The Royal Melbourne Hospital Academic Centre
(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

and

Master of Biomedical Science
COURSE CODE: MC-BMEDSC

PROJECTS 2014

Medical Research — Bench to Bedside

Affiliations:
The Royal Melbourne Hospital, The Royal Women’s Hospital, NorthWest Academic Centre (NWAC), National Ageing Research Institute (NARI), 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, Northern Clinical Research Centre, The Northern Hospital.
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3. What causes memory loss after surgery and anaesthesia?
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180. Neuropharmacology of animal models of schizophrenia and depression: Role of oestrogen – also offered as MBSc
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183. Identifying substrates for Selenium Binding Protein 1 and their functional consequence in the human brain – also offered as MBSc
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186. Investigating the stress response in a mouse model of autism
187. Investigating effects of cannabinoids on sensorimotor gating in a mouse model of autism
188. How does Age of Illness Onset affect severity and extent of MRI Brain Structural Abnormalities in Schizophrenia - also offered as MBSc
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191. Characterisation of physiological stress responses in patients with depression and epilepsy - also offered as MBSc
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194. Characterising morphological abnormalities of the cerebral cortex in established schizophrenia: A structural MRI study - also offered as MBSc
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210. Key strategies for engaging users of Social Networking Sites for health promotion - also offered as MBSc

211. Providing testing reports to general practitioners as an intervention to increase Chlamydia screening - also offered as MBSc

212. Chlamydia epidemiology in Australia - also offered as MBSc

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 MBSc

214. Risk behaviours and HIV among young gay and bisexual men - also offered as MBSc

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

216. Understanding risky single occasion drinking and links to harms in a cohort of young Melburnians - also offered as MBSc

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

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

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

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

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222. Understanding sex work in Vanuatu – also offered as MBSc

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234. How do hormones work: investigating new steroid receptors

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236. The effect of maternal diabetes on placental function: implications for fetal growth and development

237. The endothelial-trophoblast interaction during pregnancy

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2013/14 KEY DATES

HONOURS ENTRY REQUIREMENTS

COURSE WORK

HOW TO APPLY

MASTER OF BIOMEDICAL SCIENCE (MC-BMEDSC)

ENQUIRIES

RMH ACADEMIC CENTRE DEPARTMENT LINKS:
AGEING

1. Exploring data from COHORT (Cooperative Huntington’s observational research trial) - a long-term international observational study in Huntington’s disease - also offered as MBSc

   Supervisor:  Dr Anita Goh
   Other staff:  Professor Nicola Lautenschlager, Emeritus Professor Edmond Chiu, Professor David Ames, Dr Samantha Loi, Stephanie Antonopoulos
   Project Site:  Academic Unit for Psychiatry of Old Age, St George’s Hospital, Cotham Rd, Kew
   Contact:  Anita Goh T: 9816 0513 E: goha@unimelb.edu.au

   Project Description: This long-term observational study was conducted at North American and Australian Huntington Study Group (HSG) sites. The goal of COHORT was to collect information in order to learn more about HD, potential treatments, and to plan future research studies of experimental drugs aimed at postponing the onset or slowing the progression of HD. This study recruited individuals of any age who have clinically diagnosed features of HD in the setting of a confirmatory family history, adults, 18 years of age and older & older adolescents (15-17 years old) who are at-risk for developing HD and adults, 18 years of age and older that are part of an HD family. At each visit, individuals participating in COHORT underwent a clinical evaluation, including blood draws for genetic testing of the CAG polymorphism and for other genetic changes.

   This project involves mining the updated cut of the COHORT database. This revised cut of the COHORT database contains clinical, family history and genotyping data collected from 2/14/06 to 7/07/11. Data is available for about 3,200 subjects. The dataset includes:
   - 1,512 Individuals with manifest HD
   - Approximately 450 Individuals at-risk for HD who carry an expanded number of CAG repeats
   - Approximately 430 Individuals at-risk for HD who do not carry an expanded number of CAG repeats
   - 691 Individuals who have married into the family and serve as controls
   Data from 7,380 visits are included. Some subjects have as many as 6 visits.

   Opportunities:
   - The data and samples will provide researchers with a valuable resource to address a wide variety of research questions in Huntington’s disease.
   - The project offers students an opportunity to develop research skills in a comprehensive international dataset, as well as develop skills in literature reviewing, data analysis, and epidemiological study skills
   - Internationally renowned study and research team with international recognition.
   - Dataset is already complete and accessible (thesis easily achievable in time frame)
   - Publication of results

2. Understanding and controlling seizures in people with Alzheimer’s disease - also offered as MBSc

   Supervisors:  Professor Patrick Kwan, Dr Chris French, 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 Chris French, E: frenchr@unimelb.edu.au

   Project Description: Project description: Alzheimer’s disease (AD) is the most common cause of dementia. Its prevalence is set to rise further with the ageing of the population. Seizures occur in up to 64% of people with AD during their course of illness, imposing additional burden on medical care and disability. Recurrent seizures and their treatment with conventional antiepileptic drugs (AEDs) may exacerbate the progression of AD, yet the reasons for the increased risk are unknown, and there are no specific treatments for seizures in AD patients. The relationship between the pathological processes of AD and neuronal hyperexcitability is poorly understood.

   This project aims to better understand the electrophysiological properties of AD using the Tg2576 transgenic mice which are a well-established AD model. We have performed pilot study in Tg2576 mice using repeated electrical stimulation via
the left amygdala. In line with clinical observation, these mice demonstrated increased susceptibility to the development of acquired epilepsy.

**Project 1: Neuronal excitability and response to AEDs in vitro.** In vitro electrophysiology will be used initially to observe and then characterize possible “seizure proneness” in the Tg2576 mouse. Slices of brain (hippocampus) tissue will be obtained from the wildtype and transgenic animals. General observations quantifying the threshold of pharmaceutically induced seizures will first be made. Properties of synaptic transmission and neural plasticity (factors closely involved in the development of epilepsy) will then be characterised by measuring “long term potentiation”. Higher resolution experiments will then be performed using single neuron recording to provide a detailed assessment of excitatory and inhibitory neurotransmission, to particularly look for imbalances that are likely to result in seizure activity. Finally, responses of in vitro seizures to different classes of drugs will then be measured. The student will learn valuable skills in cell culture and electrophysiology.

**Project 2: Sensitivity to epileptogenesis of AD mouse model.** The sensitivity to the development of secondary epilepsy (“epileptogenesis”) in AD will be tested using the electrical amygdala kindling model, one of the most widely accepted rodent model of acquired epilepsy. Ability of established AEDs and novel compounds to retard epileptogenesis will be studied. The brains will be sectioned to confirm bipolar placement and assessed for the histological endpoints. The student will acquire techniques in animal handling, injections, dissection, immunohistochemistry, western blotting.

3. **What causes memory loss after surgery and anaesthesia?**
   - **Supervisor:** Dr. Jennifer Callaway
   - **Co-Supervisors:** Prof Colin Royse, Dr Trisha Jenkins (RMIT)
   - **Project Site:** Dept of Surgery, RMH and Dept of Pharmacology UoM
   - **Contact:** Dr Jennifer Callaway T: 8344 8304; E: callaway@unimelb.edu.au

   It is remarkably common to experience loss of memory and concentration following surgery and anaesthesia. While this is more likely to be long-lasting and cause significant problems in people over the age of 65 year, it can and does happen in young patients. This phenomenon is now recognised and is referred to as Post-Operative Cognitive Dysfunction (POCD) and the cause is currently unknown. We are currently investigating the possibility that type of anaesthesia, age, and inflammation or infection may interact to cause POCD.

   This project will involve considerable hands-on work in anaesthetised and conscious rats. The techniques involved will include surgery, blood sampling, memory testing methods as well as investigation of brain pathology and assessment of inflammatory and other markers using immunohistochemistry and ELIZA assays. This exciting project will give the right student the opportunity to work in a research science laboratory as well as to interact with anaesthetists and surgeons with direct interest in POCD research.

   **Two projects are on offer for Honours 2014.**

4. **Lifestyle Factors for healthy Ageing – also offered as MBSc**
   - **Supervisor:** A/Professor Cassandra Szeoke
   - **Project Site:** Dept of Medicine, UoM, Parkville, Vic 3052.
   - **Women’s Healthy Ageing Project (WHAP)**
   - **Contact:** A/Professor Cassandra Szeoke 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.

   Major benefits from this study are:-
   1. There is opportunity for publication within one year
   2. Rich database with lifestyle data from mid-life and spanning over 20 years
   3. This project will suit a candidate with an interest in media or commercialisation in the lifestyle and ageing area

5. **Causes of Depressive Symptoms in Early Ageing – also offered as MBSc**
   - **Supervisor:** A/Professor Cassandra Szeoke
   - **Project Site:** Dept of Medicine, UoM, Parkville, Vic 3052.
   - **Women’s Healthy Ageing Project (WHAP)**
   - **Contact:** A/Professor Cassandra Szeoke 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 - also offered as MBSc
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 at risk populations in an epidemiologically sampled cohort of women. These measures include the use of Magnetic Resonance Imaging (MRI) neuroimaging quantifying the accrual of white matter hyperintensities (WMH) as a measure of cerebrovascular disease (CVD). It has been found that white matter hyperintensity volume could predict 1-year cognitive decline, and therefore should be considered as a variable of interest in AD trials.

Major benefits from this study are:-
The study has data over 20 years already collected
There is opportunity for a publication
This project will suit a candidate with an interest in neuroimaging

7. Vitamin D deficiency and balance - also offered as MBSc
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 an interest in media or commercialisation.

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

*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: cszoene@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 ground breaking research

**NATIONAL AGEING RESEARCH INSTITUTE (NARI)**

NARI is an independent, NHMRC accredited, Medical Research Institute located in Parkville. The central mission of the organisation is to be a centre of excellence in Australia for medical, psychological and social research into all aspects of ageing and thereby improve the health and quality of life for older people. The Institute conducts a full array of research activity, from the basic biology of ageing through clinical research programs and public health/service evaluation research. Within the Clinical Research laboratory there are existing programs examining dementia and memory function, painful diseases common in older persons (e.g. osteoarthritis), falls and balance, depression and disability as well as the study of better measurement techniques (psychometric and physiological) for use in older adults. We have a number of Honours, Masters, PhD and DPsych students working in these areas of research and are currently seeking new students to study within the broad areas of neurophysiology and psychophysiology of pain. Scholarships may be available to a limited number of applicants. Some examples of current and available projects are listed below:

10. **Assessing the burden of caregiving of older people with type 2 diabetes - also offered as MBSc**

*Supervisors:* Dr Irene Blackberry and Dr Briony Dow

*Project Site:* National Ageing Research Institute, 34-54 Poplar Road, Parkville, Vic 3052.

*Contact:* Dr Irene Blackberry T: 8344 3373 E: iblackberry@unimelb.edu.au

*Project Description:* Type 2 diabetes is highly prevalent among the elderly. Yet little is known about their caregivers, who provide a significant amount of informal care to alleviate diabetes burden, support self-care and assist older people to remain in the community. Research evidence on caregiving has primarily been derived from people with cognitive decline or disability and this may not be readily transferrable to type 2 diabetes, a progressive chronic condition. Given that 80% of type 2 diabetes management in Australia is undertaken in general practice and general practice is the first point of call to access care and services, this gives an ideal opportunity to target and provide support for both caregivers and older people with type 2 diabetes living in the community to achieve better diabetes control. This project will answer key questions about burden and challenges faced by the caregivers and their unmet needs in caring for older people with type 2 diabetes using mixed qualitative and quantitative methods. It will have important implications as disease management and self-care activities are increasingly being placed upon older people with type 2 diabetes and their caregivers.
This project offers student an opportunity to develop communication skills with research participants, as well as research skills including literature review, quantitative and qualitative data analysis, and epidemiological study skills.

11. Diabetes management in residential aged care facilities - also offered as MBSc  
Supervisors: Dr Irene Blackberry and Dr Briony Dow  
Project Site: National Ageing Research Institute, 34-54 Poplar Road, Parkville, Vic 3052.  
Contact: Dr Irene Blackberry T: 8344 3373 E: i.blackberry@unimelb.edu.au  

**Project Description:** The number of older people living in a Residential Aged Care Facility (RACF) increases with the ageing population. It is estimated that the proportion of Australians aged 65 year and over will be 22% by 2031, of which nearly 10% will be in RACFs. Management of diabetes among older people is complex due to deterioration of physical function and increased prevalence of co-morbid conditions. In addition, geriatric syndromes such as cognitive impairment, falls, incontinence, low body mass index, dizziness, vision impairment or hearing impairment are present in half of people aged 65 years and over. Evidence around diabetes management for older people living in RACF is currently lacking. This project aims to address this research gap by utilising mixed quantitative and qualitative methods to describe current diabetes management and explore unmet needs among health care professionals.  
This project offers student an opportunity to undertake medical records audit, become familiar with diabetes medications, biochemical and clinical measures. Semi structured interviews will be conducted with health care professionals providing care in RACF.

