Prof Terence J O'Brien T: 8344 5479 E: obrientj@unimelb.edu.au
Professor Margaret Morris E: m.morris@unsw.edu.au

Project Description: Absence epilepsy is one of the most common idiopathic generalised epilepsy syndromes. The underlying neurophysiological correlate of absence epilepsy is a pathological activation of rhythmic thalamocortical activity. However, the underlying aetiology for this disorder is still unknown.

There is increasing evidence that neuropeptide Y has a role in modulating seizures in acquired focal epilepsies, however there has been little investigation of its possible role in generalised epilepsy syndromes.

This study will investigate the effect of intracerebral microinfusions of neuropeptide Y into selected intracerebral thalamocortical brain regions on the number and total duration of absence seizure in the Genetic Absence Epilepsy Rats of Strasbourg (GAERS) model. Absence seizures will be quantified on the basis of the SWDs recorded on EEG for 90 minutes following the infusion. The effect of infusion antagonists and agonists of various neuropeptide Y receptors will also be evaluated.

The second stage of the project will investigate the effect of enhancing NPY expression focally in selected thalamocortical using an recombinant adenosivus viral vector.

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

110. 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.
111. Epigenetic regulation of gene expression in epilepsy - also offered as MBiomedSc

Supervisors: Dr Nigel Jones, Dr Kim Powell
Project Site: Department of Medicine, MBC Neurosciences Building, Parkville.
Contact: Dr. Nigel Jones T: 9035 6402 E: nncjones@unimelb.edu.au
Dr. Kim Powell T: 9035 6394 E: kpowell@unimelb.edu.au

Background: Epigenetics describes the way chromatin/DNA structure can influence gene expression. This field of molecular biology is well-advanced in organism development and in cancer research, but has received little to no attention with respect to neurological conditions such as epilepsy, despite compelling reasons to suggest it is involved. Changes in gene expression are heavily implicated in the disease process of epilepsy (referred to as epileptogenesis) which turns a normal healthy brain into an epileptic brain, and epigenetic mechanisms are strong candidates to mediate such gene expression changes. This program seeks to investigate epigenetic changes associated with epilepsy to determine whether such modifications in chromatin structure contribute to epileptogenesis. Using animal models of epilepsy and human patient brain samples, several projects, available as Honours, Masters or PhD projects, are exploring this hypothesis:

Research project 1: Characterisation of DNA methylation changes in epilepsy
Using genome-wide and gene specific approaches, this project will characterise the changes in DNA methylation which occur during the course of epilepsy development, and in chronic disease. For this, we will use tissue from animal models, and also surgically resected brain tissue from epilepsy patients.

Research project 2: Epigenetic signatures in blood as biomarkers of disease.
The potential to predict the onset of disease, and to map disease trajectory would have far-reaching implications for neurological disorders, including epilepsy. This project will attempt this by comparing epigenetic marks after brain injury in inflammatory genes from blood-derived T cells and brain cells. We will also take serial blood samples and examine these same marks over time in their ability to predict the onset and severity of the epilepsy.

Research project 3: Pharmacological inhibition of epigenetic machinery and the development of disease
This project will use well-established inhibitors of DNA methylation to prevent the aberrant changes in DNA methylation after epileptogenic brain injury. We will then assess the ability of these interventions to block the development of epilepsy.

Research project 4: Viral-mediated manipulation of epigenetic machinery and the development of disease
This project will use lentivirus technology to down-regulate genes which are involved in catalysing DNA methylation. We will inject these viruses into brain, and assess whether changing expression of such epigenetic modifiers can interfere with the development and severity of epilepsy.

Skills: Small animal handling; animal models of epilepsy; small animal surgery and EEG recording; experience with lentiviral constructs; techniques specific for epigenetic analysis, including bisulfite conversion, pyrosequencing, Methyl-DNA immunoprecipitation, allelic sequencing, and other molecular biology techniques, such as real-time qPCR, Western blotting, gel electrophoresis.

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

Supervisors: Dr Kim Powell, Professor Terence O’Brien
Project Site: Department of Medicine (RMH), MBC Neurosciences Building, Parkville
Contact: Dr. Kim Powell T: 9035 6394 E: kpowell@unimelb.edu.au
Professor Terence O’Brien T: 8344 5479 E: obrientj@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 TARPs 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 postsynaptic 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).

113. **Dynamin activation in acute epileptic seizures and chronically epileptic rats** - *also offered as MBiomedSc*

**Supervisors:** Dr Nigel Jones, Dr Caroline Ng, Professor Terence O’Brien, Prof Phil Robinson (University of Sydney)

**Project Site:** Department of Medicine (RMH), MBC Neurosciences Building, Parkville

**Contacts:** Dr Nigel Jones T: 9035 6402 E: ncjones@unimelb.edu.au
Dr Caroline Ng T: 9035 6445; Professor Terence O’Brien T: 8344 5479 E: obrientj@unimelb.edu.au.

**Project Description:** The Epilepsy and Neuropharmacology Research group is currently investigating novel anti-epileptic drugs that act to inhibit dynamin. This protein is critical to the rapid recycling of synaptic vesicles required for excessive neurotransmitter release that occurs during epileptic seizures. Dynamin activation is regulated through calcium-dependent dephosphorylation of key serine residues in the protein’s C-terminal region. Using mass spectrometry techniques, it is possible to determine the extent to which dynamin is phosphorylated at these different residues. In this way, the activation of dynamin can be assayed.

A group of compounds have proved effective as dynamin-inhibiting agents in the *in vitro* models of our collaborators at the Children’s Medical Research Institute (Westmead, NSW) but have failed to reduce seizure severity in our epilepsy models. This project aims to determine whether putative dynamin-inhibiting drugs have any effect on the activation of dynamin *in vivo*, both in non-seizing but chronically-epileptic rats, and during acute epileptic seizure. This will be carried out by preparing synaptic subcellular fractions from different brain regions from drug-treated and non-drug treated epileptic rats, purifying the dynamin from these fractions and quantifying the level of (de)phosphorylation to determine the level of activation of dynamin.

Specifically, this project will entail

- inducing epilepsy in rats through daily electrical stimulation of the amygdala (the Amygdala-kindling model of acquired epilepsy)
- treating the epileptic animals with drugs that inhibit dynamin *in vitro*
- preparing *synaptosomes* from the amygdala, hippocampus and cerebral cortex of drug treated and control epileptic animals; synaptosomes are isolated presynaptic terminals capable of neurotransmitter release *in vitro*
- purifying dynamin from these synaptosomes using GST-pulldown techniques
- quantifying the phosphorylation of the dynamin purified in this way

Skills: The skills expected to be learnt in this project include small animal handling and neurosurgery (*electrode implantations, kindling, drug treatments*); biochemical subcellular fractionation (*preparation of synaptosomes*); protein purification (*GST-pulldowns, large format SDS-PAGE protein gels*); understanding of trypsin digestion and *mass spectrometric analysis of phosphoproteins and phosphopeptides*.

114. **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, Professor 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 double 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.

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**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, Professor 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:** 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 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 ion channels are an attractive candidate for investigating molecular mechanisms of SUDEP. Our research has identified a cardiac transcriptional channelopathy of HCN2 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 and epigenetic mechanisms contributing to the epilepsy-induced HCN2 transcriptional repression.

**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 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).
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.

116. Projects in network analysis of genetic epilepsy

Supervisors: A/Professor Steve Petrou & A/Professor Chris Reid
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; Chris Reid E: careid@unimelb.edu.au

Project description: Epilepsy impacts around 3% of the population and in many cases has clear genetic underpinnings. Our laboratory has created several genetically engineered models of epilepsy that have helped provide the most detailed understanding of how a single gene mutation can lead to behavioural seizures. Perhaps the largest gap in our understanding lies at the level of the network that bridges cellular and synaptic function with the actual seizure phenotype itself.

117. Multi-site patch clamp recording of cortical micro networks

Supervisors: A/Professor Steve Petrou & A/Professor Chris Reid
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; Chris Reid E: careid@unimelb.edu.au

Project description: In this project the candidate will be trained in the use of an emerging method in brain slice electrophysiology that allows for the simultaneous intracellular recording of 4 connected neurons. Using this recording mode it is possible to examine how neurons function in coupled micro networks in epileptic and normal brains to lead to a deeper understanding of the functional basis of epilepsy. If the candidate makes sufficient progress and is motivated this project may also expand into network analysis using multiphoton imaging where 50 or more neurons in a living brain can be labelled with a Ca²⁺ indicator dye and imaged in real time.

118. High density multi-electrode array recording of in vitro networks in epilepsy

Supervisors: A/Professor Steve Petrou, A/Professor Chris Reid
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; Chris Reid E: careid@unimelb.edu.au

Project description: In this project the candidate will use high density extracellular multielectrode array recordings to investigate large scale network function. This a level of organization beyond that studied in Project 1 and will reveal fundamental properties of how the hippocampal and thalamocortical networks are altered in genetic models of epilepsy. The goal of these studies is to not only understand more about the neurobiology of epilepsy but also to create novel disease state models for creating anti-epileptic drugs. The method will involve cutting fresh brain slices and using 60 site multi-electrode arrays that enable electrical stimulation and recording from all sites simultaneously. Slices will be subject to various stimulation and pharmacological protocols to reveal aspects about excitability, synaptic transmission and plasticity.

119. In vivo electrophysiological analysis in mouse models of genetic epilepsy

Supervisors: 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

Project description: In this project the candidate will use multi-site in vivo unit recording in mouse models of genetic epilepsy to investigate network function and dysfunction in freely moving mice. Using digital high density electrode recording the candidate will implant multiple sites and then record from mice housed in a controlled environment with video monitoring. One possible addition to these experiments is the incorporation of optogenetic stimulation whilst recording to probe network function in connected networks of behaving mice. This will provide some of the first views into how real time intervention of networks modulates seizure initiation and termination.
120.  “CLARITY” based glass brain imaging in health and disease  
Supervisors:  A/Professor Steve Petrou, Dr Verena Wimmer, Dr Kay Richards  
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;  
Project description:  Recent improvements in the histochemical method of optically clearing whole tissues and the joint development of special optics that can image deep into them have created unprecedented views into the wiring of networks. Changes in wiring of cortical neurons have been implicated in a number of disorders such as epilepsy, schizophrenia and depression. In this project the candidate will prepare brains from mice with fluorescently labelled neurons and use 2-photon excitation or custom light sheet based microscopy to create 3D images in regions of the mouse cortex. 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.

121.  MRI tractography in mouse models of genetic epilepsy: Creation of prognostic and diagnostic structural biomarkers  
Supervisors:  Dr Kay Richards, A/Professor Chris Reid, Professor Alan Connelly, A/Professor Fernando Calamente, 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;  Kay Richards  E: kay.richards@florey.edu.au  
Project Description:  Our earlier classical histological analyses have shown that neuronal numbers and positioning are both altered in genetic forms of epilepsy prior to the appearance of overt seizures suggesting that structural changes precede epilepsy. These changes, however, would be below the level of detection of current clinical MRI scanning technology and have led to the potentially erroneous conclusion that idiopathic generalised epilepsy (IGE) is characterised by a complete absence of structural change. By combining recent developments in super resolution MRI (developed by members of the supervisory team) and high field MRI acquisition (16.4T) the candidate will seek to reveal structural changes, or biomarkers, that precede or are a consequence of epilepsy. Because these approaches are directly translatable into the clinic any finding could be rapidly tested in patients. The candidate will develop skills in preparing fixed mouse brains for MRI scanning at 16.4T at the Queensland Brain Institute for analysis using the MRtrix suite of software on a custom workstation to compare brains from control and genetic mouse models.

122.  High content automated analysis of ion channels in epilepsy  
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:  Discovery of gene mutations in neurological disorders such as epilepsy is outstripping the ability to functionally validate them. Because many epilepsy genes code for ion channels we have established high content automated patch clamp platforms based on the Nanion Patchliner 16 and the Fluxion HT 64 systems to bridge the "discovery" gap between genetics and functional validation. Several new mutations have been found by our geneticist collaborators that are awaiting detailed functional analysis and the candidate will first have to produce mutant cDNAs then transiently transfected into HEK293 or CHO 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.