### ALCOHOL

12. Alcohol health promotion using mobile phones - also offered as MBSc  
Supervisor: Professor Paul Dietze, Co-Head, Alcohol & Other Drug Research, Centre for Population Health, Burnet Institute  
Project Site: Burnet Institute  
Email: E: pdietze@burnet.edu.au  

**Project Description:** Binge drinking is a serious and common problem among Australian youth. Novel methods of health promotion are urgently needed to address this problem. This project is a scoping study investigating the potential uses of and acceptability of various health promotion approaches to binge drinking, including mobile phone SMS and smartphone apps.  
The project will involve a mixed methods approach working with young people. The project will begin by scoping and evaluating existing health promotion interventions using smart phones. Studies will include quantitative methods - for example, online surveys and analysis of existing data. Qualitative methods including focus groups and in-depth interviews with young people will also be applied. The project could lead to or include the development of a smart phone app and testing of health promotion messages to be sent via SMS.

13. Street drinking in Footscray - also offered as MBSc  
Supervisor: Professor Paul Dietze, Co-Head, Alcohol & Other Drug Research, Centre for Population Health, Burnet Institute  
Project Site: Burnet Institute  
Email: E: pdietze@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.

14. Why do some people with hepatitis C continue to drink? - also offered as MBSc  
Supervisor: Professor Margaret Hellard, Head, Centre for Population Health, Burnet Institute  
Project Site: Burnet Institute  
Email: 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.

**ARTHITIS AND INFLAMMATION RESEARCH**

15. **Anterior cruciate ligament injury during high risk movements – also offered as MBSc**

   **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 systems.

   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.

16. **Examining the Quality of Orthopaedic Care in Australia - also offered as MBSc**

   **Supervisors:** Dr Megan Bohensky /Professor Danny Liew  
   **Project Site:** Melbourne EpiCentre, Royal Melbourne Hospital (Block E, Level 7), Department of Medicine, University of Melbourne  
   **Contact:** Dr Megan Bohensky T: 9342 8285|E: megan.bohensky@unimelb.edu.au; Professor Danny Liew T: 9342 8285|E: dyliew@unimelb.edu.au

   **Background and hypothesis:** This study is part of a larger study examining various dimensions of healthcare quality in orthopaedic care. This first phase of the study seeks to identify the incidence of adverse outcomes from major and minor orthopaedic surgeries using routinely collected data. The second phase of the study will employ cost-modelling and decision-modelling to understand the cost implications if preventative methods were to be utilised according to different strategies.

   **Methods:** We have data from the department of health on all orthopaedic surgeries (public & private hospitals) performed in Victoria from a previous study (July 2000- June 2009) that we plan to follow-up to identify adverse outcomes (specifically thromboembolism and infections) using data linkage. By linking our data to disease registries and emergency presentation data, we can identify adverse outcomes related to orthopaedic surgeries.

   **Acquired skills:** This project would suit a student that is seeking to learn skills in data analysis, data linkage, regression analysis, database management and cost-effectiveness analysis. Work hours would also be flexible.

**ARTHRITIS AND INFLAMMATION RESEARCH CENTRE**

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

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

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

17. 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.

18. 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.

19. The role of Interferon Regulatory factors in Arthritis  
   **Supervisors:** Dr Derek Lacey, Dr Andrew Cook and Prof John Hamilton  
   **Project Site:** Arthritis Research and Inflammation Centre, Department of Medicine (RMH), University of Melbourne  
   **Contact:** Dr Derek Lacey  T: 8344 3292  E: dlacey@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.

20. The role of a novel macrophage inflammatory mediator in arthritis  
   **Supervisors:** Dr Derek Lacey, Dr Andrew Cook and Prof John Hamilton  
   **Project Site:** Arthritis Research and Inflammation Centre, Department of Medicine (RMH), University of Melbourne  
   **Contact:** Dr Derek Lacey  T: 8344 3292  E: dlacey@unimelb.edu.au  
   **Project Description:** Through a microarray screen of inflammatory macrophages we have identified a novel potential therapeutic target for the treatment of arthritis. Macrophages are key cells involved in the destruction of joints during rheumatoid arthritis. In this project you will investigate the expression of this potential therapeutic target in patients’ tissue samples and in an inflammatory model of arthritis, and determine if targeting this protein would be a beneficial treatment. In this project you will be cutting tissue sections and measuring the expression of this novel protein. You will
be inducing a murine model of arthritis and measuring a number of clinical parameters, collecting and processing tissue, and measuring gene/protein expression by histology, real-time PCR, Western blotting and FACS analysis. You will also be using siRNA, and nanoparticles to deliver therapeutic drugs in the arthritis model.

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

### 21. Therapeutic drug delivery by nanoparticles

**Supervisors:** Dr Derek Lacey, Dr Yan Yan and Prof John Hamilton  
**Project Site:** Arthritis Research and Inflammation Centre, Department of Medicine (RMH), University of Melbourne  
**Contact:** Dr Derek Lacey T: 8344 3292 E: dlacey@unimelb.edu.au

**Project Description:** Nanoparticle delivery of therapeutic drugs in medical applications is an exciting and innovative concept. Macrophages are key cells involved in the destruction of joints during rheumatoid arthritis. This project will explore whether nanoparticles can be used as drug delivery vehicles for targeting macrophages in the treatment in inflammatory diseases. You will investigate how macrophages take up nanoparticles and what properties are needed in nanoparticles for optimal uptake. You will be culturing cells, making nanoparticles and measuring various cellular endpoints. 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

### 22. 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 3290 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).

### 23. 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 3290 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).
24. Bone health in children and young people with epilepsy treated with anti-epileptic drugs (AEDs) – also offered as MBSc

Supervisors: Professor 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.

25. Real world assessment of falls risk using novel mobile technology – also offered as MBSc

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.

26. Enhancing fracture risk prediction in osteoporosis - also offered as MBSc

Supervisors: Professor John Wark, Dr Ashwini Kale and Dr Andrew Briggs
Project Site: Department of Medicine (RMH), University of Melbourne, Parkville Campus
Contact: Prof. John Wark: E: jdwark@unimelb.edu.au; Dr Andrew Briggs: E: A Briggs@curtin.edu.au; Dr Ashwini Kale: E: akale@unimelb.edu.au

Project Description: Osteoporosis is a common condition where bones are fragile leading to fractures, predominately of hip, spine, forearm and ribs. Dual energy Xray absorptiometry (DXA) performed using anteroposterior projection scanning of the spine is the current method of choice for estimating vertebral fracture risk in a clinical setting, but has limitations in predictive value. Our preliminary data suggest that lateral projection DXA using subregions of the lumbar vertebral bodies as regions of interest provides superior fracture risk prediction and could be a major advance in clinical assessment of osteoporosis.

Aims and Methods: This project will involve recruiting and evaluating several patient groups using this novel approach to osteoporosis assessment. Once validated, this methodology will allow more reliable identification of patients at high fracture risk. The ultimate aim is to refine diagnostic methods for the improved care of osteoporosis patients.

27. Validation of bone density testing in women of south Asian background - also offered as MBSc

Supervisors: Professor John Wark, Dr Ashwini Kale
Project Site: Department of Medicine (RMH), University of Melbourne, Parkville Campus
Contact: Prof. John Wark: E: jdwark@unimelb.edu.au; Dr Ashwini Kale: E: akale@unimelb.edu.au

Project Description: Osteoporosis is a common condition where bones are fragile leading to fractures, predominately of hip, spine, forearm and ribs. Osteoporotic fracture incidence varies widely in different countries and ethnic groups, potentially related to genetic, nutritional, environmental and lifestyle factors. Bone density measurement by dual energy Xray absorptiometry (DXA) is currently the most useful way of assessing bone strength and an individual's fracture risk. However, normal ranges for bone density vary between ethnic groups and measurements of bone density have mostly been done in white or western people. Bone density in people of south Asian background typically has been interpreted
using reference data taken from white people. This may not provide an accurate reflection of true fracture risk in this population.

**Aims and Methods:** This project will involve recruiting and evaluating bone density by DXA in females of south Asian background and above the age of 30 years, and comparing their bone density values to Caucasian Australian females. Peak bone density will be estimated and age-ethnicity-specific bone density reference curves for women of south Asian background will be constructed.

Ultimately, this study will allow for appropriate estimation of fracture risk in this section of the Australian population.

28. **Does the use of health and community-based services following an osteoporotic fracture vary by socioeconomic status? - also offered as MBSc**

  **Supervisors:** Dr Sharon Brennan and A/Prof Kerrie Sanders
  **Project Site:** NWAC Sunshine Hospital, St Albans
  **Contact:** Dr Sharon Brennan T: 5226 7915 E: sbrennan@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 AusICUROS 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.

29. **Are annual physical functioning assessments predictive of falls risk in older women? - also offered as MBSc**

  **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:** 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’. Approximately 50 participants in the placebo group have had annual assessments of balance, gait, and muscle strength in conjunction with data collection on medication use and medical conditions.

  This project would investigate an association between risk of falling and the longitudinal results of their annual physical functioning assessments among these women who were randomised to receive placebo. The work is unique in the 5-year duration of follow-up and robust methodology used to ascertain falls. The results will produce sound evidence to support or otherwise the validity of physical function assessments in older women at increased risk of falls and fractures in predicting future risk of falls.

30. **Are there differences in the characteristics of older women who fall at home compared with those who fall outside the home? - also offered as MBSc**

  **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.

31. **How does dietary calcium intake affect health outcomes? - also offered as MBSc**

  **Supervisors:** Prof Peter Ebeling, Prof Dallas English and A/Prof Kerrie Sanders
  **Project Site:** NWAC Sunshine Hospital, St Albans
  **Contact:** Prof Peter Ebeling T: 8395 8115 E: peterre@unimelb.edu.au

  **Project Description:** There is a concern that calcium supplement use is associated with an increased risk of adverse cardiovascular outcomes. Increasing dietary calcium may improve bone health and reduce fractures without increasing the risk of adverse cardiovascular events, including acute myocardial infarction. We have established a database of health
outcomes over 20 years from the Health 2020 cohort, a longitudinal study of over 41,000 Victorians. All participants have had dietary calcium intake assessed on two occasions. Through database management skills and basic statistical analysis this project involves relating diet calcium with health outcomes during the study. The results will provide important data regarding effects of diet calcium on health outcomes in a large established cohort.

32. **How does being born with extremely low birth weight or extremely pre-term affect bone mass, body composition and insulin sensitivity? - also offered as MBSc**  
**Supervisors:** Prof Peter Ebeling, Prof Glenn McConell and Dr Gunveen Kaur  
**Project Site:** NWAC Sunshine Hospital, St Albans  
**Contact:** Prof Peter Ebeling  
T: 8395 8115  
E: peterre@unimelb.edu.au  
**Project Description:** There is a rapidly increasing prevalence of extremely low birth weight (ELBW; <1000g birth weight) and extremely preterm (EPT; <28 weeks’ gestational age) survivors. Although 55% of <1000g babies have low bone mineralization, the long-term consequences of metabolic bone disease (MBD) of prematurity on later bone health are not well described. In particular, the influence of surviving ELBW/EPT birth on the peak bone mass achieved has not been assessed. Similarly, ELBW/EPT survivors also develop obesity and insulin resistance, that continues into young adulthood, increasing their lifetime risk for type 2 diabetes. Through database management skills and basic statistical analysis this project involves assessing bone mass, body composition and insulin sensitivity in ELBW/EPT survivors from an established cohort at 8 years of age. The results will provide important data regarding bone mass, body composition and diabetes risk in a large established cohort.

33. **A critical analysis of Sunsmart behaviour in young Australian women - also offered as MBSc**  
**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. **Vitamin D, mood and body weight: how are they linked? - also offered as MBSc**  
**Supervisors:** Prof John Wark, Ms Nicola Reavley, Ms Stefanie Hartley, Prof Suzanne Garland  
**Project Site:** Department of Medicine, (RMH) Parkville Campus  
**Contact:** E: jdwark@unimelb.edu.au  
**Project description:** Vitamin D deficiency is linked to a range of chronic health conditions including poor cardiovascular and metabolic health, and psychological morbidity. Furthermore, overweight and obesity (rapidly escalating concerns in young women) appear to be associated with low vitamin D levels; however, this relationship is not fully understood or elucidated. How are overweight and obesity associated with vitamin D and mood? The student will examine objective measures of BMI and serum vitamin D levels, and self-reported mood data. The independent association between weight and vitamin D status will be characterised.