123.  Optogenetic modulation of the area tempestas – an epilepsy hot spot  
Supervisors:  Kay Richards, A/Professor Steve Petrou, A/Professor Chris Reid  
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;  Kay Richards  E: kay.richards@florey.edu.au  
Project description:  Several lines of study have recently converged to reveal a new target for controlling epileptic seizures. Early work by Piredda and Gale (Nature 1985, 317:623) provided unequivocal evidence that the prepiriform cortex, subsequently coined the “area tempestas”, was a hot spot for initiation and spread of epileptic seizures. Within this region a population of specialised inhibitory neurons called neurogliaform cells (NG) shows a stereotypic pattern of firing that implicates them seizures. In this project the candidate will use in vivo electrophysiological recording and optogenetic stimulation to examine real time modulation of the control of seizures to develop a role for the in vivo function of NG cells and explore their potential utility in seizure suppression.
124. Zinc and seizures  
Supervisors: A/Prof Chris Reid, A/Professor Steve Petrou, Dr Paul Adlard 
Project Site: Florey Institute of Neuroscience & Mental Health, Division of Epilepsy, Kenneth Myer Bldg 
Contact: Chris Reid E: christopher.reid@florey.edu.au / careid@unimelb.edu.au 
Project description: Zn$^{2+}$ is an essential element having a multitude of biological functions throughout the body. Febrile seizures are common affecting approximately 3% of children. There is good evidence that febrile seizures can trigger a cascade of events that lead to more severe forms of epilepsy later in life. Clinically, several studies have suggested that Zn$^{2+}$ levels are significantly lower in blood and CSF of children that suffer febrile seizures but these studies are not conclusive. In this project we will directly test the hypothesis that low brain Zn$^{2+}$ may be one environmental factor in increasing the chance of having a febrile seizure. In this project the student will learn a range of experimental techniques aimed at understanding the role Zn$^{2+}$ plays in changing neuronal excitability. The results have clear clinical implications and could be particularly important in for developing countries, where epilepsy rates are high and nutritional supplementation is a potential practical therapy.

125. Will HCN channel antagonists be good antiepileptic drugs?  
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: Our laboratory has discovered that some antiepileptic drugs act on certain HCN channel subtypes. We now need to address whether this mechanism is part of the anti-seizure effect of these drugs. In this project we will use a combination of selective HCN subtype-selective channels in a variety of seizure models to establish this. We will also extend the project to look specifically at mechanisms using electrophysiological methods that directly measure neuron excitability. Establishing if these channels are good targets will motivate drug discovery programs. These channels are also thought to be important to the generation of pain and may be useful in this condition as well.

126. Inhibitory neuron subtypes in cortical circuits: an examination of their structure, function, and connectivity  
Supervisors: Verena C Wimmer, Kay Richards, Steven Petrou, Ion Channels and Disease Group, Florey Neuroscience Institutes, The University of Melbourne, Parkville, 3010. 
Project Site: Florey Neuroscience Institutes, The University of Melbourne, Parkville. 
Contact: Verena Wimmer E: vwimmer@florey.edu.au 
Project 1: In the brain there are numerous subtypes of inhibitory neurons with specific functions and connectivity. While some of these subtypes are well understood the role of others remains enigmatic, for example VIP (vasoactive intestinal polypeptide) expressing GABAergic neurons. Using a mouse model expressing a fluorescent protein in VIP-positive neurons and quantitative anatomy approaches we will study the distribution of VIP-cells throughout the brain, their morphology and examine the ion channel composition that governs the function of those cells. We aim to develop a better understanding of the neuronal circuits VIP neurons are involved in and generate a testable model of input integration. Methods include immunohistochemistry, state-of-the-art confocal microscopy, mosaic imaging and automated analysis of large data sets.  
Project 2: Historically, some epilepsy syndromes have been defined as ‘idiopathic’ or ‘of unknown origin’, because the anatomy of the brain seems normal. Our group has recently shown that genetic ‘idiopathic’ epilepsy mutations impact the formation of neuronal networks during embryonic development and lead to microscopic changes in the wiring of the cortex, specifically affecting inhibitory neurons. This project looks at the exact changes in synaptic connectivity and aims to quantify the synaptic contacts made between parvalbumin-positive inhibitory neurons and excitatory neurons across the cortical layers in normal and epileptic mice. These results will greatly aid our understanding of how epileptic seizures develop and reveal novel mechanisms by which genetic mutations lead to long term changes in the brain of epilepsy patients. Methods include immunohistochemistry, state-of-the-art high resolution confocal microscopy and super-resolution techniques as well as deconvolution and automated analysis of large data sets.

127. Identification of serum glycoproteins inhibiting innate immunity - also offered as MBSc  
Supervisors: Dr Ben Gu, Professor James Wiley 
Project Site: Ion channel & Human Disease, Florey Neuroscience Institutes, Level 1, Kennenth-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.
128. How does the brain remove the excess number of neurons during development and aging - also offered as MBSc

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.

129. The nature of the P2X4 receptor - also offered as MBSc

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: The P2X4 receptor is a two trans-membrane ion channel activated by ATP. It is highly expressed on monocytic lineage cells (monocytes, macrophages and microglia) and certain neuronal cells and has been shown to play an important role in neuropathic pain. However, the cellular traffic of this receptor and its co-associated molecules is unclear. This project will use anti-P2X4 monoclonal antibody to examine the surface and intracellular expression of P2X4 in different cells, and identify the possible membrane complex associated with P2X4. The result could help to better understand this receptor and its role in neuropathic pain.

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

130. Search the P2X7 related biomarkers for Alzheimer’s disease? - also offered as MBSc

Supervisors: Dr Ben Gu, Dr. Alan Rambach, 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 Alan Rambach E: a.rembach@unimelb.edu.au James Wiley E: james.wiley@florey.edu.au

Project description: Alzheimer’s disease is an age-related dementia with major impact in people aged 60 or over. Typical symptoms including memory loss and cognitive impairment but the pathogenesis is unclear and treatment options are limited. Recent evidence suggests the P2X7 receptor may be involved in the pathogenesis of this disease. This project will study the peripheral blood cells obtained from Alzheimer’s disease patients, subjects with minor cognitive impairment and age matched healthy controls. The P2X7 expression and function on mononuclear cells and various phenotyping and serological assays will be performed. The diagnostic and prognostic values of P2X7 expression and function will be evaluated. This work may provide a useful biomarker for the diagnosis and prognosis of Alzheimer’s disease, as well as the possible pathogenesis mechanism.

Techniques involved are flow cytometry, ELISA and cell culture.

131. The role of P2X7 in a mouse model of oligodendrocyte apoptosis - also offered as MBSc

Supervisors: Dr Ben Gu, Dr. Tobias Merson, 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 Tobias Merson E: tmerson@unimelb.edu.au James Wiley E: james.wiley@florey.edu.au

Project description: Oligodendrocytes support the function of nerve cells by producing a fatty substance called myelin that insulates the axons of nerve cells, much like plastic insulation around an electricity cable. Dying (apoptotic) cells are normally cleared from the brain by specialised scavenger cells called microglia that engulf and digest them. Previous studies of our group have shown that the P2X7 protein found on the surface of these scavenger cells recognizes the dying cells and helps their engulfment. If dying cells are not removed, they leak molecules causing inflammation of the brain, which worsens symptoms of neurological disorders. It appears that P2X7 is important in limiting the extent of this
neurodegeneration in MS since genetic variations in P2X7 in humans can confer either an increased risk or protection against developing MS. In this project, we will investigate the role of P2X7 in regulating the ability of microglial to remove dying oligodendrocytes from the brain using an established mouse model. The results will provide insight on the role that P2X7 plays in orchestrating the inflammatory response to oligodendrocyte death. This knowledge will aid in our long-term goal of developing methods to protect neurons from permanent damage.

Techniques involved are small animal handling, tissue collection, immunohistochemical staining, cell culture, flow cytometry.

132. **Identify the transcriptional regulatory factors of the P2X7 receptor - also offered as MBSc**

**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 chromatin-immunoprecipitation, as well as cell culture, flow cytometry.

**IMAGING**

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: frenche@unimelb.edu.au

**Website:** [http://sites.google.com/a/hfbg1.net/crf_lab/](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-sensitive 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 electrophysiological 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.

INFECTIONOUS DISEASES AND IMMIGRANT HEALTH

135. 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 quantitatively, disease burdens and the provision of services to address these needs, with a view to reports for Faculty, the Gastroenterological Society of Australia, the World Gastroenterology Organization and the Australian Government (AusAid).

INJECTING DRUG USE

136. 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: pauld@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.

137. Mapping public injecting drug use in urban Melbourne - also offered as MBiomedSc
Supervisor/s: Paul Dietze, Rebecca Winter, Peter Higgs

Project Site: Burnet Institute, 85 Commercial Road, Melbourne
Contact: Paul Dietze  E: pauld@burnet.edu.au; Peter Higgs  E: peterh@burnet.edu.au

Project Description: The risks associated with injecting drug use are determined by interactions between individual injecting behaviours and the ‘environment’ (e.g., physical, social, legislative) in which injecting occurs. Using a mixed methods approach, this project will undertake ethnographic mapping and quantitative secondary data analysis to document aspects of public injecting drug use in inner urban Melbourne. The ethnographic mapping exercise will involve neighbourhood-level observational research to examine sites of public injecting, levels of public injecting and document associated injecting practices and potential risks. Additional secondary data analysis will be undertaken to examine indicators of the impacts of public injecting, such as fatal and non-fatal overdose and impacts on public amenity.

138. The experiences of people who inject drugs transitioning from prison into the community
Supervisors: Ass. Prof Mark Stoove; Prof Paul Dietze

Project Site: Burnet Institute, 85 Commercial Road, Melbourne
Contact: Mark Stoove  E: stoove@burnet.edu.au, Paul Dietze  E: pauld@burnet.edu.au

Project description: People who inject drugs (PWID) are vastly over-represented in Australian prison populations and experience extremely high rates of re-incarceration. The immediate post-release period is a particularly vulnerable time for PWID that is characterised by a return to crime, including problematic patterns of drug use, unstable accommodation and a range of psych-social outcomes that act as barriers to successful reintegration and the avoidance of recidivism and re-incarceration.

This project will use data from Australia’s largest and most significant cohort study of the experiences of PWID following release from prison. Quantitative data from a large sample of prisoners with histories of injecting drug use collected both
pre-release and in the months following release from prison will be available to answer a range of questions relating to reintegration into the community. Opportunities will be available for students to engage directly in data collection and to examine epidemiological data to inform policy and practice at a time of rapidly expanding rates of incarceration in Victoria.

139. Factors impacting on the potential for HIV Treatment-as-Prevention to reduce transmissions in Victoria

   Supervisors: Ass. Prof Mark Stoové; Prof Margaret Hellard; Dr James McMahon  
   Project Site: Burnt Institute  
   Contact: Mark Stoove E: stoove@burnet.edu.au, Margaret Hellard E: Hellard@burnet.edu.au  

Globally, the control of HIV has entered a new era of combination prevention, in which biomedical prevention approaches are increasingly prominent. In Australia, treatment-as-prevention – where individuals are encouraged to commence HIV therapy as early as possible to achieve reduced viral load and subsequent reductions in the transmissibility of HIV to others – has received particular attention as a strategy to reduce the record high numbers of HIV notification currently being reported. Recent policy changes to facilitate early commencement of HIV therapy have been introduced in Australia to support HIV prevention.

This project will use an array of disease surveillance, clinical and epidemiological data to examine trends in HIV testing, diagnosis, referral to care and treatment commencement, alongside data on gay community attitudes to HIV treatment-as-prevention. The focus of this study will on the examination of local trends in HIV treatment commencement, factors associated with these trends and the potential barriers and facilitators to the success of treatment-as-prevention approach to HIV in Australia.

140. Understanding and reducing the barriers to community based point of care hepatitis C testing in people who inject drugs

   Supervisor/s: Margaret Hellard  
   Project Site: Burnet Institute, 85 Commercial Road, Melbourne  
   Contact: Margaret Hellard E: Hellard@burnet.edu.au T: +61 3 9282 2163  

Project description: Hepatitis C infection predominately infects people who inject drugs with around 50% becoming infected within five years.

Surprisingly, despite this high risk of infections, there are no Australian guidelines on how frequently PWID should be tested. Also there are many barriers to PWID being tested for HCV including limited engagement with health services due to stigma and discrimination and the lack of a licensed rapid point of care HCV test in Australia despite them being available elsewhere in the world.

This means that many people infected with hepatitis C may have their diagnosis delayed. If someone is not aware of their infection they are a) at greater risk of accidently transmitting the infection to other and b) delaying their presentation for hepatitis C care and treatment.

This project will identify the best rapid-point of care HCV tests available and licensed world-wide. It will also examine PWIDs attitudes to rapid point of care tests administered in the community by peers or outreach workers or that are self-administered test.

This will be a qualitative research study where the student will conduct an estimated 20 to 30 interviews with PWID about their attitudes and understandings of HCV point of care tests. As well they will interview key informants from key community based organisations - Harm Reduction Victoria and Hepatitis Victoria.

The student will also review the gray and standard literature to identify jurisdictions that have implemented community based point of care testing for HCV. They will also examine the legislative barriers to making these tests available in Australia.