35. **Measuring bone and muscle health in young women - also offered as MBSc**  
**Supervisors:** Prof John Wark, Ms Alexandra Gorelik, Ms Stefanie Hartley, Prof Suzanne Garland  
**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.

36. **Does air quality influence vitamin D status in young Victorian women? - also offered as MBSc**  
**Supervisors:** Prof John Wark, Ms Alexandra Gorelik, Ms Stefanie Hartley, Prof Suzanne Garland  
**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 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. This project would suit a student interested in statistical analysis, data modelling and environmental health.

37. Assessing the clinical usefulness of peripheral quantitative CT in fracture prediction - *also offered as MBSc*

Supervisors: Prof John Wark, Mrs Ashwini Kale, Ms Alexandra Gorelik, Dr Christopher Yates

Project Site: Department of Medicine, (RMH) Parkville Campus

Contact: jdwark@unimelb.edu.au

Project description: Bone density measurement by dual energy X-ray absorptiometry (DXA) is currently the most useful way of assessing bone strength and an individual’s fracture risk. However, at a population level, most low trauma fractures occur in people who have DXA bone density values below the young normal range but above the range defined as osteoporosis (so-called “osteopenia”). While DXA has a number of attractive attributes, it is not able to assess bone biomechanical indices nor to selectively measure the density of trabecular and cortical bone. These bone properties contribute to the risk of fracture and can be assessed using peripheral quantitative computed tomography (peripheral QCT). In this project we will assess the diagnostic role of pQCT in patients with bone fragility.

**Aims and Methods:** This project will involve recruiting patients who have sustained low trauma fractures despite not having osteoporosis by conventional DXA criteria, and assessing measures of fracture risk determined using pQCT. The contribution of this new technique to the specific diagnosis of osteoporosis will be evaluated and potentially a better understanding of the pathogenesis of low-trauma fractures will be obtained.

**BIOLOGY —WOMEN’S HEALTH**

38. Characterization of dysmenorrhea in young women

Supervisors: Prof John Wark, Dr Yasmin Jayasinghe, Ms Stefanie Hartley, Prof Suzanne Garland.

Project Site: Department of Medicine, (RMH) Parkville Campus

Contact: E: jdwark@unimelb.edu.au

**Project description:** Dysmenorrhea has not been well-studied in unselected populations of young women and has been largely neglected in the public health domain. What are the prevalence, risk factors and impact of dysmenorrhea in young Victorian women? This study will establish the prevalence of dysmenorrhea in a cohort of at least 200 young women and explore correlations with risk factors derived from a comprehensive health and lifestyle questionnaire. The impact of dysmenorrhea on mental health, productivity and lifestyle will also be examined.

39. Factors associated with self-perception of body image in young women - *also offered as MBSc*

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.

40. Acceptance of delayed cervical screening to 25 years of age, attitudes of health providers.

Supervisors: Prof Suzanne Garland, Dr Yasmin Jayasinghe and Ms Stefanie Hartley

Project Site: Molecular Microbiology Laboratory, Department of Microbiology and Infectious Diseases, RWH, Bio21 Institute

Contact: Prof Suzanne Garland: E: Suzanne.Garland@thewomens.org.au; Dr Yasmin Jayasinghe: E: yasmin.jayasinghe@unimelb.edu.au; Ms Stefanie Hartley: E: Stefanie.hartley@mcri.edu.au

**Project description:** Renew programs exploring new recommendations for onset and frequency of Pap testing in Australia with a possibility to delayed screening to 25 years of age. This is because cervical cancer is very rare in young women and screening largely picks up the low grade changes that may progress on their own. The aim of cervical cytology is to pick up high grade lesions which with appropriate treatment prevent cervical cancer. With the high uptake of the human papillomavirus (HPV) vaccine and changes being seen already with reduction in infection, and cervical lesions, and the fact that a lot of the changes of low grade in young women relate to the effects of HPV infection, it is being recommended by WHO and others, to start screening at 25 years of age, not 18 years as is current practice in Australia. How acceptable this will be is unknown, and we plan to audit the practitioners who take Pap cytology: gynaecologists, general
practitioners and nurse practitioners working in women’s health. Such information will highlight deficiencies of knowledge and attitudes and assist with education programs prior to any potential change and recommendations.

41. Understanding why some young women do not accept the HPV Vaccine?

Supervisors: Prof Suzanne Garland and Ms Stefanie Hartley
Project Site: Molecular Microbiology Laboratory, Department of Microbiology and Infectious Diseases, RWH, Bio21 Institute
Contact: Prof Suzanne Garland: E: Suzanne.Garland@thewomens.org.au; Ms Stefanie Hartley: E: Stefanie.hartley@mcri.edu.au

Project description: The Australian Government is funding an ongoing school-based program to combat human papillomavirus (HPV) related disease and has been doing so since 2007 for young girls. Recently they also agreed to funding young boys as an ongoing program. We know that the take up rate has been high with resulted reduction in infection and disease related to the HPV types. Within a vaccine effectiveness study, we have an online questionnaire which asks about cervical cancer screening, knowledge, as well as HPV vaccination status and knowledge. In this project we will explore by extending the questionnaire, with an educative intervention to measure better vaccine acceptance.

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

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.

43. Oxybutynin for menopausal symptoms

Supervisor: Professor Martha Hickey
Project Site: Royal Women’s Hospital
Contact: Professor Martha Hickey E: Martha.hickey@thewomens.org.au

Project Description: Hot flushes and night sweats affect around 80% of women at menopause. These can be distressing and impact on quality of life. Estrogen-containing HRT is effective, but many women wish to avoid hormones. Preliminary data indicate that oxybutynin (Ditropan) may be effective for sweating at menopause, but this has not yet been formally tested.

This study will be the first prospective trial of oxybutynin for hot flushes and sweats at menopause. This may lead to a novel non-hormonal therapy for menopausal symptoms.

44. Cognitive behavior therapy for menopausal symptoms

Supervisors: Professor Martha Hickey and Professor Myra Hunter (UK)
Project Site: Royal Women’s Hospital
Contact: Professor Martha Hickey Martha.hickey@thewomens.org.au

Project Description: Hot flushes and night sweats affect around 80% of women at menopause. These can be distressing and impact on quality of life. Estrogen-containing HRT is effective, but many women wish to avoid hormones. Cognitive behaviour therapy is effective in reducing the impact of vasomotor symptoms, but has not previously been compared with conventional therapies.

This will be the first study to compare standard pharmacological therapies for hot flushes with CBT
45. Sleep disturbance at menopause
Supervisors: Professor Martha Hickey and Dr Jeremy Goldin
Project Site: Royal Women’s Hospital and Royal Melbourne Hospital
Contact: Professor Martha Hickey Martha.hickey@thewomens.org.au

Project Description: Sleep disturbance affects around 40% of women at menopause. There is preliminary evidence that surgical menopause may lead to worse sleep disturbance than spontaneous menopause but this has not previously been addressed in prospective studies.
This prospective study will measure both subjective and objective parameters of sleep in women undergoing surgical menopause.

BRAIN INJURY

46. Targeting Tau phosphorylation to treat and prevent acquired epilepsy, neurodegeneration and neuropsychiatric disease following a brain injury - also offered as MBSc
Supervisors: Dr Sandy Shultz, Professor Terence O’Brien, Associate Professor Chris Hovens, Dr. Nigel Jones, Dr. Dennis Velakoulis.
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.

47. Post traumatic brain injury and epilepsy onset: Imaging the brain to investigate neural circuits and appropriate therapy interventions - also offered as MBSc
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 E: 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 cellular 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;

**Project 3:** Post-traumatic brain injury and neurogenesis: Tracking neurological changes in post-traumatic brain injury using advanced fluorescence imaging techniques.

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.

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**48. Repeated brain concussions – understanding mechanisms and proposing new treatments - also offered as MBSc**

**Supervisors:** Dr. Sandy Shultz, Prof. Terence O’Brien, Prof. Seong-Seng Tan

**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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**CANCER**

**49. 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: 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%. 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.

50. 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.

51. 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.

52. 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
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.
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.

53. **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 & 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

**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 upregulated 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.

54. **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 & 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

**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.

55. 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
E: Nuzhat.Ahmed@thewomens.org.au

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

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

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

Outcomes/Benefits: This proposal will compare the inherent traits and chemotherapy response of ovarian cancer cells in the presence and absence of MSC. MSC will be isolated from the ascites of ovarian cancer patients as well as from the placenta of women undergoing caesarean section. Differences in the biological phenotype of ovarian cancer cells in the presence and absence of MSC will be assessed by methods such as Western blot, quantitative PCR, immunofluorescence, flow cytometry, MTT and 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.

56. Synchrotron radiotherapy for the treatment of cancer

Project leaders: Prof Peter Rogers, Dr Yuqing Yang, Dr Premila Paiva and Dr Jeff Crosbie

Project Site: Department of Obstetrics & Gynaecology, Royal Women’s Hospital and Australian Synchrotron Facility, Clayton

Contact: Prof Peter Rogers E: parogers@unimelb.edu.au or Dr Yuqing Yang E: Yuqing.Yang@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, 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. 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.

57. 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 E: rluwor@unimelb.edu.au
**Project Description:** Traditionally, key-lock or on-off models dominate the molecular understanding of cellular signalling and disease development, with most studies focusing on linear molecular signalling cascades. With the advent of large scale molecular techniques such as proteomics and microarrays, cross-talk between signalling networks has been implicated to play critical roles in cancer development. It challenges the physiological validity of the switch on-off model.

Our lab, using molecular, cellular and gene targeted animal models as well as human patient samples, has established that the moderation of signalling sensitivity by other pathways, rather than a black-white switch on-off, specifically of the TGF (Transforming Growth Factor-) signalling pathways determines cancer progression. These findings have been published in top-ranking biomedical journals including *Nature Medicine* (11:845-52, 2005). Given the medical significance, current works in our lab are supported by 4 NHMRC and 1 Cancer Council grants totalling more than $2 million.

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

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

- **Project A:** Converting oncogene signalling to tumor killing in brain cancer
- **Project B:** Stat3 mediated impairment of TGF - signalling in head&neck and breast cancer
- **Project C:** Targeting TGF - signalling expansion in brain tumor invasion
- **Project D:** Regulation of TGF - signaling by Wnt pathway in the development of colon cancer

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

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

58. **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.

59. **Prostate Cancer – has it got all of its DUX in a row?**

**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:** Genome wide analysis has revealed that cancer most often occurs as a consequence of mutations or mis-regulation of particular molecular pathways. The same end effect – cancer – can arise through disruption at any point in the pathway. Recently, we have found that particular drugs known to kill Prostate cancer induce expression of a gene called DUX4. In other systems it has been shown that activation of this gene is capable of killing cells. A number of different factors are required upstream to turn the DUX4 gene on and downstream for it to elicit its killing effect. Interestingly, a number of these upstream and downstream factors are commonly mutated in Prostate cancer. We
therefore hypothesise that Prostate cancer avoids the inbuilt checks and balances that would otherwise kill cells that have become cancerous by mutating factors required for DUX4 activation and effect.

**Project Description:** To test our hypothesis we will knockdown elements of the DUX4 pathway and examine whether this makes Prostate cancer cells resistant to drug treatments. A number of different “second generation” drugs have been described recently that have a similar molecular mechanism to the one we are currently using. These will also be tested for their ability and effectiveness in inducing DUX4 and directing tumor cell death both in cell culture models and in pieces of prostate tissue obtained from patients.

60. **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.

61. **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 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 clinicalinformatics 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.

62. **Stat3 mediates Resistance to EGFR targeted therapy in Cancer - also offered as MBSc**

**Supervisors:** Dr Rodney Luwor

**Location:** Dept of Surgery, Level 5, Clinical Sciences Building, Royal Melbourne Hospital

**Contact:** Dr Rodney Luwor T: 9342-7703, E: rluwor@unimelb.edu.au

**Project Description:** During physiological processes the intracellular protein Signal Transducer and Activator of Transcription 3 (Stat3) is activated by many growth factors and cytokines (e.g. EGF, IL-6, IL-11...) 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 control over cancer progression.
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 interaction using in vitro models together with in vivo experiments using models of metastatic spread.

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.