141. The impact of new and highly effective treatment for hepatitis C on injecting risk behavior in people who inject drugs

   Supervisor/s: Margaret Hellard  
   Project Site: Burnet Institute, 85 Commercial Road, Melbourne  
   Contact: Margaret Hellard E: Hellard@burnet.edu.au T: +61 3 9282 2163  

Position description: People who inject drugs (PWID) are at high risk of hepatitis C infection. The evidence suggests that many PWID reduce their injecting risk behavior following hepatitis C treatment using the current therapies (pegylated interferon/ribavirin +/- telaprevir/boceprevir) which have significant side effects and require 24 to 48 weeks of treatment. Some people believe that PWID reduce their injecting risk behavior due to reluctance to go through treatment again if they became re-infected because treatment was so difficult.
New highly effective and tolerable treatments for hepatitis C infection (DAAs) will become available in Australia in the next few years. There is concern that PWID will be less fearful about retreatment and therefore not alter their injecting behavior leading to high levels of hepatitis C reinfection.

This is a concern because the new treatments will be very expensive - it is estimated that a course of treatment will be around $80,000. This study will compare injecting risk behaviours in a PWID following treatment with pegylated interferon/ribavirin +/- telaprevir/boceprevir with PWID following treatment with DAAs using data from historical cohorts.

142. The feasibility of paying people who inject drugs a modest financial incentive to remain free of hepatitis C (HCV) infections - also offered as MBiomedSc

Supervisor/s: Margaret Hellard, Mark Stoové

Project Site: Burnet Institute, 85 Commercial Road, Melbourne

Contact: Mark Stoove E: stoove@burnet.edu.au; Margaret Hellard E: Hellard@burnet.edu.au

Project Description: The predominant blood borne virus (BBV) transmitted through injecting drug risk practices in Australia is hepatitis C (HCV) and it leads to substantial morbidity and mortality in people who develop chronic infection. There are currently no vaccines for these infections, and whilst treatments are improving, prevention of transmission in people who inject drugs (PWID) remains vitally important. Various education and behavioural interventions have been trialled but to date no-one has provided a financial incentive to PWID to remain HCV free.

This project will explore the feasibility of providing a financial incentive to current PWID who have not been exposed to HCV to remain HCV free. It will also explore what would be considered a reasonable incentive to ensure PWID remain HCV free. A series of focus groups and one on one interviews will be conducted with current PWID, community based organisation representing PWID and relevant government officials.

143. Risk environments and injecting drug use – the impact of CCTV - also offered as MBiomedSc

Supervisor: Dr Mark Stoove, Head, Head of HIV, AIDS and STI Research, Centre for Population Health, Burnet Institute

Project Site: Burnet Institute

Contact: stoove@burnet.edu.au

Project Description: The risks associated with injecting drug use are determined by complex interactions between individual behaviours, drug using networks, socio-political influences, legislative responses and service provision. These factors combine to create an overall risk environment for people who inject drugs that mediate blood borne virus transmission, overdose risk, the frequency of drug use and other injecting drug related outcomes. This project offers an opportunity to examine risk environments for injecting drug use from a public health, epidemiological and/or policy perspective, in the context of the introduction of closed circuit television (CCTV) monitoring systems in key locations. Depending on the epistemological approach, this study will involve a combination of document review, media analysis, secondary data analysis, and primary quantitative and qualitative data collection from people who inject drugs and other key stakeholders.

144. Barriers to successful reintegration among people with a history of injecting drug use transitioning from prison to the community - also offered as MBiomedSc

Supervisor: Dr Mark Stoove, Head, Head of HIV, AIDS and STI Research, Centre for Population Health, Burnet Institute

Project Site: Burnet Institute

Contact: stoove@burnet.edu.au

Project description: Although release from prison is a challenging and particularly vulnerable period for people with a history of injecting drug use, this transition also offers opportunity for intervention and support. This Honours project will involve a targeted epidemiological examination of health and social outcomes among a cohort of people who inject drugs recently released from prison. Individual and structural barriers and facilitators related to successful reintegration outcomes (e.g., avoidance of problematic drug use and recidivism, stable accommodation, accessing drug dependence treatment, supportive social relationships) will be examined.

145. Who’s talking about whom? An evaluation of techniques used to match individuals who inject drugs who have named each other in a research study - also offered as MBiomedSc

Supervisor: Professor Margaret Hellard, Head, Centre for Population Health, Burnet Institute

Project Site: Burnet Institute

Contact: Hellard@burnet.edu.au

Project Description: The Networks Study aims to understand how hepatitis C is transmitted between people who inject drugs (PWID) by modelling the structure of the injecting network. We have collected five years of social network data from PWID including first names, nicknames and some other characteristics of the people with whom participants inject
drugs. A number of links have been made between named injecting partners and study participants but some may have been missed and multiple participants may have named the same partners who have not been recruited into the study.

This project aims to identify more matches using (a) traditional probabilistic matching techniques, (b) a technique that explicitly accounts for whether the participants have other common injecting partners? What is the influence of the additional matches on the structure of the social network? Is the second technique biased because it assumes social clustering and what are the implications of this for social network analysis?

146. A systematic review of the structural features of injecting networks - also offered as MBiomedSc

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

Project Description: Hepatitis C and other blood-borne viruses are transmitted through sharing needles and other injecting equipment. These risk behaviours are embedded in social relationships but there is little known about the types and structures of social relationships in which these behaviours take place. A number of empirical studies have been conducted of injecting networks. This study would involve systematic searches of scientific literature in order to identify published empirical injecting networks, characterising common structural features of injecting networks (if these exist), and describing how these injecting networks differ from other types of contact networks.

INNATE IMMUNITY AND HOST DEFENCE

147. Immune Cell Signalling Regulation During Inflammation

Supervisors: Dr Paul Licciardi and Dr Rodney Luwor
Location: Murdoch Childrens’ Research Institute, The Royal Children’s Hospital and Dept of Surgery,
Level 5, Clinical Sciences Building, Royal Melbourne Hospital
Contact: Dr Paul Licciardi; T: 9345-5554, E: paul.licciardi@mcri.edu.au or 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.

MALARIA

148. Malaria parasite adhesion to the human placenta - also offered as MBiomedSc

Supervisor: Dr Philippe Boeuf
Project Site: Department of Medicine (RMH), Peter Doherty Institute
Contact: Dr Philippe Boeuf T: 8344 3263 E: pboeuf@unimelb.edu.au

Project Description: Pregnant women are more susceptible to malaria infection than their non-pregnant peers. This is thought to be due to the adhesion of malaria parasites to the placenta, triggering pathways leading to low birth weight. A better understanding of the mechanisms of malaria parasite adhesion to the human placenta would allow for the design of intervention strategies, including a vaccine. In this project, you will use placentas from women delivering at the Royal Women’s Hospital as a matrix for malaria parasite adhesion. By studying the adhesion of various parasite lines under different experimental conditions, you will gain insights in the characteristics of this adhesion.
This project is based at the Department of Medicine, Royal Melbourne Hospital, in the malaria lab that has a long-term experience of malaria parasite adhesion. The lab is made of 1 lab head, 3 post-docs (including your supervisor), 2 research assistants, 6 PhD students and 2 mid-term honour students as well as visiting scientists from all over the world. Techniques involve (but are not limited to): malaria parasite culture, biochemistry, flow cytometry, confocal microscopy and western blotting.

149. Cross reactive antigens expressed in severe malaria

Supervisors: Dr Michael Duffy
Project Site: Department of Medicine (RMH), Peter Doherty Institute, Cnr Grattan St and Elizabeth St, University of Melbourne
Contact: Dr Michael Duffy; T: 8344 3264; E: mduffy@unimelb.edu.au

Project description: Severe, cerebral malaria is caused by Plasmodium falciparum and is associated with adhesion of infected erythrocytes to microvasculature via the PfEMP1 variant surface antigen. Each parasite encodes 60 different PfEMP1s that also differ between isolates and regions. Different PfEMP1s adhere to different host receptors. Antibodies to PfEMP1 correlate with protective immunity, but parasites avoid immunity by switching between the PfEMP1s expressed. Recently a subset of PfEMP1 domain cassettes were shown to be associated with severe disease and to bind a novel receptor, these domains may be vaccine targets.

Hypothesis: That parasites causing severe malaria express a conserved subset of PfEMP1 variant surface antigens that elicit cross-reactive antibodies.

Aim: To test PfEMP1 domains abundantly transcribed in severe malaria for cross-reactivity with severe malaria sera. We have identified the PfEMP1 domains expressed in patients with severe and non-severe malaria in West Papua. Sera from these patients will be tested for reactivity with recombinant PfEMP1 domains from their infecting strain and from both severe and non-severe heterologous infections. We predict that patients with acute severe malaria will lack antibodies to their infecting strain PfEMP1s and to PfEMP1s from other parasites causing severe malaria whilst patients with non-severe malaria will be immune and possess antibodies to the PfEMP1s expressed by parasites causing severe malaria.

Significance: Discovery of conserved PfEMP1 domains expressed in severe malaria in West Papua will be an essential step towards a globally effective vaccine to prevent adhesion.

150. Are novel bromodomain proteins required for malaria parasite growth and gene regulation?

Supervisors: Dr Michael Duffy
Project Site: Department of Medicine (RMH), Peter Doherty Institute
Contacts: Dr Michael Duffy; T: 8344 3264; E: mduffy@unimelb.edu.au

Novel anti-malarial drugs are urgently required to combat the increasing resistance to existing anti-malarials. Inhibition of factors binding acetylated histones has recently emerged as a totally novel therapeutic strategy targeting a central epigenetic pathway. This approach has shown promise for the treatment of cancer, inflammation and HIV.

Histone acetylation is a fundamental epigenetic mechanism; it affects the packaging of DNA into chromatin and the histone acetylations bind regulatory protein complexes that determine gene activity. Bromodomains are protein motifs that bind selectively to different acetylated lysine residues in histones. They are present in a range of proteins that modify chromatin structure directly or recruit enzymatic complexes to specific positions in the genome.

We hypothesise that unique P. falciparum proteins containing bromodomains interact with acetylated histones and are essential for gene regulation and survival of the malaria parasite. We will determine the role in parasite biology and gene regulation of six novel P. falciparum bromodomain proteins and will identify and characterize specific, small molecule inhibitors that interfere with their function.

The specific aims of this project are:
1. To analyse the function of the bromodomain proteins using mutant parasites.
2. To characterize six putative P. falciparum bromodomain proteins by determining their location across the genome and how their presence correlates with gene transcription.

151. Gene regulation mechanisms in the transmissible stages of the malaria parasite – also offered as MBiomedSc

Supervisors: Dr Michaela Petter and Dr Michael Duffy
Project Site: Department of Medicine (RMH), Clinical Sciences Building, Royal Melbourne Hospital, University of Melbourne
Contacts: Dr Michael Duffy and Dr Michaela Petter; T: 8344 3264; E: mduffy@unimelb.edu.au, mpetter@unimelb.edu.au

Project Description: During infection with the malaria parasite Plasmodium falciparum, some malaria parasites infecting red blood cells differentiate into sexual stages called gametocytes. Gametocytes are transmitted to the mosquito when it feeds on an infected human. The mechanisms that trigger the differentiation of malaria gametocytes are poorly understood. In many eukaryotes, epigenetic mechanisms are crucial for the regulation of cellular differentiation processes. This project aims to identify epigenetic gene regulation mechanisms which are important during the
differentiation of malaria gametocytes. The project will involve cultivating *P. falciparum* gametocytes in vitro and the analysis of the expression of candidate epigenetic regulators by using advanced molecular and imaging techniques such as fluorescence microscopy, Western Blot analysis, and chromatin immunoprecipitation, combined with classical molecular biology.

152. **Characterizing new surface proteins of the malaria parasite - also offered as MBiomedSc**  
**Supervisors:** Dr Michaela Petter  
**Project Site:** Department of Medicine (RMH), Peter Doherty Institute  
**Contacts:** Dr Michaela Petter; T: 8344 3264; E: mpetter@unimelb.edu.au  
**Project Description:** The malaria parasite evades the host immune system by constantly changing its appearance, a process called antigenic variation. This is mediated by large protein families encoded in the parasites genome. Due to their important role in the patho-physiology of the disease, a better understanding of these surface proteins may reveal new targets for interventions. This project aims to characterize members of a particular protein family, called RIFIN. You will generate and analyse transgenic parasite lines expressing RIFIN proteins fused to fluorescent markers and use these tools to characterize the protein family with respect to their expression, cellular localization, membrane topology and function.  
Techniques include: Cell culture, PCR and cloning, SDS-PAGE and Western blotting, FACS analysis, Immunofluorescence microscopy.

153. **Functional assays for immunity to malaria - also offered as MBiomedSc**  
**Supervisor:** Professor Stephen Rogerson  
**Project Site:** Department of Medicine, Royal Melbourne Hospital  
**Contact:** Prof Stephen Rogerson, T: 8343259; E: sroger@unimelb.edu.au  
**Project Description:** Identifying antibody responses that protect against malaria and its complications is an important but elusive goal. This may be in part because total, rather than functional, antibody measures have been widely used. In the context of studies of malaria in pregnancy in Papua New Guinea and Malawi, you will learn novel assays developed in our laboratory to measure functional opsonising antibodies, and will apply this to the study of sample sets from pregnant women, integrating results of your laboratory measurements with extensive clinical data bases available on these women. The aim is to discover which antibody responses help clear malaria infection, and which responses prevent complications of malaria like anaemia and low birth weight.  
This project is based at the Department of Medicine at the Peter Doherty Institute, in the malaria laboratory. We have extensive experience in malaria parasite culture and analysis of immune responses. The lab comprises 4 post-docs, 2 research assistants, and 6 PhD students as well as visiting scientists from all over the world.  
Techniques will include, but not be limited to, malaria parasite and human monocyte cell culture; flow cytometry, and statistical analysis.

154. **Vaccines to protect pregnant women from malaria**  
**Supervisors:** Prof Stephen Rogerson  
**Project Site:** Department of Medicine, Peter Doherty Institute  
**Contact:** Prof Stephen Rogerson, T: 83443259, E: sroger@unimelb.edu.au  
**Project Description:** Researchers have identified proteins that may be targets of protective immunity against malaria in pregnant women. The main protein is called VAR2CSA, and we have several versions of this recombinant protein to test. Using these proteins, and samples we have collected from pregnant women in African and Papua New Guinea, you will measure antibody responses and investigate whether antibody levels are associated with protection against malaria infection or its major consequences, such as anaemia and low birth weight.  
Techniques to be used include ELISAs and statistical analysis. Students will receive detailed training in Stata, one of the best statistical packages for biomedical research.

155. **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: aac@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 \textit{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.

156. Immunity, drug efficacy and the spread of anti-malarial drug resistance - also offered as MBiomedSc

Supervisor: Dr Freya Fowkes, Head, Malaria Epidemiology Group, Centre for Population Health, Burnet Institute

Email: Fowkes@burnet.edu.au

Project Description: Malaria caused by Plasmodium falciparum remains a major cause of morbidity and mortality globally. It is now extremely alarming that resistance to the first-line treatment for falciparum malaria, artemisinin-based combination therapy (ACT), has recently been reported in Asia. The assessment of antimalarial resistance is severely impeded by the presence of host immunity to malaria in patients living in malaria endemic regions. Naturally acquired blood-stage immunity increases the probability of parasite clearance independently of the drugs used, and regardless of their antimalarial resistance. However, the precise immunological targets and mechanisms which enhance antimalarial drug efficacy are unclear. The overall objective of this project is to identify and quantify immunological biomarkers that determine ACT therapeutic efficacy in a malaria endemic area of Thailand, both in the context of clinical disease and malaria transmission.

Laboratory techniques will include ELISA and functional antibody assays. Findings will help assess to what extent immunity in populations can mask the presence of drug resistance and are vital for monitoring the global spread of drug resistance.

157. 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

Email: 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 worldwide 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.

158. The impact of malaria control measures on the acquisition of immunity to malaria

Supervisor: Dr Freya Fowkes, and Professor James Beeson, Malaria Epidemiology Group, Centre for Population Health, Burnet Institute

Email: Freya Fowkes E: Fowkes@burnet.edu.au, James Beeson E: beeson@burnet.edu.au

Project description: Malaria caused by Plasmodium falciparum remains a major cause of morbidity and mortality globally. It has decreased substantially over the past decade due to increased control measures and access to efficacious treatments. People living in these areas are exposed less and less to malaria over time due to declining transmission. Naturally acquired blood-stage immunity develops to malaria after repeated exposure that controls blood-stage parasitaemia, thereby reducing clinical symptoms and life-threatening complications. Antibodies are important mediators of this acquired immunity. However, it is unclear how declining malaria transmission impacts on the acquisition of malarial immunity.

The overall objective of this project is to quantify the impact of declining transmission on the acquisition of malarial immunity in a malaria endemic area of Thailand, both in the context of clinical disease and malaria transmission. Laboratory techniques will include ELISA and functional antibody assays and/or epidemiological analyses. Findings will help us understand how immunity develops and is maintained against infectious diseases in populations with declining transmission.
159. Identifying antigen targets of the acquired immune response during severe malaria

**Supervisor:**  Professor James Beeson, Dr Freya Fowkes, Dr Jack Richards, Professor Stephen Rogerson  
**Project site:** Burnet Institute  
**Email:**  Professor James Beeson E: beeson@burnet.edu.au T: 9282 2111

**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 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.

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

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

161. Developing new diagnostics and treatments for malaria

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

**Project Description:** Access to affordable malaria diagnostics and antimalarial treatments are vital for the effective management of individuals and for malaria control at a population level. With an increasing emphasis on malaria elimination in some parts of the world, there is a need to develop diagnostics with improved sensitivity to detect low levels of parasites and to identify individuals with glucose-6-phosphate deficiency. There is also an urgent need to develop new anti-malarial drugs to combat drug resistance. This project seeks to develop and assess new tools for the diagnosis of malaria and to identify and develop novel drug compounds that block the blood stage replication of malaria parasites.

162. Vaccines against malaria

**Supervisor:**  Professor James Beeson, Dr Jack Richards, Dr Freya Fowkes  
**Project site:** Burnet Institute  
**Email:**  E: beeson@burnet.edu.au Richards@burnet.edu.au, Fowkes@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, EBS, 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.
163. Evaluation of potent inhibitory antibody combinations for experimental malaria vaccines.
   Supervisor: Dr Paul Gilson, Dr Freya Fowkes and Professor James Beeson
   Project site: Burnet Institute
   Email: Gilson@burnet.edu.au Fowkes@burnet.edu.au
   Project Description: Malaria parasites invade and replicate within human red blood cells which can cause debilitating disease symptoms and even death. Parasites recognize, attach to and penetrate red blood cells using a surfeit of surface ligands, the understanding of which is important for vaccine development. We have recently established the potential functions of several malaria surface proteins and the order in which they work. This project aims to capitalize on this discovery by finding the best combinations of invasion inhibitory antibodies to block the surface proteins and prevent growth. This work could prove highly informative for future vaccine development.
   Techniques involved: Cell culture, luciferase based growth assays, live cell microscopy of parasites.

164. Host cell modification in malaria parasites. – also offered as MBiomedSc
   Supervisor: Dr Paul Gilson, Dr Freya Fowkes and Professor James Beeson
   Project site: Burnet Institute
   Email: Gilson@burnet.edu.au Fowkes@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, parasite molecular cell genetics, fluorescence microscopy, flow cytometry.

MEDICATION SAFETY

165. Safe and appropriate medication prescribing of older patients in hospital – also offered as MBiomedSc
   Supervisors: Professor Elizabeth Manias and Dr Snezana Kusljic
   Project Site: Royal Melbourne Hospital, Parkville Campus; Melbourne School of Health, The University of Melbourne
   Contact: Professor Elizabeth Manias T: 0450 308 060 E: emanias@unimelb.edu.au
   Project description: Older people often have a number of chronic conditions and therefore are prescribed many medication to treat these conditions. Administration of many medications, also known as polypharmacy, puts older people at risk of developing adverse events such as falls, gastrointestinal bleeding, and cognitive impairment. In addition, older people are often denied potentially beneficial medications without a valid reason. In this study, the STOPP (Screening Tool of Older Persons' Prescriptions)/START (Screening Tool to Alert doctors to Right Treatment) screening tool will be applied to a random sample of older people admitted to Geriatric Evaluation and Assessment Units of The Royal Melbourne Hospital. Use of this screening tool will determine what medications have been inappropriately commenced in older people and what medications have been inappropriately stopped or not commenced in older people. The adverse events experienced by older people will also be examined to determine whether the medications they are prescribed may be associated with these adverse events. Medical histories of older people 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 in hospitals.

166. How do cognitive and functional impairment relate to the use of anticholinergic medications in patients aged 65 years and over in rehabilitation and geriatric evaluation and management settings? – also offered as MBiomedSc
   Supervisors: Professor Elizabeth Manias and Dr Snezana Kusljic
   Project Site: Royal Melbourne Hospital, Royal Park Campus; Melbourne School of Health, The University of Melbourne
   Contact: Professor Elizabeth Manias T: 0450 308 060 E: emanias@unimelb.edu.au
   Project description: Anticholinergic medications can cause many adverse events such as drowsiness, urinary retention, tachycardia, constipation, blurred vision, dry mouth and increased intraocular pressure. These medications can reduce levels of cognition, therefore causing decreased arousal, sedation, and confusion. These effects are more likely to be pronounced in older people because of altered pharmacokinetics and reduced levels of cognition that occur with increased age. Examples of anticholinergic medications include tricyclic antidepressants, antihistamines, and ocular mydriatic agents. This study will involve the conduct of a prospective audit of anticholinergic medications prescribed to older patients (aged 65 years and over) admitted to hospital. Data will also be collected on all medications prescribed to these patients. Prescription of anticholinergic medications will be considered in relation to the cognitive levels...
experienced by older patients as determined by the Mini-Mental State Examination. The prevalence and severity of anticholinergic symptoms, including dry mouth, constipation, blurred vision, confusion, urinary hesitation, dry eyes, and drowsiness will also be assessed. Following conduct of this study it will be possible to make recommendations about how medication safety can be improved in the use of anticholinergic medications in older people.

MULTIPLE SCLEROSIS/NEUROLOGY

167. How does steroid therapy change the course of multiple sclerosis relapses?
Supervisors: Dr Tomas Kalincik, Dr Vilija Jokubaitis and A/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: Clinical relapses triggered by episodic inflammatory activity are a typical feature of multiple sclerosis (MS). Typically, patients experiencing relapses of MS activity receive short courses of high-dose intravenous steroids. However, the evidence supporting this approach is scarce.

This project will examine the outcomes of steroid therapy for MS relapses. We hypothesise that intravenous steroids decrease duration of MS relapses and improve recovery. This project is an extension of our recently published work on relapse incidence and phenotype. It will utilise a large longitudinal collection of data recorded in the international observational MS registry based at Melbourne Brain Centre - MSBase.

This project will suit people with interest in statistics and health outcome analysis. During the course of the project, you will become familiar with quasi-randomisation and the analysis of observational data. Knowledge of elementary statistics is a requisite and the statistical package used to conduct the analyses is R. You will contribute to the evidence-based clinical management of MS.

168. Predicting treatment response in multiple sclerosis
Supervisors: Dr Tomas Kalincik, Dr Vilija Jokubaitis and A/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: The range of treatments available to patients with multiple sclerosis has recently grown and more disease modifying agents are expected to become available soon. These comprise agents with various mechanisms of action, efficacy and potential adverse effects. Since MS is a variable disease whose course is difficult to predict in individual patients, pre-treatment estimation of future response to various agents is crucial for maximising treatment efficacy, and for implementation of individually-tailored treatment regimens in clinical practice. Even though some predictors of treatment response have previously been suggested (e.g. intensity of relapsing activity or severity of MRI changes), a retrospective analysis of treatment response within a large and heterogeneous sample of patients representative of the MS population has been missing.

This project uses the MSBase - a large international, observational database of MS patients - to evaluate routinely available demographic and clinical information as potential predictors of response to several commonly used therapeutic agents. It aims at recognising these predictors in individual patients prior to the treatment initiation, in order to allow clinicians to choose the most appropriate therapeutic regimen.

This project would suit people with interest in statistics and health outcome analysis. The project will enable you develop your analytical and statistical skills, whilst undertaking research using a large, well powered data collection. Knowledge of elementary statistics is a requisite and the statistical package used to conduct the analyses is R. You will become familiar with retrospective evaluation of potential predictive markers, validation of the resulting predictors and planning their clinical implementation.

169. Management of radiologically active relapsing-remitting multiple sclerosis
Supervisors: Dr Tomas Kalincik, Dr Vilija Jokubaitis and A/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: Regular imaging of the central nervous system is a common practice in relapsing-remitting multiple sclerosis (MS). Only approximately 1 in 10 new MS-related brain lesions present with clinical symptoms of a relapse. It is unclear whether silent brain lesions observed on routine brain MRI’s warrant change of disease modifying therapy or whether these lesions do not add any prognostic information to the management algorithm.

This project compares disease outcomes (relapse and disability outcomes) in patients with multiple sclerosis with recent clinically silent MRI activity. It utilises the MSBase - a large international, observational database of MS patients, to conduct retrospective analysis of prospectively recorded data.
This project will suit people with interest in statistics and health outcome analysis. During the project, you will improve your statistical skills, learning some of the more complex statistical analytical techniques, including propensity score matching procedures. Knowledge of elementary statistics is a requisite and the statistical package used to conduct the analyses is R. You will contribute to the evidence-based clinical management of MS.