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

67. Fertility issues in children and adolescents with cancer

Supervisors: Dr Yasmin Jayasinghe, Dr Lisa Orme, Dr Leanne Super

Project site: The Royal Children’s Hospital and The Royal Women’s Hospital, Melbourne

Contact: E: yasmin.jayasinghe@unimelb.edu.au

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

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

1. An audit of fertility preservation consultations for patients seen at The Royal Children’s Hospital between 2002 and 2014. This project is ethics approved. Specifically the audit will report the proportion of subjects who underwent such discussions, the procedures offered, barriers to uptake of the procedures, and complications.

2. Evaluation of a ‘Fertility Preservation Toolkit’. This is a recently introduced resource for health providers, patients and families which aims to improve knowledge and awareness of fertility preservation options for patients and families by providing information in a standardized manner.

3. Mining the haematology oncology database at the Royal Children’s Hospital to examine recovery of gonadal function according to cancer treatment in the young.

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

CANCER – WOMEN’S RESEARCH

68. microRNAs as puppeteers of ovarian cancer chemoresistance - also offered as MBSc

Supervisor: Dr Nuzhat Ahmed and Dr Mark Ziemann

Project Site: Women’s Cancer Research Centre, Royal Women’s Hospital

Contact: Dr Nuzhat Ahmed, Women’s Cancer Research Centre, RWH. Tel: 8345 3734; E: Nuzhat.Ahmed@thewomens.org.au

Project Description: Ovarian cancer is the second most common gynaecological cancer diagnosed in Australian women. Approximately 80% of patients diagnosed with ovarian cancer initially respond to chemotherapy. However, most (almost all) return after few months with resistant recurrent disease resulting in mortality within five years. Recent data in our laboratory suggests that a set of small non-coding RNAs commonly known as microRNAs (miRs) associated with cancer
stemness may be responsible for chemoresistance (platinum and taxol) in ovarian cancer patients. The aim of this study is to investigate the involvement of these miRs in the development of chemoresistance in ovarian cancer.

Methods: Selected miRs identified by next generation sequence will be validated in ovarian cancer cell lines (treated with or without chemotherapy), and also in tumor cells isolated from the ascites of chemonaive and chemoresistant ovarian cancer patients by quantitative real-time polymerase chain reaction. Levels of targeting miRNA will be manipulated in ovarian cancer cell lines by mimics and inhibitors. Functional assays in the manipulated cells such as sensitization of cells to chemotherapy, changes in the metastatic features such as migration/invasion, and activation of signaling pathways will be determined by MTT assay, XCELLigence, Western blot, immunofluorescence, q-PCR, etc.

**CARDIOLOGY**

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

Supervisors: Professor Judy Savige and A/Prof Deb Colville
Project Site: NWAC, Northern Hospital, Epping.
Contact: Professor Judy Savige, T 8344 3260, jsavige@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.

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

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

**Project Description:** Acute myocardial infarction (AMI) occurs following acute occlusion of a coronary artery. It is important to re-open the blocked artery to re-establish blood supply to the ischemic myocardium (reperfusion) to save ischemic myocardium from necrosis, i.e. infarct size limitation. Clinically, post-ischemia reperfusion can be achieved most commonly by catheter-based percutaneous primary coronary intervention (PCI) or by thrombolytic drugs. Clinical studies indicate that delayed time with PCI is associated with increased transmurality of the infarct and higher prevalence of in-hospital and late mortality.

AMI in mice can be induced surgically by coronary artery occlusion (CAO), which has been commonly used for research on post-infarct cardiac outcomes. Like human patients, mice with AMI develop cardiac wall rupture, a malignant complication due to post-infarct myocardial inflammation and damage to the extracellular matrix (ECM) architecture of infarct myocardium. In our recent study on mice, reperfusion was done following 1, 2 or 4 hours after CAO. We observed that the onset of cardiac rupture was completely prevented not only by early, but also by delayed reperfusion (Gao XM, et al: Pharmacol Ther. 2012). This finding clearly indicates benefits achieved by delayed reperfusion that is independent of myocardial salvage. This project is designed to explore the mechanism responsible for such cardiac protection by delayed reperfusion focusing on the extent of inflammation and ECM damage. This project is for honours degree.

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

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

**CLINICAL RESEARCH**

71. **Hospital-acquired electrolyte disorders – also offered as MBSc**

   - **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.

72. **Are readmissions to The Northern Hospital related to hospital acquired diagnoses in a previous admission? - also offered as MBSc**

   - **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.
73. **The Effect of an Enhanced Recovery After Surgery (ERAS) programme on the Management of Emergency Surgical Patients**

*Supervisors:* Ms Karen Barclay  
*Project Site:* The Northern Hospital, Epping  
*Contact:* Ms Karen Barclay  
E: karen.barclay@nh.org.au

**Project description:** Enhanced Recovery after Surgery (ERAS) programmes aim to optimise peri-operative care and decrease the physiologic stress response to surgery. Benefit in terms of decreased complications and reduced cost and length of stay have been shown. At our hospital, the programme is in place for elective patients however the same medical and nursing staff care for both emergency and elective patients on the same wards. The aim of this retrospective audit is to see if the introduction of an ERAS programme has had a flow-on beneficial effect on the management of emergency patients.

74. **Documentation of Pre-Operative Decision making in Surgery**

*Supervisors:* Ms Karen Barclay  
*Project Site:* The Northern Hospital, Epping  
*Contact:* Ms Karen Barclay  
E: 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.

75. **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  
E: 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.

76. **Complications of surgical implants in hospital care – also offered as MBSc**

*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.
77. 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.

**COLORECTAL MEDICINE AND GENETICS**

78. Bioinformatics in colorectal cancer genetics and prevention - *also offered as MBSc*  
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 further 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?

79. The Human Variome Project (HVP) and familial bowel cancer - *also offered as MBSc*  
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 world wide 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

80. Biogrid and IBD data basing - *also offered as MBSc*  
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 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

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

83. 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: 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 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).

84. Dietary prevention of adenomas in familial adenomatous polyposis - also offered as MBSc
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.

CSIRO MATERIAL SCIENCE AND ENGINEERING

CSIRO Materials Science and Engineering (MSE), Parkville:

CSIRO Preventative Health Flagship:

85. Synchrotron beam studies of Neurodegenerative disease proteins
Supervisors: Dr Victor Streltsov; Dr Lance Macaulay; Dr Stewart Nuttall.
Project Site: CSIRO MSE and Preventative Health Flagship, 343 Royal Pde, Parkville.
Contacts: Dr Victor Streltsov: Victor.Streltsov@csiro.au; 03 9662 7311
Dr Lance Macaulay: Lance.Macaulay@csiro.au; 03 9662 7335
Dr Stewart Nuttall: Stewart.Nuttall@csiro.au; 03 9662 7324
Project Description: Alzheimer’s disease (AD) and Parkinson’s disease are progressive neurodegenerative disorders characterized by the presence of misfolded protein depositions, for example amyloid plaques which consist predominantly of amyloid β-peptide (Aβ) as well as α-synuclein. Frustratingly, obtaining structural data at an atomic resolution for such proteins has been difficult, due in part to their propensity to form amyloid fibrils and aggregates,
rather than crystal-like lattices. However, we have partially resolved this bottleneck by the use of protein scaffold technologies, and have developed several protein fusion systems which show promise in allowing us to determine the structures of neurodegenerative disease proteins.

This project will utilize our protein systems to address the question of which structures neurodegenerative disease proteins adopt. It will be heavily based upon synchrotron x-ray protein crystallography, x-ray small angle scattering in solution and three dimensional structure determinations. As such, it is ideally suited to a biochemistry student with a strong interest in biophysics and a talent in the mathematics/physics disciplines.

**Skill acquisition:** Instruction in protein crystallography (crystal growth and preliminary x-ray structure solution) and small angle scattering in solutions will be provided, including data collection at the Australian synchrotron, and structural analysis. Laboratory-based recombinant protein expression and biophysical analysis (for example dynamic light scattering) will also be included.

86. **Antibody-based targeting of Neurodegenerative disease proteins**

**Supervisors:** Dr Stewart Nuttall; Dr Lance Macaulay; Dr Julie Nigro.

**Project Site:** CSIRO MSE and Preventative Health Flagship, 343 Royal Pde, Parkville.

**Contacts:** Dr Stewart Nuttall: Stewart.Nuttall@csiro.au; 03 9662 7214
Dr Lance Macaulay: Lance.Macaulay@csiro.au; 03 9662 7335
Dr Julie Nigro: Julie.Nigro@csiro.au; 03 9662 7216

**Project Description:** Alzheimer’s disease (AD) and Parkinson’s disease are progressive neurodegenerative disorders characterized by the presence of misfolded protein depositions, for example amyloid plaques which consist predominantly of amyloid β-peptide (Aβ) as well as α-synuclein. Antibodies are assuming an ever-increasing importance in the therapeutic biological pipeline, in a market estimated at $67 billion by 2015. Such monoclonal antibodies, suitable for human therapy, can be generated by traditional *in vivo* monoclonal antibody procedures, or can be selected from large *in vitro* libraries of antibody fragments. This recombinant antibody technology is in place at CSIRO Parkville.

This project will select and analyse novel recombinant antibodies targeting neurodegenerative disease protein isoforms, with a focus on the Aβ peptide and α-synuclein. Antibodies will be purified and characterised by protein chemistry, labelled using a variety of techniques, and tested for functionality in cell-based assays of neuronal toxicity.

**Skill acquisition:** Instruction in recombinant antibody methodologies including library selection, cloning, and protein production and analysis will be provided. The candidate, who should have an interest in protein function and/or biochemistry will also receive training in the planning and execution of properly controlled cell biology experiments.

87. **Selection of imaging agents targeting Aβ oligomers in alzheimer’s disease**

**Supervisors:** Dr Victor Streltsov; Dr Lance Macaulay; Dr Julie Nigro.

**Project Site:** CSIRO MSE and Preventative Health Flagship, 343 Royal Pde, Parkville.

**Contacts:** Dr Victor Streltsov: Victor.Streltsov@csiro.au; 03 9662 7311
Dr Lance Macaulay: Lance.Macaulay@csiro.au; 03 9662 7335
Dr Julie Nigro: Julie.Nigro@csiro.au; 03 9662 7216

**Project Description:** Alzheimer’s disease (AD) is currently Australia’s third overall leading cause of death, after heart disease and stroke. A major obstacle in a successful treatment for AD is that moderately accurate clinical diagnosis is only achieved ten to fifteen years after disease onset, when neurodegenerative changes are irreversible. Thus, techniques are needed to diagnose AD in the early presymptomatic phases of disease and to monitor disease progression. Only when this is achieved, can the efficacy of potential drug and lifestyle changes be monitored. Therapeutically, even small delays in the onset of clinical disease have the potential to have significant impact. The Aβ deposits can be detected by expensive brain positron emission tomography (PET) scans with a radioisotope labelled compound [C-11]PiB (Pittsburgh compound B). This is largely a research tool because of its limited availability, expense and short isotope half-life (~20min). Thus, alternative Aβ-specific imaging agents are urgently required.

We have developed Aβ-binding compounds and this project will select and test their use *in situ* and *in vivo* models of AD, in particular, in neuronal cells and roundworm *Caenorhabditis elegans* (*C. elegans*) AD models. Additionally, promising compounds can be tested in mice brain tissue sections using synchrotron x-ray fluorescence microscopy.

**Skill acquisition:** Instruction in properly controlled cell biology experiments, toxicity assays and analysis will be provided. The candidate, who should have an interest in cell biology and/or biochemistry will also receive training in biophysical analysis including synchrotron based experiments.