NEPHROLOGY

170. Understanding Why Fibrosis is Progressive in Chronic Kidney Disease
Supervisors: A/Prof. Tim Hewitson, Prof. Steve Holt
Project Site: Department of Nephrology, The Royal Melbourne Hospital, Parkville.
Contact: A/Prof. Tim Hewitson T: 9342 7726 E: tim.hewitson@mh.org.au

Project Description: Although the kidney can recover from acute injury, persistent and/or severe injury results in scarring (fibrosis) and progressive renal failure. Understanding the mechanisms that regulate the transition from acute kidney injury to chronic fibrotic disease is important, because once fibrosis is initiated it can be incredibly difficult to switch off or reverse. Our recent work suggests that epigenetic histone modifications in the kidney are responsible for a perpetual activation of collagen producing cells (fibroblasts) that cause progressive scarring. To test this we will use a combination of in vitro and in vivo methodologies to determine what epigenetic modifications distinguish cells in fibrotic tissue from their unscarred counterparts, and what the functional significance of these modifications are. Techniques involved include cell culture, immunohistochemistry, animal (mice) models and molecular biology.

171. Demonstrating the Value of Bioimpedance Spectroscopy in Managing Dialysis Patients in Remote Sites
Supervisors: Prof. Steve Holt, A/Prof Nigel Toussaint, Dr Scott Wilson, A/Prof Genie Pedagogos
Project Site: Department of Nephrology, The Royal Melbourne Hospital, Parkville.
Contact: Prof. S. Holt T: 9342 7058 E: steve.holt@mh.org.au

Project Description: One of the most important functions of dialysis is removal of excess salt and water which accumulates in kidney failure causing oedema in various tissues, most dangerously in the lungs. Patients undertaking haemodialysis (HD) are given a target weight (TW); that being the weight that needs to be achieved after a dialysis session, where all the fluid is essentially in the correct place. The TW is arrived at by careful clinical examination and determination of a TW requires considerable nephrological expertise. Once patients have been prescribed a TW, they can then be weighed on arrival at a dialysis centre and the fluid that must be removed during the HD session corresponds to the difference between their current weight and their TW. However, over time changes in flesh weight and fat mass may mean that target weights become inaccurate and must be reviewed. In remote dialysis sites this may be difficult. The RMH has over 22 dialysis satellite centres, many of which are remote. In this environment it is difficult for patients to have an accurate, timely TW assessment. Recent data suggest that bioimpedance spectrometeroscopy is helpful in determining fluid volumes in various compartments (Hur et al., 2013). This project will examine how the use of such devices might make HD in remote dialysis centres safer for patients by assisting with recognition of changes in flesh and fluid weight before they become dangerous. Such observations may allow earlier adjustments to the dialysis schedule and better individualise the dialysis prescription to improve long-term outcomes. Project based in Parkville, with some travel required (driving licence an advantage).

172. Finding genetic mutations in new types of inherited kidney disease: focal segmental glomerulosclerosis – also offered as MBiomedSc
Supervisors: Professor Judy Savige and Dr Yanyan Wang
Project Site: NWAC, Northern Hospital, Epping.
Contact: Professor Judy Savige, T 8344 3260, jsavige@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 proteinuria 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**

**173. The role of dopamine receptor 1 vs 2 in adolescent vulnerability to anxiety.**

**Supervisors:** Dr Jee Hyun Kim; Dr Heather Madsen  
**Project Site:** The Florey  
**Contact:** Dr Jee Hyun Kim Ph: 9035 6623; Email: jeek@unimelb.edu.au  
**Project description:** Anxiety disorders are a major worldwide public health concern, and according to the Australian Bureau of Statistics (ABS; 2007) ~1 in 4 Australians suffer from a clinically diagnosed anxiety disorder at least once in their lifetime. While these disorders can affect people of all ages, adolescence represents a particularly vulnerable period. For example, the median age of onset for anxiety disorders is 14, and people who experience anxiety early in life are more likely to exhibit more severe symptoms later on in life. One of the main focuses of our laboratory lies in determining what neurobiological factors underlie this increased vulnerability observed in adolescents, with the aim of developing more effective therapeutic interventions. Fear conditioning is the most commonly used model for studying anxiety disorders in rodents. Extinction refers to the decrease in fear due to the fear-eliciting cue no longer being accompanied by an aversive event, and this forms the basis of exposure therapies used for the treatment of anxiety disorders in humans. Using a fear conditioning/extinction paradigm we have shown that extinction training is less effective in P35 (adolescent) compared to P70 (adult) rats due to maturational differences in the prefrontal cortex (PFC). This difference may be due to the well-established disrupted balance of dopamine receptor 1 (DR1) vs 2 (DR2) signalling during adolescence, however this has yet to be directly demonstrated. The aim of this project is to investigate potential age-related differences in the activation of D1R vs D2R in the PFC of adult vs adolescent mice in response to extinction of conditioned fear. Mice that express green fluorescent protein- (GFP) tagged D1R and D2R will be utilised, and Fos/GFP immunohistochemistry will be performed to identify activated D1R and D2R neurons. The effect of the D2 partial agonist Aripiprazole upon extinction consolidation and D1R/D2R activation in the PFC will also be examined.

**174. Neural circuitry underlying extinction of fear across development.**

**Supervisors:** Dr Jee Hyun Kim; Dr Despina Ganella  
**Project Site:** The Florey Institute  
**Contact:** Dr Jee Hyun Kim Ph: 9035 6623; Email: jeek@unimelb.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 the process of extinction. Extinction is the decrease in fear responses expressed to a fearful stimulus due to the repeated exposure to the stimulus without any aversive outcome. We have accumulated powerful evidence supporting that extinction is erasure in juvenile rats whereas extinction is new learning in adult rats. This developmental transition from erasure to new learning appears to be driven by changes in the functionality and the circuitry between the amygdala, the hippocampus, and the medial prefrontal cortex (mPFC). This project will characterise the functional organisation of that neural circuitry using intracranial microinusions of retrograde tracers (cholera toxin b subunit and fluorogold), using Pavlovian fear conditioning as a model of post-traumatic stress disorder in developing rats.

**175. Towards a brain-based measure of human anxiety sensitivity (offered as MSc only) – ONLY available as MBiomedSc**

**Supervisors:** Assoc Prof Ben Harrison and Dr Chris Davey  
**Project Site:** Melbourne Neuropsychiatry Centre, and Department of Psychiatry, The University of Melbourne  
**Contact:** Assoc Prof Ben Harrison; T: 03 8344 1876 E: habj@unimelb.edu.au  
**Project Description:** Anxiety disorders are the most prevalent and costly of all mental disorders for Australians aged between 18 and 45 years. Despite this, we lack a clear understanding of the biological mechanisms that give rise to their symptoms and how to effectively treat them. This PhD project will test the hypothesis that human anterior insular cortex activity underlies individual differences in trait “anxiety sensitivity”: an established psychological risk factor for clinical anxiety disorders. The project will recruit a large
cohort of adolescent and young adult participants and assess them with functional magnetic resonance imaging (fMRI) combined with psychophysiological monitoring. As well as characterising the brain basis of human anxiety sensitivity, it is expected that this project will identify a novel biological risk marker of clinical anxiety, in particular, panic disorder. We have close collaborations with Orygen Youth Health and headspace Western Melbourne, and there is scope for the project to be extended to patient groups from these clinics.

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

176. **Predicting treatment response in young people with major depression using functional neuroimaging - ONLY available as MBiomedSc**

Supervisors: Dr Chris Davey and Assoc Prof Ben Harrison

Project Site: Melbourne Neuropsychiatry Centre, and Department of Psychiatry, The University of Melbourne

Contact: Dr Chris Davey, T: 03 9342 2800 E: c.davey@unimelb.edu.au

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

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

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

177. **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.

178. **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.
179. Neuroimaging in schizophrenia-spectrum disorders – also offered as MBiomedSc  
Supervisors: Dr Vanessa Cropley, Dr Cali Bartholomeusz, 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 Cali Bartholomeusz; T: (03) 8344 1878; E: cbarc@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 studies conducted within our Centre as well as 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. These data are collected across five research sites within Australia, including MNC. The data are 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 structural neuroimaging correlates of schizophrenia and related disorders. These projects will utilise MRI scans and associated clinical and cognitive data collected from our Centre or as part of the ASRB. Example projects for 2015 include:

- Comparison of morphological abnormalities in schizophrenia, schizoaffective disorder and bipolar disorder
- Shape analysis of the hippocampus and its association with cognitive profiles in established schizophrenia
- Examining the effect of symptom profile and illness severity on pituitary volume in first episode psychosis, established schizophrenia and schizoaffective disorder

Students will have the opportunity to develop their own projects in-line with their specific research interests given the availability of data and resources.

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

There are 3 honours places available for 2015.

180. 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.

181. 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.

**182. 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

**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.

**183. Antidepressants in epilepsy**

**Supervisor:** Dr Nigel Jones and Dr Sandy Shultz

**Project Site:** Kenneth Myer Building/Dept of Medicine RMH

**Contact:** Nigel Jones E: ncjones@unimelb.edu.au Sandy Shultz E: sandy.shutz@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
184. Temporal lobe epilepsy, the HPA axis and depression - also offered as MBiomedSc

**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.

185. Determining whether muscarinic cholinergic receptors contribute to the pathophysiology of Parkinson’s disease – also offered as MBiomedSc

**Project description:** Anticholinergic drugs and cholinesterase inhibitors have been used as adjunct therapies in Parkinson’s disease to reduce tremors/ rigidity and symptoms of dementia respectively. With the recent advances in targeting specific muscarinic receptors, it is hoped that more effective drugs can be developed targeting muscarinic M4 receptors to alleviate the tremor/rigidity and M1 receptors to reduce the impact of cognitive decline. Therefore, it is surprising that relatively little is known about the levels of muscarinic receptors in the brains of people with Parkinson’s disease.

This project will use *in situ* radioligand binding and autoradiography to determine levels of muscarinic M1, M2/4 and M3 receptors in cortical (involved in cognition) and sub-cortical (involved in fine motor control) brain regions from 10 subjects with Parkinson’s disease and 10 age and sex matched control subjects.

If compounds targeting specific muscarinic receptors are to be developed for the treatment of Parkinson’s disease, it is critical that we know whether the expression of the target receptors is altered in the brains of people suffering from the disease.

This project is suitable for either an Honours or an MSc (BHS) student. The project will be offered to one (1) student in 2015.

*An autoradiograph showing the density of binding to muscarinic M1 receptors in the caudate putamen from a subject with no history of neurological disorder.*

186. Understanding the role of the zinc transporter ZIP12 in schizophrenia

**Project description:** Schizophrenia is a debilitating mental illness that affects approximately 1% of the population. The biological basis of schizophrenia remains largely unknown. Using human post-mortem brain tissue, we recently discovered that the gene for zinc transporter member 12 (ZIP12) is upregulated in cortical regions in people with schizophrenia. This increase was not detected in brain tissue from people with bipolar disorder or major depressive disorder, indicating the change is disease specific.
Research Plan: This project will involve: 1) Measuring ZIP12 expression, using real-time PCR, in the caudate-putamen from people with schizophrenia, compared to control subjects, to determine how widespread the change of expression is throughout the brain. 2) As we have now shown that human ZIP12 is capable of increasing zinc uptake in the cell, total and subcellular zinc levels will be measured in human brain preparations, using ICP-MS, to determine if zinc regulation is affected by increased ZIP12 expression in these individuals. 3) Finally, total and subcellular zinc levels will be measured in brain tissue from rats treated with antipsychotic drugs to see whether the changes we observe in the brains from people with schizophrenia are influenced by medication.

187. 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: njones@unimelb.edu.au
   - 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.

188. High Frequency Brain Wave Patterns in a Rodent Model of Schizophrenia
   Supervisors: Dr Chris French, A/Prof Anthony Hannan, Dr Nigel Jones, Prof Terrence O’Brien
   Project Site: Melbourne Brain Centre
   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.

189. Estrogen, antipsychotics and schizophrenia – also offered as MBiomedSc
   Supervisors: Dr Andrea Gogos and Dr Snezana Kusljic
   Project Site: 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 hypothesised to explain the observed gender 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 is currently using a number of different rodent models to study the role of estradiol and testosterone in mediating several behaviours with relevance to schizophrenia and depression. The behavioural tests we use focus on drug-induced locomotor hyperactivity, sensorimotor gating, and learning and memory.
   We have a number of projects available in this area. The aim of one study is to investigate the role of sex steroids in modulating the effects of antipsychotic treatment in rats. This will include both behavioural testing and analysis of cyclic adenosine monophosphate (cAMP) levels in the brains of these rats. Another study is focused on investigating the role of selective estrogen receptor modulators (SERMs) in regulating cognition. SERMs are potentially a safer alternative to estradiol, in terms of side-effects.
190. **Understanding the role of neurotrophic factors in adolescent brain development – also offered as MBiomedSc**

**Supervisor:** Dr Rachel Hill and Dr Xin Du  
**Project Site:** Behavioural Neuroscience Laboratory, The Florey Institute of Neuroscience and Mental Health  
**Contact:** Rachel Hill T: 9035 6661 E: rachel.hill@florey.edu.au

**Project description:** There is increasing evidence that the neurotrophin BDNF is involved in schizophrenia. BDNF plays a major role in neurodevelopment and the survival of neuronal cells in response to stress. Studies have shown that BDNF levels are disrupted in schizophrenic and depressive patients and that BDNF expression is decreased by stress exposure. Our laboratory uses a number of genetically modified mice with mutations in the gene encoding BDNF and its receptor TrkB to determine the role of this gene in regulating brain development and behaviour.

Project 1 will involve a thorough molecular analysis of the genetically modified BDNF heterozygous brain throughout adolescent development, including expression analysis of neurotrophins, estrogen and androgen receptors, and a number of neurotransmitters associated with schizophrenia including GABAergic interneurons, NMDA receptors, dopaminergic receptors and serotoninergic receptors.

191. **A role for sex steroid hormones in psychiatric disorders – also offered as MBiomedSc**

**Supervisors:** Dr Rachel Hill, Dr Xin Du and Dr Andrea Gogos  
**Project Site:** Behavioural Neuroscience Laboratory, The Florey Institute of Neuroscience and Mental Health  
**Contact:** Rachel Hill T: 9035 6661 E: rachel.hill@florey.edu.au

A role for sex hormones in the development of schizophrenia has been hypothesised to explain the observed gender difference in the age of onset with women presenting symptoms on average 3-4 years later than in men. In addition, women experience worsening of symptoms during periods of low estradiol (e.g. post-menopause) and improvements during periods of high estradiol (e.g. during pregnancy). Our laboratory are currently using a number of different rodent models to study the role of estradiol and testosterone in mediating several behaviours with relevance to schizophrenia and depression, including drug-induced locomotor hyperactivity, sensorimotor gating, and learning and memory. We have a number of projects currently available in this area assessing:

1. The role of selective estrogen receptor modulators (SERM’s) in regulating cognition.  
2. A novel pathway by which estrogen regulates cognition via GABAergic interneurons.  
3. The role of testosterone in regulating dopaminergic function.

192. **Investigating the effect of antipsychotic drugs on the levels of TNF receptor in the brain**

**Supervisors:** Dr Andrew Gibbons, Dr Caitlin McOmish, Prof Brian Dean  
**Project Site:** Florey Institute of Neuroscience and Mental Health  
**Contact:** Email: agibbons@unimelb.edu.au / Phone: 9035 6746

**Project description:** There is growing evidence to suggest that proteins that are involved in inflammation are also affected in schizophrenia. Research from our group suggests that the signalling pathway of the pro-inflammatory cytokine, Tumour Necrosis Factor (TNF), is involved in the pathophysiology of schizophrenia. We have recently shown that the levels of the TNF receptor, TNFR1, are increased in the frontal cortex of people with schizophrenia. Studies are currently underway within our laboratory to further investigate how TNF signalling is affected in this disorder.

This project aims to investigate whether antipsychotic drugs can affect the levels of TNFR1 in the frontal cortex. TNFR1 protein will be measured in frontal cortical tissue from rats that have been treated with antipsychotic drugs. TNFR1 protein will also be measured in the frontal cortex from mice treated with the psychotomimetic phencyclidine (PCP) to investigate whether TNFR1 levels are altered in a mouse model of psychosis.

The techniques that the student will use in this project will include but not be limited to:

- Processing of post-mortem tissue, SDS-PAGE separation of protein extracts, Western blotting and protein expression analysis.

193. **Investigating the involvement of the serotonin 2A receptor in the incidence suicide.**

**Supervisors:** Dr Andrew Gibbons, Dr Caitlin McOmish, Prof Brian Dean  
**Project Site:** Florey Institute of Neuroscience and Mental Health  
**Contact:** Email: agibbons@unimelb.edu.au / Phone: 9035 6746

**Project description:** There is a high risk of suicide amongst people suffering with major depression. Furthermore, many antidepressant drugs that target the serotonergic system may contribute to suicidal ideation. A recent study by our group showed that subjects with major depression have lower levels of the serotonin receptor, 5-HT2A receptor, in the cingulate cortex compared to control subjects. Amongst those subjects, people with mood disorders who died as a result of suicide also had lower levels of 5-HT2A receptor in the cingulate cortex compared to non-suicide cases. Therefore, we are interested in understanding whether 5-HT2A receptor could be involved in the pathophysiology of suicide, itself.
This project aims to determine whether the levels of 5-HT_{2A} receptor are altered in the brains of people who have committed suicide. Levels of the 5-HT_{2A} receptor will be measured in the cingulate cortex, taken post-mortem, from subjects with no prior history of psychiatric illness who died as a result of suicide and compared with tissue from non-suicide, control subjects.

The techniques students will use in this project will include but not be limited to: Processing of post-mortem tissue, Radiolig and binding assays, autoradiography.

**NEUROVASCULAR**

194. 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 (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. 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.

195. 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.
196. Acute stroke rescue: Does imaging characteristics predict the histopathology 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 immunohistochemistry 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.

197. What are the 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, lab work and how to interpret DNA sequence abnormalities.

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

198. Small vessel disease causing stroke and dementia – 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 undergoing brain MRI and correlating any small vessel disease in the retina with strokes/’white matter ischemia’. This study is to investigate whether retinal photographs might be useful in predicting patients who will develop a stroke and in whom greater attention to blood pressure control might prevent disability and even death.

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

Feasibility: We already have Human Research Ethics Committee Approval for this project, and 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).

199. The Contribution of Endothelial Progenitor Cells to Retinal Vascular Regeneration

 Supervisor: Dr R C Andrew Symons (Department of Ophthalmology, RMH; Department of Surgery (RMH), University of Melbourne)
 Project Site: Department of Surgery, Royal Melbourne Hospital
 Contact: Dr Andrew Symons Tel: 9342 2166 Email: andrew.symons@mh.org.au

Aim: To determine the role of endothelial progenitor cells in retinal revascularization in the oxygen induced retinopathy model of retinopathy of prematurity.

Retinal vasculopathies are some of the most important causes of blindness. Diabetic retinopathy is the most significant cause of visual disability in working adults in the developed world. Retinopathy of prematurity is one of the most significant causes of childhood blindness. It is unknown how important vascular regeneration is to delaying development of diabetic retinopathy, and it is unknown to what extent the arrest of vascular development that precedes the development of retinopathy of prematurity may be modulated by modifying angiogenic processes. Treatments that optimize vascular regeneration may potentially have an enormous impact on reducing visual loss in these diseases.

Our previous work has found a gene that controls numbers of endothelial progenitor cells in the bone marrow, and also the number of endothelial progenitor cells being recruited to the retina during vascular regeneration after hyperoxic vaso-obliteration. The number of retinal endothelial progenitor cells appears to control the rate of revascularization and the severity of the pathological angiogenesis in the oxygen induced retinopathy model of retinopathy of prematurity.

This project involves the use of reporter mice expressing green fluorescent protein under the control of the Id1 allele to identify endothelial progenitor cells in the retina. Mice homozygous for this allele will be used to determine whether endothelial progenitor cell deficiency leads to a deficit in retinal vascular regeneration.

Future work on this project may lead to development of therapeutic strategies to reduce the severity of retinopathy of prematurity and diabetic retinopathy.

Skills: Animal handling skills, design of mouse breeding strategies, retinal fluorescein-dextran perfusions, immunofluorescence microscopy, flow cytometry, data analysis.

Please note: this subject is only offered for Round 2 - late applications. Late applications will open in early December. Please check the ‘How to Apply’ website for details: http://sc.mdhs.unimelb.edu.au/how-apply

PHARMACOGENETICS AND PERSONALISED MEDICINE

200. 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 gauge the clinical utility of TPMT genotyping and the clinical decision support tools that will be built into the program, and thiopurine metabolite testing, in the management of inflammatory bowel disease.

201. 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.
202. Development of novel rapid genotyping techniques to detect genetic variants predictive of response to drugs for application in personalized medicine - also offered as MBiomedSc

Supervisors: Professor Patrick Kwan, Dr Marian Todaro
Project Site: Department of Medicine (RMH)
Contact: Patrick Kwan, Department of Medicine (RMH) E: patick.kwan@unimelb.edu.au; Dr Marian Todaro, Department of Neurology E: Marian.Todaro@mh.org.au

Project Description: This study is part of a large project aiming to bring personalised medicine into widespread clinical practice. Personalised medicine based on pharmacogenetics knowledge promises to revolutionise healthcare by harnessing individual genetic information to improve drug safety and effectiveness. However, conventional genotyping platforms in the clinical setting typically rely on polymerase chain reaction (PCR) or direct sequencing, which require complex sample handling and are performed in laboratories using expensive equipment operated by highly skilled personnel. Testing is expensive and typically takes days to weeks for the results to become available to the requesting physician. These logistic barriers cause delay in starting appropriate treatment, and add administration time for extra clinic visits or patient contacts.

To overcome these logistic and economic barriers, we propose an innovative combination of biochemical and engineering technologies that will perform genotyping rapidly using compact ‘smart’ devices at the point of care. The protocol developed will be adapted for use in a compact automated device through collaboration with electronic engineers. There is very strong potential for technological innovation and eventual application and commercialisation of the device in clinical practice. This project will be suitable for students with background in molecular biology interested in learning new DNA amplification technologies and developing new protocols that will have direct clinical application in the near future.

203. Lab-on-a-chip nanotechnology testing device for personalized medicine - also offered as MBiomedSc

Supervisors: Professor Patrick Kwan and Professor Stan Skafidas
Project Site: Centre for Neural Engineering, Department of Electrical Engineering
Contact: Professor Patrick Kwan, Department of Medicine, E: patick.kwan@unimelb.edu.au Professor Stan Skafidas, Department of Electrical Engineering, E: sskaf@unimelb.edu.au

Project Description: A novel rapid genotyping platform has been identified by the study team. However, identification of the amplified DNA is subjective and insensitive. To overcome this limitation and to improve sensitivity, we propose the use of silicon nanowire for more rapid and objective detection. The platform developed will be engineered into a compact device prototype that can carry out the genotyping steps and product detection using silicon nanowire technology in automated operation. There is very strong potential for technological innovation and eventual application and commercialisation of the device in clinical practice. This project is suitable for students with background in electrical engineering.

204. Electrophysiological characterization of effects of MDR1 (ABCB1) polymorphisms on efflux transport of antiepileptic drugs - also offered as MBiomedSc

Supervisors: Professor Patrick Kwan and Dr Chris French
Project Site: Melbourne Brain Centre @ RMH, Parkville
Contact Details: Dr Chris French, E: frenchc@unimelb.edu.au; Professor Patrick Kwan, E: patrick.kwan@unimelb.edu.au

Project Description: Pharmacoresistance of antiepileptic drugs (AEDs) is a major public health problem and epilepsy resists pharmacotherapy in 30-40% of patients. Polymorphisms of MDR1 or ABCB1, which encodes the multidrug transporter P-glycoprotein (Pgp) at the blood-brain barrier, are associated with drug responsiveness. Drug-resistant epilepsy patients more frequently have the 2677T/A and 3435T MDR1 alleles compared with drug responsive patients. Using cells transfected with MDR1 variants, we found that Pgp with 2677T allele had higher transport function of pumping AEDs from basolateral to apical side than 2677G allele in cell monolayers, suggesting that polymorphisms of MDR1 influence the transport of AEDs. Pgp is an ATP-transporter, and some AEDs have an electrostatic dipole. To elucidate the molecular mechanisms of the associations between the polymorphisms and pharmacoresistance, this project will use electrophysiological methods to 1) investigate possible functional effects of MDR1 polymorphisms on intrinsic function of Pgp, and 2) to assess effects of these polymorphisms on AED transport. The results will provide a clearer basis for the design of genetic-based personalised treatment of epilepsy with the prospect of significantly enhanced therapeutic effectiveness.

Research Plan: LLC-PK1 cells transfected with MDR1 haplotypes of 2677G>T/A and 3435C>T have been established and validated in our laboratory. Western blotting and real-time PCR will be used to measure expression of Pgp (wildtype and mutants) in the stably transfected cell lines. Single channel and whole cell currents will be measured to study the effect of polymorphisms on the Pgp properties, and transport of phenytoin, a Pgp substrate and a widely used AED. Cell uptake assay for rhodamine-123 will be performed to confirm the functional difference of MDR1 variants by flow cytometry.