88. **Does the Alzheimer’s disease peptide (amyloid-β) interact with growth factor receptors in neuronal/other cell lines?**

**Supervisors:** Dr Julie Nigro, Dr Lance Macaulay

**Project Site:** CSIRO MSE and Preventative Health Flagship, 343 Royal Pde, Parkville.

**Contacts:** Dr Julie Nigro: Julie.Nigro@csiro.au; Dr Lance Macaulay: lance.macaulay@csiro.au

**For Project Description: please contact supervisors for further details**
ELECTROPHYSIOLOGY

89. Investigating inhibitory synaptic function in a mouse model of Autism - also offered as MBSc
Supervisors: Dr Elisa Hill & Professor Terence O’Brien.
Project Site: Department of Medicine, University of Melbourne
Contact: Phone: 8344 3261 Email: elhill@unimelb.edu.au
Prof Terence O’Brien: obrientj@unimelb.edu.au
Aim of Project: This project involves the study of altered inhibitory synaptic function in the NL3 mouse model of Autism Spectrum Disorder. Specifically, the project will investigate:
   i. electrophysiological characteristics of 2 interneuron subtypes, and
   ii. the effect of the NL3 mutation on endogenous cannabinoid pathways in brain slices.
Autism Spectrum Disorder (ASD) is a prevalent neurological disorder characterised by impairments in social interactions, communication, and repetitive behaviour. Up to 30% of ASD patients also experience seizures, suggesting alterations in neuronal network function. While the cause of ASD is unknown, an imbalance of excitation and inhibition in brain circuitry has been proposed as an underlying mechanism. NL3 mice express a mutation in the Neureilgin-3 gene identified in two brothers with autism and show increased synaptic inhibition in the somatosensory cortex.
In order to investigate mechanisms underlying the observed increase in synaptic inhibition, this project will compare the functional properties of neuronal subtypes in the NL3 and Wild Type control mice. Specifically, this project will focus on action potential firing and network characteristics of Fast Spiking (FS) and Regular Spiking Non Pyramidal (RSNP) neurons. FS neurons are strong candidates for influencing synaptic inhibition as they play an important role in modulating cortical networks via their synapses onto pyramidal cell bodies. In contrast, RSNPs (expressing somatostatin) synapse preferentially at dendritic locations. Altered network inhibition will be further assessed in these mice by pharmacological modulation of the endogenous cannabinoid pathway.
Skills: Characterisation of cortical inhibitory neurons using patch clamp electrophysiology in acute slices, and biocytin histochemistry in fixed slices for cellular morphology.

90. How do Anti-Epileptic Drugs Work? - also offered as MBSc
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.

91. How do Antipsychotic Drugs Trigger Seizures? - also offered as MBSc
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 antipsychotic 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.

92. Multi-Electrode Recording in the Rat Brain - also offered as MBSc
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/
**BENCH TO BEDSIDE - MEDICAL RESEARCH**

**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 be 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**

**93. Assessment of changes of spatial heterogeneity of DMB in aging – also offered as MBSc**

*Supervisors: A/Prof Peter Pivonka and Prof Peter Ebeling*

*Project Collaborators: Prof John Clement*

*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.

**94. Does vitamin D with calcium affect circulating mediators of insulin sensitivity in men and women with pre-diabetes?**

*Supervisors: Professor Peter Ebeling and Dr Claudia Gagnon*

*Project Site: NWAC Sunshine Hospital, St Albans*

*Contact: Professor Peter Ebeling T: 8395 8115 E: peter.re@unimelb.edu.au*

**Project Description:** Vitamin D deficiency is common and affects 31% of Australians. We have shown that vitamin D deficiency is associated with an increased risk of both type 2 diabetes mellitus and its precursor, metabolic syndrome. For every 25nmol/L increase in serum 25OHD, the risk of diabetes mellitus is decreased by 24%. We have recently completed a 6-month randomised controlled trial of vitamin D with calcium versus placebo with calcium to study changes in insulin sensitivity in 92 men and women with pre-diabetes.

Through database management skills and basic statistical analysis this project involves examining changes in two mediators of insulin sensitivity, uncarboxylated osteocalcin and adiponectin during the study. The results will provide unique data particularly relating to the responses of these two mediators to vitamin D supplementation and whether these changes have an impact on insulin sensitivity. The work could provide an understanding of a mechanism whereby vitamin D can reduce the risk of type 2 diabetes.

**95. Sarcopenia, Physical Performance and Vitamin D in Older Adults**

*Supervisors: Dr David Scott, A/Professor Kerrie Sanders, Professor Peter Ebeling*

*Project Site: NWAC Sunshine Hospital, St Albans*

*Contact: Dr David Scott T: 8395 8108 E: d.scott@unimelb.edu.au*

Sarcopenia is the term used to describe age-related declines in skeletal muscle quality and physical performance. This study will investigate how specific changes in skeletal muscle quality contribute to performance declines and risk of falls in older adults. The study will also examine the association of increased abdominal and intramuscular fat with muscle quality and function, and determine whether vitamin D status plays a role in this relationship. The Honours student will be based at the NorthWest Academic Centre (Sunshine Hospital) for the duration of the project and will have the opportunity to develop skills including administering physical performance tests (such as gait and balance assessment) and radiographic measurement of body composition (using dual-energy X-ray absorptiometry and peripheral quantitative computed tomography). For further information on this project, please contact David Scott using the details listed above.
EPILEPSY AND NEUROPHARMACOLOGY

96. Keeping the Brain and the Heart in Sync – HERG channels in the CNS - also offered as MBSc
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.

97. Modelling Epilepsy and Epilepsy Drug Effects–Computational Neuroscience Project
Supervisor: Dr Chris French
Project Site: Department of Medicine, MBC Neurosciences Building, Parkville
Contact: Dr Chris French T: 9035 6376 E: frenchc@unimelb.edu.au

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

98. Genetics of epilepsy in Han Chinese - also offered as MBSc
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: 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.

99. Evaluation of Dynamin Inhibitors as Novel Therapies for Epilepsy - also offered as MBSc
Supervisors: Prof. Terence J. O’Brien, Professor Phil Robinson and Dr. Nigel Jones.
Project Site: The Department of Medicine, Melbourne, and the Department of Physiology, Children’s Medical Research Institute, Sydney.
Contact: Prof Terence J. O’Brien T: 8344 5479 E: obrientj@unimelb.edu.au Professor Phil Robinson E: probinson@cmri.com.au Dr. Nigel Jones T: 9035 6402 E: ncjones@unimelb.edu.au

Project Description: The group of Phil Robinson at the CMRI have discovered the principle that dynamin modulators can control synaptic transmission. Consequently, they have engineered the first generation of small molecule dynamin inhibitors and have preliminary evidence for their effectiveness as anticonvulsant drug candidates using in vivo models. The GTPase activity of the enzyme dynamin is a novel molecular target for epilepsy. Blocking dynamin produces inhibition of neuronal synaptic vesicle endocytosis (SVE) and reduced synaptic transmission. The common feature of all
anti-epileptic drugs (AEDs) is a reduction in synaptic transmission. For most AEDs the mechanistic basis of this reduction is uncertain. In a 2006 publication in Nature Neuroscience Professor Robinson’s group showed that inhibition of SVE by blocking dynamin leads to an activity-dependent run-down in synaptic transmission. The unique aspect of this discovery is the lack of effect on acute or brief bursts of synaptic transmission - being inhibited only after high or prolonged stimulation. We propose that molecules based on SVE inhibition would reflect a new and better AED design, especially in those cases where sufferers fail to respond to or tolerate conventional treatments. SVE inhibition has the unique ability to block sustained neuronal burst firing, as occurs during an epileptic seizure, while allowing normal neuronal transmission to occur under most physiological situations. By targeting only neurons experiencing prolonged or unusually high frequency stimulation, such drugs may have fewer effects in the absence of a seizure thus reducing the risk of many of the side-effects associated with AED therapy. This project would test one or more of these candidate dynamin inhibitor treatments for anti-epileptic and anti-epileptogenic effects in “true” epilepsy models of generalized genetic (i.e. GAERS) and acquired focal epilepsy (post-status epilepticus and electrical amygdala kindling) to provide data predictive of efficacy for human epilepsies. 

**Skills:** Small animal handling and neurosurgery (electrode implantations), rat electroencephalography recordings, brain perfusion and fixation, brain histological techniques, drug administration and neuropharmacological principles.

### 100. Investigations into the role of neuropeptide Y in a genetic rat model of absence epilepsy - also offered as MBSc

**Supervisor:** Prof Margaret Morris, Prof Terence J O’Brien, Dr Kim Powell

**Project Site:** Department of Medicine and Department of Pharmacology, University of New South Wales.

**Contact:** Prof Terence J O’Brien T: 8344 5479 E: obrientj@unimelb.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 adenosivirus viral vector.

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

### 101. Antiepileptic drugs and effects on bone health - also offered as MBSc

**Supervisor:** Dr Damian Myers, Dr Andrew Stevenson, Professor John Wark, and Professor Terence O’Brien.

**Project Site:** Department of Medicine, The Royal Melbourne Hospital.

**Contact:**

Dr Damian Myers T: 8344 6449/0401 766608 E: damianem@unimelb.edu.au

Dr Andrew Stevenson E: andrew.stevenson@csiro.au

Professor John Wark T: 9342 7109 E: jdwark@unimelb.edu.au

**Project Description:** Recent clinical studies have confirmed that long-term administration of antiepileptic drug (AED) therapies affect bone mineral density (BMD) and increase risk of bone fracture. Epilepsy is a common neurological disorder typically requiring life-long treatment with neuroactive drugs such as carbamazepine and valproate. The problem of AED-associated bone disease must be addressed. Our research group has developed a model to study AED-induced changes in bone and the emphasis of this project will involve the use of bone protective therapies to overcome the AED-induced bone loss.

The common aim of the projects listed below is to determine whether the loss of bone associated with anti-epilepsy therapies can be prevented by the administration of bone protective therapies. The two protective agents to be tested are bisphosphonate and parathyroid hormone (PTH).

**Project 1: AED-induced changes in bone macrostructure, microstructure and bone strength:**

**AIM:** To image and quantify, in *in vivo* longitudinal studies, the effects of anti-epilepsy drugs on bone using peripheral quantitative computed tomography (pQCT) (for changes in bone macrostructure & strength) and phase-contrast X-ray imaging (PCI tomography to assess bone microarchitecture at high resolution). The two interventions, bisphosphonate and PTH will be assessed on bone parameters; images will be acquired at 8, 16 and 24 weeks.

**Project 2: AED-induced changes in measures of bone turnover:**

**AIM:** To measure biochemical markers of bone turnover and key metabolic factors in the serum (vitamin D, PTH, osteocalcin, calcium) in our model of AED-induced bone loss and to determine whether the interventions, bisphosphonate or PTH, affect the biochemical outcomes
Project 3: AED-induced changes in macro- and micro-architectural features of bone:

AIM: To assess whether the bone-protective agents, bisphosphonate or PTH, inhibit bone remodelling after treatment with the AED. Microarchitectural changes to bone will be imaged using phase-contrast X-ray (PCX) imaging and tomography. These techniques provide high resolution images (in micron range) using X-ray projection-based techniques. These projects involve collaborations with other institutes. This work will be conducted in the Department of Medicine at the Royal Melbourne Hospital and advanced imaging techniques will be performed in collaboration with the CSIRO Materials Science and Engineering division in Clayton.

102. Investigation of the role of Y receptors in the seizure suppression effect of valproate in a rat model of genetic generalised epilepsy - also offered as MBSc

Supervisor: Prof. Terence O’Brien and Prof. Margaret Morris, Dr Kim Powell
Project Site: The Department of Medicine, The Royal Melbourne Hospital and The Department of Pharmacology, The University of New South Wales.
Contact: Professor Terence O’Brien T: 8344 5479 E: obrientj@unimelb.edu.au
Prof. Margaret Morris: E: m.morris@unsw.edu.au
Dr Kim Powell T: 9035 6394 E: kpowell@unimelb.edu.au

Project Description: Description: Valproate is the drug of choice for treatment of primary generalised epilepsy, but its mechanisms of action is still uncertain. There is a delayed onset of maximal effect following commencement of valproate treatment, suggesting that upregulation of a secondary messenger may be involved in its anti-epileptic action. Recent work has demonstrated that chronic valproate administration in rats results in upregulation of expression of neuropeptide Y (NPY) in brain regions critical to the generation of generalised seizures. We have evidence that NPY has powerful seizure suppression effects in the genetic absence epilepsy rats from Strasbourg (GAERS), a genetic rat model of absence epilepsy, predominantly via effects on the Y2 receptor subtype. This project will investigate if the anti-seizure effects of NPY are mediated through NPY related mechanisms, and if so identify the receptors mediating this effect. A positive outcome of the study may lead to new drugs that more specifically target the epilepsy reducing some of the common undesirable side effects of valproate.

Skills: Small animal handling and neurosurgery (electrode/cannula implantations), rat electroencephalography recordings, drug administration, brain perfusion and fixation, brain histology, immunohistochemistry, stereological neuronal cell counting and analysis techniques.

103. Sodium Channels in Epilepsy - also offered as MBSc

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.

104. Epigenetic regulation of gene expression in epilepsy - also offered as MBSc

Supervisors: Dr Nigel Jones, Dr Kim Powell
Project Site: Department of Medicine , MBC Neurosciences Building, Parkville.
Contact: Dr. Nigel Jones T: 9035 6402 E: ncjones@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 lenti-viral 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 lenti-viral 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.

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

**Supervisors:** Dr Kim Powell, Professor Terence O’Brien

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

**Contacts:** Dr. Kim Powell T: 9035 6394 E: kpowell@unimelb.edu.au
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 TARP role for stargazin may have major functional implications on the homeostatic balance of neuronal excitation, and potentially for the pathophysiology of epilepsy. Recent work from our lab has shown increased expression of stargazin at neuronal membranes in the somatosensory cortex of epileptic GAERS animals, a brain region thought to be involved in the generation of absence seizures. These animals also show increased membrane AMPA receptor expression, which may be driven by elevated stargazin levels. Stargazin is known to interact with other synaptic proteins to localise AMPA receptors to the 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).
Dynamin activation in acute epileptic seizures and chronically epileptic rats - also offered as MBSc

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.

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 MBSc

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 Ca3.2 T-type calcium (Ca2+) channel gene (Cacna1h) resulting in an amino acid from arginine to proline (R1584P). The R1584P mutation correlates with the epileptic phenotype in GAERS doubled crossed with Non-Epileptic Control (NEC) rats. Additionally, the R1584P mutation increases the rate of recovery from channel inactivation in a splice variant specific manner, producing a predicted gain-of-function phenotype.

We have a knock-in mouse model of the R1584P Ca3.2 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 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.

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

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: k.powell@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.

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 (Ih) 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).

109. Do balance deficits in patients chronically taking anti-epileptic medications reflect neurodegeneration of the cerebellum? - also offered as MBSc

Supervisors: Professor Terence O'Brien, Professor John Wark, Dr Frances Batchelor and Professor Patricia Desmond.
Project Site: Departments of Medicine and Radiology, The Royal Melbourne Hospital, University of Melbourne
Contact: Prof Terence O’Brien: obrientj@unimelb.edu.au; Prof. John Wark: jdwark@unimelb.edu.au; Dr Frances Batchelor: F.Batchelor@nari.unimelb.edu.au; Prof. Patricia Desmond: PatriciaDesmond@mh.org.au

Background: Anti-epileptic medications are taken chronically by many people of all ages, for epilepsy and for a range of other high prevalence medical conditions. The adverse effects of the chronic use of these medications on bone and fracture risk is well recognised, but only recently has the negative impact of these medications on balance performance been documented by our group and others. Using a matched twin-sibling pair design we found that worse performance on several sway measures for AED users with longer duration of AED use. The association between chronic AED use, particularly with phenytoin, and cerebellar atrophy has long been recognized, but this has not previously been correlated with measures of balance function.

Aims of Project: To investigate whether the magnitude of cerebellar volume on MRI, compared with a matched twin or sibling control, is associated with the severity of quantitative measures of balance dysfunction.

Methods: 35 AED use discordant twin or sibling pairs have had a detailed falls and balance assessment. The T1-weighted volumetric MRI images on these patients will be used to quantitatively measure cerebellar, cerebral and brain stem volumes. The relative cerebellar volume will be compared between the AED user and their matched twin/sibling pair for the study population. The within pair difference in cerebellar volumes will then be correlated with that of the within pair difference for the balance measurements.

Skills: MRI image analysis, balance assessment interpretation, clinical pharmacology and statistical analysis of data.
110. Do older patients have poorer outcomes after epilepsy surgery?
Supervisors: Dr Anne McIntosh, Professor Patrick Kwan.
Project Site: Department of Medicine, Comprehensive Epilepsy Programs at Royal Melbourne Hospital and Austin Health.
Contact: Dr Anne McIntosh. E: a.mcintosh@unimelb.edu.au, T: 93424419 or 90357007.

Individuals who have severe epilepsy that is refractory to medication may undergo surgical resection of the seizure focus, usually a lesion (non-malignant) or other structural abnormality. Epilepsy outcome research in the Department of Medicine at Royal Melbourne Hospital and Austin Health offers the opportunity to utilise two large well-established surgical cohorts to study post-surgical outcome and contribute to the growing international evidence base in this area. Although the majority of patients who have epilepsy surgery achieve seizure freedom or a significant decrease in seizures, not all suitable surgical candidates will be offered this opportunity. Worldwide, older patients are one group where there appears to be a reluctance to offer surgery, possibly due to concerns about increased likelihood of seizure recurrence or complications. The aim of this project is to examine whether older patients have a poor outcome after surgery compared to younger patients.

The student will collate data regarding several factors (i.e. histopathology, surgery type, seizure outcome, cognitive outcome, post-surgical complications) from the medical records of patients who have undergone epilepsy surgery at The Royal Melbourne Hospital or Austin Health. In a number of cases, follow-up telephone interviews with patients will be required in order to obtain up-to-date seizure outcome information. Outcome information will be analysed according to age at surgery.

This information will contribute directly to the assessment, counseling and management of patients undertaking surgery at Austin Health and RMH. The study will contribute to the international epilepsy surgery literature.

The skills expected to be learnt from this project include: Patient telephone interviews, outcomes assessment, clinical epilepsy, statistics.

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.

111. Projects in network analysis of genetic epilepsy
Supervisors: A/Professor Steve Petrou & Dr 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.

112. Multi site patch clamp recording of cortical micro networks
Supervisors: Dr Verena Wimmer, A/Professor Steve Petrou, Dr Chris Reid
Project Site: Florey Institute of Neuroscience & Mental Health, Division of Epilepsy, Kenneth Myer Bldg
Contact: Verena Wimmer E: vwimmer@florey.edu.au; 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 Ca" indicator dye and imaged in real time.
114. In vivo electrophysiological analysis in mouse models of genetic epilepsy

Supervisors: A/Professor Steve Petrou, Dr Antonio Paolini
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 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.

115. The glass brain: “Connectomics” in epilepsy

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 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.

116. MRI tractography in mouse models of genetic epilepsy: Creation of prognostic and diagnostic structural biomarkers

Supervisors: A/Professor Steve Petrou, Dr Kay Richards, Dr Chris Reid, Dr Alan Connelly, Dr Donald Tournier, Dr Fernando Calamente
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: 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.

117. High content automated analysis of ion channels in epilepsy

Supervisors: A/Professor Steve Petrou Dr Carol Milligan, Dr 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
Zn$^{2+}$ levels are significantly lower in blood and CSF of children that suffer febrile seizures but these studies are not cascade of events that lead to more severe forms of epilepsy later in life. Clinically, several studies have suggested that seizures are common affecting approximately 3% of children. There is good evidence that febrile seizures can trigger a

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 transfect 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.

118. Optogenetic modulation of the area tempestas – an epilepsy hot spot
Supervisors: A/Professor Steve Petrou, Dr Antonio Paolini, Dr 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: 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.

119. Exploring the role of GABA mediated tonic inhibition in depression
Supervisors: A/Professor Steve Petrou, Dr Robert Richardson, Dr 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: Depression is a serious neurological disorder that can impact people of all ages and genders. Elegant studies led by Istvan Mody at UCLA have shown that in post-partum depression levels of GABA tonic inhibition determine disease severity. Tonic inhibition is a long term form of inhibition caused by the chronic opening of a certain type of GABA receptor that result in a continued inhibitory response. Changes in the function of this receptor by sex steroids may implicate this channel in the depression seen during puberty. In this project the candidate will first examine the genetic variation of the key GABA receptor involved in tonic inhibition in both patients and controls and then compare function using patch clamp electrophysiology. In a second series of experiments the candidate will use mouse models we have developed that possess low, normal and high levels of tonic inhibition and analyse their depression phenotypes using standard behavioural tests. These experiments will provide vital links between levels of tonic current, GABA receptor function and depressive behaviour and will inform future clinical studies.

120. In vitro study of the mechanism of action of a naturally occurring pain killer
Supervisors: A/Professor Steve Petrou, Dr Peregrine Osborne
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: Opioids are a common and effective way of treating pain but have serious side effects including addiction, tolerance, respiratory depression and chronic constipation. Despite significant efforts in industrial and academic laboratories, next generation, non-opioid pain medications have yet to materialise. Recently, however, conolidine, a non-opioid natural compound isolated from the stem bark of Tabernaemontana divaricata (Tarselli et al. 2011, Nature Chemistry 3:449) was shown to be a potent analgesic in rodent models. In this project the candidate will undertake a series of in vitro experiments to begin to define why this molecule has such remarkable pain killing properties. Brain slice patch clamp electrophysiology will be used to reveal potential neuronal and synaptic mechanisms of action. This project will be the first phase of a broader collaboration with industry in an effort to establish in vitro and in vivo assays to test various conolidine analogues with improved drug properties and efficacy for the treatment of persistent pain.

121. Zinc and seizures
Supervisors: A/Professor Steve Petrou, Dr Paul Adlard
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: 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.

122. **HCN channels, epilepsy and memory**  
**Supervisors:** Dr Chris Reid, Dr Marie Phillips  
**Project Site:** Florey Institute of Neuroscience & Mental Health, Division of Epilepsy, Kenneth Myer Bldg  
**Contact:** Chris Reid E: careid@unimelb.edu.au  
**Project Description:** Humans with epilepsy often have other problems that can include memory loss, anxiety and depression. We have data that shows that our epilepsy model learns more slowly than a non-epileptic animal. We also know that seizures change HCN channel expression in the epilepsy mouse. HCN channels are neuronal ion channels important for normal brain function including the ability to learn. The candidate will investigate if changes in HCN channels are responsible for a reduction in the ability to learn in epilepsy. The project will use whole animal behavioural studies, molecular techniques and potentially electrophysiology to investigate this question.

123. **Identification of serum glycoproteins inhibiting innate immunity - also offered as MBSc**  
**Supervisors:** Dr Ben Gu, Professor James Wiley, A/Professor Steven Petrou  
**Project Site:** Ion channel & Human Disease, Florey Neuroscience Institutes, Melbourne Brain Centre, Parkville  
**Contact:** Ben Gu T: 03 9035 6317 E: gub@unimelb.edu.au; James Wiley E: james.wiley@florey.edu.au; Steven Petrou E: spetrou@unimelb.edu.au  
**Project Description:** Innate immunity is the first line defense of host against invaded 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 new therapies to boost resistance against infectious diseases. Techniques involved are chromatography, cell culture, flow cytometry, electrophoresis, western blotting and mass spectrometry.

124. **Raising innate immunity to fight with severe infection - also offered as MBSc**  
**Supervisors:** Dr Ben Gu, Dr Rohit Ramchandra, Professor James Wiley, A/Professor Steven Petrou  
**Project Site:** Ion channel & Human Disease, Florey Neuroscience Institutes, Melbourne Brain Centre.  
**Contact:** Ben Gu T: 03 9035 6317 E: gub@unimelb.edu.au; Rohit Ramchandra E: rohit.ramchandra@florey.edu.au; James Wiley E: james.wiley@florey.edu.au; Steven Petrou E: spetrou@unimelb.edu.au  
**Project Description:** Septic shock contributes to around 8000 deaths annually in Australia. Innate immunity is the first line of host (patient) defence against invading microorganisms. The most dangerous microorganisms are those resistant to antibiotics and in such situations, phagocytosis of these microorganisms by immune cells (such as neutrophils and monocytes) becomes the only line of defence.

We have recently found that copper binding proteins (e.g. ceruloplasmin) in serum are potent inhibitors of phagocytosis of non-opsonized bacteria. Our preliminary results show that chelation of copper with 1-5 mM tetraethylenepentamine (TEPA, a drug that binds to copper) can neutralize the inhibitory effect of serum thereby restoring innate resistance against bacteria. This project aims to boost innate immunity by copper chelation (using TEPA) and show the benefit of copper chelation a sheep model of septic shock.  

Techniques involved are large animal (sheep) handling, flow cytometry, and protein separation.

125. **Identification of the unique epitope expressed on the surface of early apoptotic neuronal cells - also offered as MBSc**  
**Supervisors:** Dr Ben Gu, Professor James Wiley, A/Professor Steven Petrou  
**Project Site:** Ion channel & Human Disease, Florey Neuroscience Institutes, Melbourne Brain Centre, Parkville  
**Contact:** Ben Gu T: 03 9035 6317 E: gub@unimelb.edu.au; James Wiley E: james.wiley@florey.edu.au; Steven Petrou E: spetrou@unimelb.edu.au  
Cell death by apoptosis and clearance of these dying cells are 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. Our recent novel finding 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 during normal development and in disease. This result will have relevance to neurological diseases as well as neurodevelopment. Techniques involved are cell culture, immunoprecipitation, western blotting, flow cytometry, peptide screen, molecular biology and mass spectrometry.