Acquired skills: Single channel and whole cell electrophysiology, flow cytometry, western blotting, real-time PCR, cell culture
A decision support system for implementation of pharmacogenomics in epilepsy treatment - also offered as MBiomedSc

Supervisors: Professor Patrick Kwan, Professor Terence O’Brien, A/Professor Les Sheffield
Project Site: Department of Medicine (RMH)
Contact: Professor Patrick Kwan, Departments of Medicine and Neurology, E: patrick.kwan@unimelb.edu.au

**Project description:** Personalised medicine based on pharmacogenetics knowledge promises to revolutionise healthcare by harnessing individual genetic information to improve drug safety and effectiveness. Yet its uptake has been limited partly owing to the lack of appropriate systems that can support its widespread application in clinical practice. Through partnership with a business enterprise, The Royal Melbourne Hospital is pioneering the implementation of such a system in Australia. One of the projects relates to HLA genotyping prior to the prescription of certain antiepileptic drugs to prevent severe, life-threatening allergic skin reactions. This honours project will assist in the development, implementation and evaluation of the program by collecting and analysing the relevant clinical and test information.

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.

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.
208. **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, prasugrel 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 clopidogrel 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.

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209. **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: obrienj@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.
210. Key strategies for engaging users of Social Networking Sites for health promotion - also offered as MBiomedSc
Supervisor: Dr Mark Stoove, Head, Head of HIV, AIDS and STI Research, Centre for Population Health, Burnet Institute
Project Site: Burnet Institute
Contact: stoove@burnet.edu.au
Project description: We recently conducted a review of social networking sites (SNS) to assess their use for sexual health promotion purposes. We found that, although many organisations involved in sexual health promotion have begun to use these websites, there has been very little formal study and evaluation of them. We identified a number of organisations that appear to be using SNS more effectively than others but we were unable to further investigate the strategies that these organisations used.
This Honours project will aim to identify strategies for success in this growing area. More specifically, the findings from this study will help us better understand the content, features and approaches that successfully encourage social engagement within a SNS health promotion context. Methods will include interviewing organisations with active health promotion activities on SNS and conducting an independent comparative evaluation of these sites. Quantitative and qualitative research will be used and the project will involve novel online recruitment methods.

211. Providing testing reports to general practitioners as an intervention to increase Chlamydia screening - also offered as MBiomedSc
Supervisor: Dr Mark Stoove, Head, Head of HIV, AIDS and STI Research, Centre for Population Health, Burnet Institute
Project Site: Burnet Institute
Contact: stoove@burnet.edu.au
Project description: Chlamydia is the most commonly notified infection in Australia. An important component of chlamydia control is screening and testing; the majority of which occurs in general practice. Encouraging GPs to offer more chlamydia tests to young people is vital.
This is a study to look at the effectiveness of providing GPs with individual testing/positivity reports to examine if such reports change testing behaviour. This study would use a pre-post-test design, looking at number of tests requested in 2012 following receipt of a report presenting the number of chlamydia tests requested in 2011, and the number of positive tests. The study will use data from the Australian Collaboration for Chlamydia Enhanced Sentinel Surveillance (ACCESS).

212. Chlamydia epidemiology in Australia - also offered as MBiomedSc
Supervisor: Dr Mark Stoove, Head, Head of HIV, AIDS and STI Research, Centre for Population Health, Burnet Institute
Project Site: Burnet Institute
Contact: stoove@burnet.edu.au
Project Description: Sentinel surveillance systems that provide key indicators of testing rates, positivity rates, prevalence and incidence can enhance the capacity of Australia to evaluate interventions in priority populations to control the spread of infection. The ACCESS project is such a surveillance system; it is a comprehensive surveillance system developed to evaluate the impact of national and local strategies designed to control genital chlamydia infection in Australia and to underpin Australia’s strategic response to chlamydia. Data collected through the ACCESS project is available for analysis to measure chlamydia infection and reinfection in young Australians. This project is also listed under Infectious Diseases

213. Content analysis of the successful health promotion project “Queer as F**K delivery sexual health to gay men on Social Networking Sites - also offered as MBiomedSc
Supervisor: Dr Mark Stoove, Head, Head of HIV, AIDS and STI Research, Centre for Population Health, Burnet Institute
Project Site: Burnet Institute
Contact: stoove@burnet.edu.au
Project Description: Online social networking sites (SNS) such as Facebook have grown rapidly in popularity. The popularity of these sites, along with their interactive functions, offers a novel environment in which to deliver health promotion messages. Over the past three years the Burnet Institute, working with the VAC have developed the Queer as F**K project that aims to engage with gay males about sexual health and other issues impacting on their life. Using a mixed methods analytical approach (quantitative and qualitative), this honours project will monitor and analyse the ongoing ‘Queer as F**K’ health promotion project over seasons 1-5, assessing reach, interactivity and engagement.
214. Risk behaviours and HIV among young gay and bisexual men - also offered as MBiomedSc

Supervisor:  Dr Mark Stoove, Head, Head of HIV, AIDS and STI Research, Centre for Population Health, Burnet Institute
Project Site:  Burnet Institute
Contact:  stoove@burnet.edu.au

Project description:  In recent years, the notification of newly acquired HIV has increased among young gay men in Victoria. Studies have found that gay men in Australia are having anal sex much younger than in the past and do not test for HIV as often as older gay men do. This project will investigate reported sexual and testing behaviours of young MSM by consolidating and analysing data from various surveillance data sources, with the aim of better understanding what is contributing to the increased detection of HIV in this group.

Several ongoing projects conducted by the Burnet Institute collect behavioural data from young gay and bisexual men in Melbourne, such as the Big Day Out study, HIV passive surveillance, the Victorian Primary Care Network for Sentinel Surveillance on BBVs and STIs and focus groups conducted as part of a large campaign evaluation study. These data would be analysed and interpreted alongside other available behavioural surveillance data such as those collected annually for the Melbourne Gay Periodic Survey.

215. Mapping trajectories of methamphetamine and other drug use among an established Melbourne-based cohort - also offered as MBiomedSc

Supervisor:  Prof Paul Dietze, Dr Mark Stoové, Mr Brendan Quinn
Project Site:  Burnet Institute
Contact:  E:  pauld@burnet.edu.au  Telephone: 9282 2134

Project description:  The Burnet Institute recently established and followed a cohort of methamphetamine users for 12 months to examine a range of related issues including barriers to treatment entry for methamphetamine dependence. The ‘UnMET Study’ recruited and interviewed 255 regular, Melbourne-based methamphetamine users in 2010 with followed-up in 2011. A distinct sub-group of the sample reported that their methamphetamine use was not ‘problematic’/harmful enough to warrant utilisation of professional support. The primary aim of the proposed project will be to examine trajectories of methamphetamine and other drug use, involvement in risk behaviours and experience of related harms among this group. This will enable investigations of the characteristics of methamphetamine users who are more likely to progress to more harmful patterns of use (in addition to those who are likely to reduce/cease heavy use patterns). Given increasing use of methamphetamine among Australia’s general and sentinel drug-using populations, this timely research will be valuable for informing targeted early intervention and harm reduction initiatives.

216. 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:  pauld@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.

217. Needle and Syringe Program coverage in Melbourne – also offered as MBiomedSc

Supervisor:  Paul Dietze, Peter Higgs, Campbell Aitken
Project Site:  Burnet Institute
Contact:  E:  pauld@burnet.edu.au  Telephone: 9282 2134

Project description:  The provision of clean needles and syringes and other injecting equipment to people who inject drugs (PWID) is the cornerstone of prevention strategies aimed at reducing the incidence of blood borne viruses such as hepatitis C and HIV. Australia is a world leader in Needle and Syringe Programs (NSP) with programs running for almost 30 years. However, coverage remains incomplete and the incidence of hepatitis C in particular remains stubbornly high. Aim: The aim of this study is to examine NSP coverage in Melbourne.
The proposed study involves analysis of quantitative data on NSP coverage collected through two key data sources, (1) the survey of PWID collected through the Illicit Drug Reporting System, and (2) survey data obtained through the Melbourne Injecting Drug User Cohort Study (MIX). The student will be required to collect some interview data as part of these studies and will analyse these and other data already collected as part of the studies. There has been no equivalent study of NSP coverage in Melbourne and longitudinal analysis of MIX data on coverage will be unique internationally.

218. Evaluation of a community-based HIV rapid point-of-care service for men who have sex with men – also offered as MBiomedSc

**Supervisor:** Dr Mark Stoove, Dr Alisa Pedrana, Ms Carol El Hayek

**Project Site:** Burnet Institute

**Contact:** E: stoove@burnet.edu.au  Telephone: 9282 2134

**Project description:** In recent years, notifications of HIV have increased among gay men in Victoria. Responses to HIV prevention in Australia have involved both health promotion oriented toward reductions in risk behaviour and promotion of regular HIV testing among those at risk. To address some structural barriers to high frequency HIV testing recent policy and regulatory changes have created the opportunity for the implementation of rapid point-of-care HIV testing in Australia. In response, the Victorian Department of health has funded the Burnet Institute and the Victorian AIDS Council to trial Australia’s first community-based HIV rapid testing service targeting men who have sex with men. The primary aim of this service is to increase the frequency of HIV testing in this population and reduce the prevalence of undiagnosed HIV in the community. The Burnet Institute is leading the implementation and evaluation of Victoria’s community-based HIV rapid point-of-care service for men who have sex. This Honours project will make use of quantitative and qualitative data collected in this evaluation to address primary and secondary aims of the service. Outcomes of interest will include HIV testing and diagnosis rates, the degree to which the service is attracting key risk populations, and the acceptability of the service for clients, staff and other HIV testing services in Melbourne.

219. Trends in STI testing and positivity in priority populations in Australia – also offered as MBiomedSc

**Supervisor:** Ms Caroline van Gemert, , Ms Carol El Hayek

**Project Site:** Burnet Institute

**Contact:** E: carolinevg@burnet.edu.au  Telephone: 9282 2243

**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 Chlamydia and other STI Enhanced Sentinel Surveillance (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).

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

**Supervisor:** Ms Carol El Hayek, Dr Emma McBryde

**Project Site:** Burnet Institute

**Contact:** E: carol@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.
221. Sexual Health Promotion at Music Festivals  
Supervisor: Dr Megan Lim  
Project Site: Burnet Institute  
Contact: E: lim@burnet.edu.au  
Project description: Rising rates of sexually transmitted infections and unplanned pregnancy in Australia indicate that educating young people about sexual health is vital. However, engaging young people in this topic can be difficult; innovative ways of reaching youth are needed. For several years, the Burnet Institute and other sexual health organisations have been disseminating sexual health information at music festivals, including The Big Day Out in Melbourne and Groovin’ the Moo in Bendigo. This Honours project has two main aims; firstly to evaluate the effectiveness of different aspects of the Burnet Institute’s sexual health promotion activities, and secondly to utilise qualitative data collected at the music festivals to assess young people’s knowledge of sexual health and sexual health education needs.  

The Honours student will be part of a team of researchers and educators providing sexual health education and collecting data from young people at music festivals. The project will utilise a variety of research techniques and multiple data sources. Data will be collected from young people at music festivals using techniques such as paper questionnaires, video and audio interviews, direct observation, and mobile phone surveys. These data will be analysed using descriptive statistics, content analysis methodologies, and qualitative thematic analysis. The results of the project will inform future sexual health promotion and education initiatives.

222. What really counts as ‘sex’?  
Supervisor: Dr Megan Lim  
Project Site: Burnet Institute  
Contact: E: lim@burnet.edu.au  
Project description: Sexual health research relies on individuals accurately reporting their sexual behaviour information in order to investigate associations with sexually transmitted infections and to evaluate health promotion programs. Unfortunately, self-reported behaviour can sometimes be inaccurate or invalid. This may be because participants deliberately provide false information, forget certain details, or misunderstand questions. Sexual behaviour is a very complicated measurement and participants’ understanding of a question may be different to a researcher’s intention. For example, when we ask about ‘sex’ in a survey, do participants think only of vaginal intercourse or do they include other forms of sexual activity? The aim of this Honours project is to conduct in-depth qualitative research to improve the validity of sexual health behaviour questionnaires.  

In this project the student will investigate the prevalence of sexual activity and engagement in sexual risk behaviours using quantitative data collected in a standard sexual health behaviour survey. The student will then recruit and interview young people regarding their understanding of the questionnaire and the concepts covered in the questionnaire. Through in-depth qualitative interviews the student will elicit opinions from young people on topics such as; ‘what counts as sex,’ ‘what is the difference between a boy/girlfriend and a casual partner,’ and ‘does it count if you forget to use a condom just one time?’  

The results of the project will have a significant impact on sexual health research, globally. The data will help to validate sexual behaviour questionnaires and improve our understanding and interpretation of sexual health research findings.