126. Rescue brain cells by stopping phagocytic attack following head injury - also offered as MBSc
Supervisors: Dr Ben Gu, Professor James Wiley, A/Professor Steven Petrou
Project Site: Ion channel & Human Disease, Florey Neuroscience Institutes, Melbourne Brain Centre, Parkville
Contact: Ben Gu T: 03 9035 6317 E gub@unimelb.edu.au; James Wiley E: james.wiley@florey.edu.au; Steven Petrou E: spetrou@unimelb.edu.au

Project Description: Recent studies show that inhibition of P2X7 receptors improves recovery from spinal cord injury due to the reduction of inflammatory response. Our recent findings reveal that P2X7 can function in two alternative modes either as a pro-inflammatory receptor or as a scavenger receptor for clearance of apoptotic cells. This project will link the cognitive decline which follows traumatic brain injury with innate phagocytosis of stressed or ischemic neurones by activated microglia expressing large amount of P2X7. P2X7 antagonists given shortly after brain injury have the potential to improve functional recovery by minimizing both the immediate inflammatory response over hours and the slow phase of neuronal loss over days and weeks. Techniques involved are small animal (mouse) handling, immunohistochemical staining, flow cytometry and Magnetic Resonance Imaging (MRI).

127. The role of P2X7 receptors in multiple sclerosis - also offered as MBSc
Supervisors: Dr Ben Gu, Professor James Wiley, A/Professor Steven Petrou
Project Site: Ion channel & Human Disease, Florey Neuroscience Institutes, Melbourne Brain Centre, Parkville
Contact: Ben Gu T: 03 9035 6317 E gub@unimelb.edu.au; James Wiley E: james.wiley@florey.edu.au; Steven Petrou E: spetrou@unimelb.edu.au

Project Description: Microglia and macrophages of the brain are responsible for the prompt clearance of apoptotic (dying) cells by a process of phagocytosis. Our previous work has shown that the P2X7 receptor expressed on the surface of microglia/macrophages binds to apoptotic cells to allow their rapid engulfment. Genetic variants of the P2X7 receptor are common and affect the rate of clearance of apoptotic cells. This project aims to show that P2X7 mediated phagocytosis of apoptotic cells is important to prevent inflammation in several neurological disorders such as multiple sclerosis, age related macular degeneration (AMD) of the eye, and possibly Parkinson’s disease. In this project, we will use both genetic and cell biological approaches to investigate the role of P2X7 in the inflammation of multiple sclerosis and other neurological disorders. Techniques involved are genetic analysis, molecular biology, flow cytometry, and immunohistochemical staining.

128. Neuroanatomical determinants of susceptibility in a model of genetic epilepsy
Supervisors: Verena C Wimmer, 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 Description: Epilepsy affects ~1-2% of the population, making it the most common neurological disorder. 50% of all epilepsies are genetic generalized epilepsies (GGE), and currently more than 100,000 Australians live with this disease. These numbers highlight the dire clinical need for better therapy, diagnosis and prognosis. To achieve these goals we need to develop better knowledge of the underlying pathogenic processes. To date, research has focussed on acute functional effects of genetic mutations rather than anatomical changes in the brain as GGEs have been traditionally been considered “idiopathic” without any visible changes in brain structure. Recent results, however, indicate that subtle, microscopic alterations in brain anatomy and neuronal connectivity underlie some aspects of seizure genesis. This prompts the question whether we can understand genetic epilepsy if we are ignoring structural changes or assuming they are non-existent?

This project will examine two forms of anatomical change associated with GGE: Microdysgenesis, which refers to changes during brain development, and homestatic plasticity, which is an adaptive response to the seizures themselves. Anatomical alterations will be analysed in a mouse model carrying a human epilepsy mutation using cutting edge imaging and quantification techniques. Results will improve our understanding of pathogenic mechanisms in GGE with implications for therapy and diagnosis.

129. The role of hyperpolarization-activated channel 1 (HCN1) in network excitability
Supervisors: Verena C Wimmer, Steven Petrou, Ion Channels and Disease Group, Florey Neuroscience Institutes, The University of Melbourne, Parkville, 3010.
**Project Description:** Epilepsy is the most common disorder of the Central Nervous System with ~60 million people affected worldwide. It is not a single disorder but includes aetiologies ranging from purely genetic to acquired conditions such as seizures resulting from head trauma. The common feature of “the epilepsies” is highly synchronized activity of large numbers of neurons.

Interestingly, recent research suggests a *common functional pathway* of both inherited and acquired seizure disorders: several studies have mechanistically linked functional changes in hyperpolarization activated currents (Ih) to inherited and acquired epilepsy. Ih regulates dendritic excitability which is a key determinant of neuronal excitability. On a molecular level, Ih is exclusively mediated by *hyperpolarization activated cyclic nucleotide gated channels* (HCN-channels).

As observed in animal models and human epileptic brain tissue, the activity of HCN-channels is altered in a multitude of seizure disorders. It is yet unclear whether these changes play a compensatory, neuroprotective role or whether they are causative in epileptogenesis. Hence, the precise action of Ih in the transition from physiological to pathological network activity is not understood. This project aims at answering the following question whether a decrease in Ih itself can lead to epilepsy.

To answer this question HCN expression will be manipulated in different brain regions using stereotaxic *in vivo* injection of recombinant viruses. Effects on network excitability will be assessed by *in vivo* recording of neuronal spiking activity using tetrodes. Results will clarify specific contributions of HCN activity to the aetiology of different types of epilepsy and provide an important theoretical framework for developing specific therapeutic intervention strategies.

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**HEPATOLOGY**

130. **Hepatitis C & Depression “HEDGE project” – this project is NO LONGER AVAILABLE for 2014**

Supervisors:  
A/Professor Amanda Nicoll; Prof Ian Everall;  
RMH Department of Gastroenterology & Hepatology, & Department of Psychiatry  
Contact: Amanda Nicoll 9342 8938 /9342 7789  E: amanda.nicoll@mh.org.au

**Project Description:** chronic hepatitis C may cause mood and cognitive disorders by direct effects on the brain. Depression and anxiety are major barriers to patients receiving treatment, result in alcohol and other substance abuse, and contribute to progression to severe liver disease. Many patients complain of poor memory function and concentration. We are collecting demographic details and blood from hepatitis C patients to investigate this. They will have neurocognitive tests to examine for specific defects in cognition, and tests for the proteins mRNA and DNA SNPs associated with depression. Partial ethics approval, approval for the genetic SNPs is pending.

131. **Volatile anaesthesia & liver disease “VALDA project” - this project is NO LONGER AVAILABLE for 2014**  
Supervisors:  
A/Professor Amanda Nicoll; Dr David Moore; Dr Brad Hockey  
RMH Department of Gastroenterology & Hepatology, & Department of Anaesthesia  
Contact: Amanda Nicoll 9342 8938 /9342 7789  E: amanda.nicoll@mh.org.au

**Project Description:** Volatile anaesthetics (halothane, desflurane, sevoflurane) are known to cause acute hepatitis and in some cases fulminant liver failure. Minor liver inflammation is seen in possibly 3% of anaesthetics, but there are no good studies examining this with adequate liver information. We are assessing post-operative patients prospectively to see what the true incidence of liver injury is, and if any risk factors for its occurrence can be determined. This study has full ethics clearance and pilot data.

132. **Imaging estimation of liver fibrosis “MRE & ARFI project” - this project is NO LONGER AVAILABLE for 2014**  
Supervisors:  
A/Professor Amanda Nicoll; Professor R Gibson, Dr D Stella, Dr Jessica Howell  
RMH Department of Gastroenterology & Hepatology, & Department of Radiology  
Contact: Amanda Nicoll 9342 8938 /9342 7789  E: amanda.nicoll@mh.org.au

**Project Description:** Monitoring patients with liver disease is difficult because liver biochemistry and ultrasound are crude tools that do not necessarily reflect liver disease severity. RMH has recently established ARFI, an ultrasound based test, that estimates liver fibrosis. In 2013 we hope to also have magnetic resonance elastography, a much more sensitive and specific method of determining liver fibrosis at RMH. This study will examine a cohort of patients with various liver diseases and co-morbidities and determine their fibrosis readings and estimated prognosis. Ethics for this is currently in preparation.

133. **Biologicals, immunosuppression and chronic hepatitis B “BIRCH project” - this project is NO LONGER AVAILABLE for 2014**  
Supervisors:  
A/Professor Amanda Nicoll; Dr Sharon Van Doornam; Dr Chatura Jayasekera; Dr Peter Hughes  
RMH Department of Gastroenterology & Hepatology, & Department of Rheumatology
**Project Description:** One of the dangers of using strong immunosuppressant medications for inflammatory conditions is the potential to reactivate or flare dormant hepatitis B. This has resulted in deaths from fulminant liver failure in some cases. In Melbourne we have a higher than average hepatitis B rate, which overlaps with the inflammatory diseases. We are monitoring hepatitis B patients on biological therapies, and plan to also look at disease modifying agents such as methotrexate, cyclosporine; azathioprine, etc. and the effect on chronic hepatitisB. This will have important implications for guiding how these agents are used and monitored in hepatitis B patients in the future. Ethics is in preparation and will be submitted soon for this work.

**134. Pain management in advanced liver disease - this project is NO LONGER AVAILABLE for 2014**

**Supervisors:** A/Professor Amanda Nicoll; Dr Chatura Jayasekera; Dr Malcolm Hogg; Dr Greta Palmer  
**Project Site:** RMH Department of Gastroenterology & Hepatology, & Pain service  
**Contact:** Amanda Nicoll 9342 8938 /9342 7789  
E: amanda.nicoll@mh.org.au

**Project Description:** Advanced liver disease presents unique problems when it comes to managing pain control. Many analgesics cause sedation and constipation and may precipitate encephalopathy. As a result, many patients with liver disease are denied adequate analgesia or are burdened with recurrent encephalopathy. We have developed guidelines for the use of analgesia in patients with advanced cirrhosis. We would like to test prospectively if these guidelines result in good pain control, and avoid precipitating encephalopathy. Patients with cirrhosis in the ward will be recruited and their pain control quantitated, and episodes of sedation and confusion measured. Ethics is to be submitted.

**IMAGING**

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

**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:** 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.

**136. Neuroimaging**

**Supervisors:** Drs. Brad Moffat, Chris Steward, Professor Patricia Desmond  
**Project Site:** The Brain Imaging Laboratory, Department of Radiology, Level 2, 1B building, Royal Melbourne Hospital.  
**Contact:** Dr Brad Moffat T: 9342 8340  
E: brad.moffat@mh.org.au

**Project Description:** There is presently a paradigm shift in the way in which patients with neurological diseases (such as Brain Tumours, Stroke and Epilepsy and Dementia) are treated. Old methods are being replaced by individualised patient management protocols using spatially, molecularly and genetically targeted therapies. Similarly, there is also currently a paradigm shift occurring in the field of Neuroimaging. Imaging (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 clinicians to better understand and predict patient disease and response to treatment. Imaging techniques being studied are: Structural imaging, Functional Diffusion Mapping, Diffusion Tensor Imaging, Magnetic Resonance Spectroscopy and Perfusion MRI, functional MRI. The following are a subset of possible projects:

**Project A:** Perfusion MRI of Brain Tumour Patients  
**Project B:** fMRI in aging and dementia  
**Project C:** Diffusion tensor MRI techniques for clinical assessment of white matter integrity in mild cognitive impairment and healthy aging.  
**Project D:** MRI in healthy aging (also available as MSc)  
**Project E:** functional MRI paradigms for imaging the visual cortex.
INFECTIONOUS DISEASES

137. Primary tuberculosis infection in immunocompromised travelers – **ONLY available for Master of Science**

**Supervisors:** Dr Sharon Van Doornum, Dr Justin Denholm, Dr Irani Ratnam  
**Project Site:** Royal Melbourne Hospital  
**Contact:** Sharon Van Doornum E: svd@unimelb.edu.au

**Project Description:** Patients with autoimmune disease such as rheumatoid arthritis frequently require treatment with immune suppression to control the symptoms of their disease. However immunosuppression is associated with risks too, including increased risk of infection. One particular infection that can cause problems in immunocompromised patients is tuberculosis. Although tuberculosis is uncommon in Australia, Australian patients who travel overseas may be at increased risk of contracting tuberculosis during their travels. Little is known about the incidence and risk factors for primary infection with tuberculosis in immunocompromised patients who travel overseas to high risk countries.

This project is offered as MSc, and will evaluate the incidence of, and risk factors for, primary infection with tuberculosis in immunocompromised patients who travel overseas to high risk places. The project includes study design and travel questionnaire design, ethics committee applications, patient recruitment and informed consent, implementation of questionnaires, organisation of patient testing, database development and entry, statistical analysis and manuscript preparation.