223. How does binge drinking impact on health-related behaviours among ex-prisoners in Fiji? – also offered as MBiomedSc  
Supervisor: Ms Rebecca Winter, A/Prof. Stuart Kinner, Dr Mark Stoove  
Project Site: Burnet Institute  
Contact: E: rwinter@burnet.edu.au  
Telephone: 8506 2328  
Project description: Globally, prisoners are known to be a group at high risk of HIV and other sexually transmitted infections (STIs), and following release into the community risky behaviours such as unprotected sex and alcohol and other drug (AOD) use have the potential to spread infection. AOD use is known to be associated with risky sexual practices and poor health outcomes, and alcohol, yaqona and cannabis use are prevalent across Pacific Island Countries and Territories (PICTs). A situation analysis in Fijian prisons showed that prisoners engage in high levels of risk behaviour including unprotected sex, unsterile tattooing and genital modification. Although information about the prevalence of HIV and other STIs among prisoners in Fiji is limited, second generation behavioural surveys have demonstrated a high prevalence of (STIs) among other high-risk groups. Furthermore, although most prisoners return to the community within a relatively short period of time, little is known about patterns of risk behaviour among recently released prisoners in Fiji. This project will investigate how risky AOD use, such as binge drinking, impacts on STI risk behaviours and selected health outcomes pre and/or post-imprisonment.
224. Structural and environmental impacts on women's relationships with their children following imprisonment - also offered as MBiomedSc
Supervisor: Dr Mark Stoove, Head, Head of HIV, AIDS and STI Research, Centre for Population Health, Burnet Institute
Project Site: Burnet Institute
Contact: stoove@burnet.edu.au
Project Description: Connection with family, particularly dependent children is often a key factor in the psychological and social welfare of women in prison and those transitioning from prison to the community. This project will examine structural and environmental factors such as the operation of the Victorian criminal justice and welfare systems and the way these factors impact on women's relationships with their children. The study will involve a desktop review of key policy documents and other 'grey literature' and interviews with key informants to identify systemic barriers and enablers to maintaining connection with children, and how these ultimately impact on the in contact with the criminal justice system.

225. 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 substitution 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

226. Understanding changes in haemostasis during pregnancy and pregnancy complications – also offered as MBiomedSc
Supervisors: A/Prof Joanne Said and Dr Briony Cutts
Project Site: Centre for Health Research and Education, NorthWest Academic Centre, 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.

227. 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.

### 228. 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.

### 229. 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. Yet, in humans, maternal serum progesterone concentrations do not significantly decrease at labour onset, 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.

**Techniques:** Tissue culture, siRNA gene silencing, Real-time RT-PCR, western immunoblotting, microarray.

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.

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

### 230. 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

**231. 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

**Subject category:** Pregnancy Research

**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
2014/15 KEY DATES

Aug-November 2014: Contact potential supervisors to discuss Honours projects (Step 1)
29 August 2014: Open date to register online application
Mid September 2014: Open date to lodge project preferences through HATS
14 November 2014: Closing date to register online application (Step 2)
28 November 2014: Closing date to lodge project preferences through HATS (Step 3)
3rd wk December 2014: First round of offer letters sent by mail to students
5 January 2015: Closing date for acceptance/rejection by students of First Round offers
9 January 2015: Second round of selection and mailing of offer letters begins
25 January 2015: Deadline for Late Applications
16 February 2015: Honours 2015 Program commences / Melbourne Academic Centre at 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: students who meet the minimum entry requirements for entry to MDHS Honours does not guarantee a place in the Honours program. All successful applicants will also need to be selected for admission by the department. The University of Melbourne handbook contains detailed information about the subjects available and entry requirements for departments offering Honours. The 2011 handbook is available at https://handbook.unimelb.edu.au.

For further details see the Department of Medicine Honours Website: http://honoursrmh.unimelb.edu.au/
Faculty of Medicine, Dentistry & Health Sciences website: http://sc.mdhs.unimelb.edu.au/entry-requirements

HONOURS COURSEWORK

BIOM40001 – Introduction to Biomedical Research (12.5%) – Semester 1
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 – Advanced Coursework (12.5%) – Semester 1
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 – Research Project (75%) – Semester 1 & 2
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: Written research report (thesis) to be submitted. 80% 
Formal Thesis Oral presentation. 20%
### HOW TO APPLY - HONOURS

**Course Codes:**
- Bachelor of Biomedicine (Honours) – BH-BMED
- Bachelor of Science (Honours) – BH-SCI

Melbourne Academic Centre (RMH) Enrolling Unit is: Department of Medicine (RMH)

### 2014 APPLICATION FOR HONOURS IN THE FACULTY OF MEDICINE, DENTISTRY & HEALTH SCIENCES (FMDHS)

If you wish to be considered for Honours in 2015, and you would like to undertake your project and coursework with the Melbourne Academic Centre at RMH, Faculty of Medicine and Dentistry Sciences or affiliated institute (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 2015. [http://honoursrmh.unimelb.edu.au/](http://honoursrmh.unimelb.edu.au/)

#### STEP 2: Lodge an online application

Lodge an online application between Friday 29 August to Friday 14 November 2014: [http://sc.mdhs.unimelb.edu.au/how-apply](http://sc.mdhs.unimelb.edu.au/how-apply)

**Note:** Applicants must select MDHS Student Centre as their area of interest on their application to ensure their application is directed to the correct area.

Applications for Honours are lodged to MDHS via one of the following processes:

a) Current and previous University of Melbourne applicants (local and international) apply online and select the ‘RETURN APPLICANTS, CURRENT STUDENTS or PREVIOUS STUDENTS” option.

b) Non-University of Melbourne applicants apply online and select the ‘FIRST TIME APPLICANTS” option.

**All previous and current University of Melbourne applicants please note the following:**

Students who have an existing Student ID number in the university of Melbourne system but who apply as “First Time Applicants” will have their records data matched and merged. This will delay the processing of their application.

**All non-University of Melbourne applicants please note the following:**

Please provide an original or certified copy of your complete official Academic Transcript to the MDHS Student Centre as part of your application and ensure that you include your University of Melbourne applicant or student number.

Documents should be sent to the address below. (Please include your Applicant / Student ID in all correspondence with the University)

Attention: Honours Student Advisor  
MDHS Student Centre, Level 1, Brownless Biomedical Library  
University of Melbourne, Victoria, 3010. Australia

If you have any queries contact the MDHS Student Centre Honours Advisor Mr Victor Liu  
T: +61 3 9035 3405  
E: victliu@unimelb.edu.au

**It is essential students carry out Step 2 BEFORE they carry Step 3. Note the closing date for Step 2 is 14 November 2014.**

#### 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.

Please note that HATS is ONLY available to On-Time applicants for Start Year entry.

**HATS will open mid September 2014 and will close at 5pm on Friday 28 November 2014.**

If you have lodged your online application for Honours, you will receive an email with your HATS password in mid-September so you can lodge your project preferences.

**Please note that you must ONLY list project preferences for which you have already made contact with the supervisor**
**LATE APPLICANTS**  
Those applying after the Application Closing Date in mid November must complete Step 3 by submitting a hard copy “Late Application – Project Preference Form”. Late applications will be assessed in January as part of the Round 2 selection process. The “Late Application – Project Preference Form” will be made available on the MDHS Honours “How to Apply” web page after the Application Closing Date, but only allows applicants to list a maximum of three (3) project preferences.  

To carry out STEP 3 in HATS you will need to:

A. **Enter your Application ID into HATS**
B. **Enter your HATS password**  
HATS passwords are issued once a week. Your HATS password will be emailed to you on the Monday following the date you completed Step 2.
C. **Click on Preferences then Search Projects**  
Use this search to make sure that the project(s) you wish to apply for are present in HATS. If you cannot find the project you are interested in, you should contact the supervisor of these projects, who will be able to take steps to have the project details entered into HATS.
D. **Click on Preferences then Lodge/Update Preferences to lodge your project preferences with HATS.**  
You can update/change your preferences as many times as you wish. However, you must ensure that your final preference list (in order of 1-10; you must enter at least 1 preference, and you can enter up to 10) is lodged by **Friday 28 November 2014.** This list will be supplied to Departments to allow them to carry out their selection process in early December 2013

You will receive a round one offer letter for the highest preference project you have been offered by mail before Christmas. You can choose to accept the offer or not. If you choose not to accept, you will be considered for selection by Departments for the second round in mid January.

**Note:** The Department of Medicine (RMH) is the enrolling unit for the Melbourne Academic Centre (RMH) Honours Program.

**For further details on ‘How to Apply’ please refer to the following websites:**

- Department of Medicine Honours: [http://honoursrmh.unimelb.edu.au/](http://honoursrmh.unimelb.edu.au/)
- Faculty of Medicine, Dentistry and Health Sciences Honours: [http://sc.mdhs.unimelb.edu.au/why-honours](http://sc.mdhs.unimelb.edu.au/why-honours)
- Faculty of Medicine, Dentistry and Health Sciences Application Process: [http://www.mdhs.unimelb.edu.au/future_students/honours/application_process](http://www.mdhs.unimelb.edu.au/future_students/honours/application_process)

**IMPORTANT NOTE:**
Please note that the above process is for applications to the Biomedical and Health Sciences Departments ONLY. Students interested in submitting preferences for projects in Genetics, the Melbourne School of Psychological Sciences, Optometry and Vision Sciences, Veterinary Science or Zoology, must contact those departments directly.

**STEP 3: Offers**

Round 1 offer letters are sent to applicants via post and email around the 3rd week of December. Students MUST accept their offer by the Offer Lapse Date noted in their offer letter.

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.

**Please note:** Not all students who meet the minimum entry requirements and make contact with supervisors will be offered a place in a MDHS Honours course. Entry is conditional upon selection by the Departmental Selection Committee and is academically competitive.

**MID-YEAR ENTRY**

Students applying for Mid Year entry must contact potential supervisors to confirm if the department is offering mid-year entry (Step 1). Submit an online application for entry to the course (Step 2) and submit a hard copy “Mid Year Project Preference Form”. The Mid Year form can be obtained by contacting the MDHS Honours Student Advisor Mr Victor Liu  
T: +61 3 9035 3405 E: victliu@unimelb.edu.au
MASTER OF BIOMEDICAL SCIENCE - COURSEWORK
Previously Master of Science (Biomedical and Health Sciences)

The Master of Science (Biomedical and Health Sciences) 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 MSc is a two year course that can be taken in place of Honours.

Students must complete 200 points comprising of:

<table>
<thead>
<tr>
<th>Component</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Research Project (Literature Review, Thesis, &amp; Ora Presentations)</td>
<td>125</td>
</tr>
<tr>
<td>Core Discipline subject (Introduction to Biomedical Research BIOM40001)</td>
<td>12.5</td>
</tr>
<tr>
<td>Discipline Subjects</td>
<td>37.5</td>
</tr>
<tr>
<td>Professional Skills</td>
<td>25</td>
</tr>
</tbody>
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**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 MSc projects available with the Royal Melbourne Hospital Academic Centre please see projects listed as available for MBiomedSc in the 2015 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://medicine.unimelb.edu.au/study-here/postgraduate_coursetwork_programs/master_of_biomedical_science](http://medicine.unimelb.edu.au/study-here/postgraduate_coursetwork_programs/master_of_biomedical_science)

   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.

**Domestic Applications:**
Closing date: 28 November 2014
Offer date: 15 December 2014
Semester 1 start: 16 February 2015

**International Applications:**
Closing date: 31 October 2014
Offer date: 21 November 2014
Semester 1 start: 16 February 2015

4. Wait for your letter of offer in the mail early-mid December. If you do not receive an offer for one, you will be assessed for any other applications made.

5. Complete the Faculty acceptance form and follow enrolment instructions for 2014.
As for Honours, Commonwealth supported places (CSP) are competitively available for eligible Masters students and HECS funding arrangements for fees apply. Overseas and Australian Fee places are also offered (and Fee Help support is available for local students). Students entering the Masters program need to check the banding classification of specific subjects to determine overall fees payable as some selected Discipline and Professional Skills subjects may be in fee bands which are different (possibly lower) than fee bands which apply to natural and physical sciences, mathematics and statistics fee band subjects. Some students may qualify for scholarship funding. http://www.futurestudents.unimelb.edu.au/admissions/fees


ENQUIRIES

Melbourne Medical School Masters Coordinator
Prof Lea Delbridge
Department of Physiology
lmd@unimelb.edu.au

Melbourne Academic Centre Honours/MBiomedSc Coordinators:

Dr Chris French E: frenchc@unimelb.edu.au,

A/Professor Caroline Marshall E: Caroline.Marshall@mh.org.au

Melbourne Academic Centre (RMH) Honours/MBSc Administrator: Mary Ljubanovic E: mlju@unimelb.edu.au

RMH ACADEMIC CENTRE DEPARTMENT LINKS:

Melbourne Academic Centre (RMH): http://www.rmh.unimelb.edu.au

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.obsbgyn.unimelb.edu.au/