138. Investigating antibiotic resistance in the emerging pathogen *Mycoplasma genitalium*

**Supervisors:** A/Professor Sepehr Tabrizi, Dr Jimmy Twin  
**Project site:** Women’s Centre for Infectious Diseases (RWH), Bio21 Institute  
**Contact:** A/Professor Sepehr Tabrizi T: 8345 3672 E: sepehr.tabrizi@thewomens.org.au;  
Dr Jimmy Twin T: 8345 3679 E: jimmy.twin@mcri.edu.au

**Project Description:** *Mycoplasma genitalium* is a sexually transmitted pathogen responsible for 20-35% of non-gonococcal urethritis (NGU) as well as cervicitis, and is implicated in other conditions such as endometritis, pelvic inflammatory disease, tubal factor infertility and balanoposthitis. Current treatment is a single 1g dose of the macrolide antibiotic azithromycin, which binds to the bacterial ribosome, inhibiting translation of mRNA and protein synthesis. Disturbingly, recent studies have suggested an increase in the prevalence of antibiotic resistant *M. genitalium* strains, due to mutations in the 23S ribosomal subunit. Using molecular-based techniques such as qPCR, high resolution melt analysis and DNA sequencing, this project will measure the prevalence of wildtype and antibiotic-resistant *M. genitalium* in Australian populations. There is also the potential for exploration of culture-based techniques to grow resistant *M. genitalium* for future whole genome sequencing projects.

139. Characterization of bacteria associated with *Bacterial Vaginosis*

**Supervisors:** Dr Jimmy Twin, Assoc Prof Sepehr Tabrizi, Assoc Prof Catriona Bradshaw, Prof Suzanne Garland  
**Project Site:** Women’s Centre for Infectious Diseases (RWH), Bio21 Institute  
**Contact:** Dr Jimmy Twin jimmy.twin@mcri.edu.au, Assoc Prof Sepehr Tabrizi sepehr.tabrizi@thewomens.org.au

**Project Description:** *Bacterial Vaginosis* (BV) is a condition developed in up to 30% of women with no clear etiology. Women with BV have changes in their vaginal bacteria with primarily Lactobacillus spp. being replaced with other bacterial species. BV is associated with a number of adverse outcome like preterm delivery, low birth weight, and increased risk of sexually transmitted infections (STI) and HIV. This project aims to characterize the vaginal bacteria obtained from women with BV using both conventional culture and molecular biological methodologies. Overall, differences in strain diversity, biofilm formation will be investigated in this study in order to better understand role of potentially virulence factors leading to this condition.

INFECTIONOUS DISEASES AND IMMIGRANT HEALTH

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

**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**

141. **Mapping public injecting drug use in urban Melbourne** - *also offered as MBSc*

   **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.

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

   **Supervisor/s:** Margaret Hellard, Mark Stoove
   **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 MBSc*

   **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 MBSc*

   **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 MBSc

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. Understanding the social structures of relationships between people who inject drugs: a mixed-methods project - also offered as MBSc

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

Project Description: We have conducted an empirical study of a drug injecting network and identified a number of social-structural features of that network. Some of these were unexpected: for example, we found that there were many people who reported injecting with two other participants but the two injecting partners did not report injecting with each other (this is surprising because usually there is a high propensity for two people with a friend in common to also be friends). This project would include interviewing networks study participants in more depth about relationships that they have already reported in the past in order to understand some of the structural features. Quantitative methods would be used to identify potential interviewees and describe profiles of people with similar positions in the social network.

147. A systematic review of the structural features of injecting networks - also offered as MBSc

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.

148. The persistence of risk among people who inject drugs - also offered as MBSc

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

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

INNATE IMMUNITY AND HOST DEFENCE

149. Immune Cell Signalling Regulation During Inflammation

Supervisors: Dr Paul Licciard and Dr Rodney Luwor
Location: Murdoch Children’s Research Institute, The Royal Children's Hospital and Dept of Surgery, Level 5, Clinical Sciences Building, Royal Melbourne Hospital
**MALARIA**

1. **Malaria parasite adhesion to the human placenta - also offered as MBSc**
   
   **Supervisor:** Dr Philippe Boeuf
   
   **Project Site:** Department of Medicine (RMH), Clinical Sciences Building, Royal Melbourne Hospital, University of Melbourne
   
   **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 into 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.

2. **Severe Malaria Transcriptomics and Severe Antigens**
   
   **Supervisors:** Dr Michael Duffy
   
   **Project Site:** Department of Medicine (RMH), Clinical Sciences Building, Royal Melbourne Hospital, University of Melbourne
   
   **Contacts:** Dr Michael Duffy; T: 8344 3264;  E: mduffy@unimelb.edu.au
   
   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.

   **Aims:**
   
   1) Identify conserved PfEMP1s that are abundantly expressed in severe malaria. We will use next generation sequencing to identify and quantify all transcribed PfEMP1 domains in severe malaria patients and non severe malaria patients from West Papua.
   
   2) Test PfEMP1 domains abundantly transcribed in severe malaria for cross-reactivity with severe malaria sera. Recombinant PfEMP1 domains will be expressed in a wheat germ system and tested with West Papuan and African
children’s sera in luminex assays to compare responses by malaria syndrome and by region. Antisera to PFEMP1 domains will be tested against heterologous patient isolates.

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.

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

Supervisors: Dr Michael Duffy
Project Site: Department of Medicine (RMH), Clinical Sciences Building, Royal Melbourne Hospital, University of Melbourne
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.

153. Next Generation Sequencing to identify sequence elements important for gene expression in malaria parasites – also offered as MBSc

Supervisors: 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

Plasmodium falciparum malaria kills 800,000 people a year. Three processes are critical to malaria pathogenesis, i) erythrocyte invasion, ii) immune evasion through the parasite changing its appearance and iii) adhesion of parasite infected erythrocytes to small blood vessels. All three of these processes are regulated by epigenetic control of malaria gene expression. Epigenetic control is a rapidly moving and recent field of study with applications beyond malaria to cell development, neurology and cancer. A central component of epigenetic control is the reversible, covalent modification of histones. Recent data suggests that specific histone modifications at enhancers precede and control changes in gene expression. Studies of P. falciparum cis regulatory elements are only now emerging and there is a tremendous opportunity to experimentally identify enhancers, which could lead to therapies targeting the trans factors that bind these sequence elements. We will use an illumina platform for genome wide Chromatin immunoprecipitation sequencing (ChiPseq) to identify sequences enriched in two histone modifications that are enriched in the enhancers of other species. Identified sequences will constitute putative enhancers. We will also collect parasite RNA in parallel and perform genome wide gene expression analysis. These experiments will be performed over a timecourse of the parasite’s 48 hour lifecycle and gene expression data will then be correlated with fluctuations in histone modifications to identify putative enhancers for specific, regulated genes.

Keywords: malaria, next gen sequencing, molecular biology

154. Gene regulation mechanisms in the transmissible stages of the malaria parasite – also offered as MBSc

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.

155. **Characterizing new surface proteins of the malaria parasite - also offered as MBSc**

**Supervisors:** Dr Michaela Petter

**Project Site:** Department of Medicine (RMH), Clinical Sciences Building, Royal Melbourne Hospital, University of Melbourne

**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.

156. **Functional assays for immunity to malaria - also offered as MBSc**

**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, Royal Melbourne Hospital, 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, 4 PhD students and one Masters student 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.

157. **Malaria in pregnancy: risk factors and consequences - also offered as MBSc**

**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:** Our laboratory is part of the Malaria In Pregnancy Consortium, which seeks to understand how to better treat and prevent this condition. As part of this activity, we have a project to understand some of the risk factors for malaria in pregnancy and its consequences. In this project, you will obtain and analyse data from a number of studies, to examine several clinically important questions: Does fetal gender alter the mother’s susceptibility to malaria? If malaria infection is detected only in the placenta, are these babies more likely to be born with low birth weight than uninfected babies? Are current antimalarial drugs adequate at preventing infection?

This project offers an introduction to statistical analysis of multiple data sets. Some basic knowledge of statistics would be useful for this project.

158. **Malaria immunity and treatment outcome - also offered as MBSc**

**Supervisor:** Professor Stephen Rogerson

**Project Site:** Department of Medicine (RMH), Royal Melbourne Hospital

**Contact:** Prof Stephen Rogerson, T: 8343259 E: sroger@unimelb.edu.au

**Project Description:** Our laboratory is part of the Malaria in Pregnancy Consortium, which seeks to understand how best to treat and prevent malaria in pregnant women. A recently completed study in Malawi found that the malaria preventive drug sulphadoxine-pyrimethamine (Fansidar, or SP) is no longer protecting pregnant women from malaria, especially women in first pregnancy. In a previous cohort, we found that antibody levels were associated with treatment outcomes. Using samples from these women, you will measure antibodies in these women and relate the levels of antibodies to the outcomes of malaria treatment in this group.

Techniques will include parasite culture, flow cytometry, ELISAs and data analysis and training in basic medical statistics.
159. Investigating the effects of GM-CSF and M-CSF derived human macrophages on phagocytosing *P. falciparum* infected erythrocytes and cytokine production - *also offered as MBSc*

Supervisors: Dr. Adrian Achuthan and Dr. Louise Ludlow  
Project site: Department of Medicine (RMH), University of Melbourne  
Contact: Dr. Adrian Achuthan T: 8344-3290 E: aaa@unimelb.edu.au; Dr. Louise Ludlow T: 8344-3264 E: lludlow@unimelb.edu.au

**Project Description:** An important way in which the body clears malaria infection is through opsonisation of *P. falciparum*-infected erythrocytes (IE) and phagocytosis by monocytes/macrophages. This process leads to activation of signalling pathway and cytokine production. Current studies utilize human monocytes cultured in vitro in the presence of either granulocyte-macrophage colony stimulating factor (GM-CSF) or M-CSF to produce monocyte-derived macrophages (MDMs). Classical activation of monocytes by GM-CSF yields “M1-like” MDMs with a pro-inflammatory cytokine profile while M-CSF promotes “M2-like” MDMs that produce an anti-inflammatory cytokine repertoire. In this project you will explore the effects of IE phagocytosis by M1-like and M2-like MDMs on cytokine production and trafficking. Furthermore, you will be investigating the expression and function of signalling proteins that govern phagocytosis and cytokine secretion in these two types of MDMs.

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

160. Immunity, drug efficacy and the spread of anti-malarial drug resistance - *also offered as MBSc*

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

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

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

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

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

162. 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 to determine levels of antibodies to a range of malaria antigens by Enzyme-linked immunosorbent assay (ELISA), flow cytometry and functional antibody assays. The levels of these antibodies will then be related to clinical outcome using statistical analysis including regression techniques. These findings will help us understand how immunity contributes to protection from severe malarial disease progression. The findings are valuable for advancing vaccine development by providing evidence supporting certain malaria antigens as targets of protective immunity.

163. 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.

164. 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.

165. 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, EBAs, PfRh, MSP2), and other promising antigens. They will use novel approaches in molecular biology, cell biology and immunology to address these aims. In addition, the project could include working on optimising vaccine approaches to induce potent protective immune responses (e.g. improving antigen presentation). The project could focus on vaccines for P. falciparum and P. vivax, which are the two main causes of human malaria.

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

Medication discrepancies in hospitalised older patients

Supervisors: Professor Elizabeth Manias, Dr. Snezana Kusljic
Project Site: Melbourne School of Health Sciences, University of Melbourne
Contact: Professor Elizabeth Manias T: 8344 9463 E: emanias@unimelb.edu.au

Project description: As older patients move across transition points of care from home to hospital and back home again, medication discrepancies are likely to occur. Medication discrepancies occur when there is lack of matching of patients’ prescribed medications as they move across different settings. This lack of matching of medications as older patients move from one setting to another can relate to omission of medications, changed doses, changed routes of administration, and changed frequency of doses to be administered. Older patients are particularly vulnerable to medication discrepancies because of the complexity associated with their medication regimens. Many older patients have a number of chronic medical conditions, which means that they need to be prescribed many medications.

Using a retrospective chart audit method, this study will identify the patient, environment and medication related factors involving unexplained medication discrepancies as older patients are discharged home from medical wards. A stratified, random sampling of data will be undertaken for patients admitted to hospital through the emergency department over a 12-month period. Information will be obtained from patients’ medical records. Medications will be audited and compared for any differences or discrepancies between time points 1 and 2. At time point 1, a description of all medications that older patients have been taking at home will be collected, including the medication name, dose, frequency of use, and

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route of administration. At time point 2 the medications ordered for older patients upon discharge from a medical ward will be examined. Following conduct of the project, implications will be made on how medication management can be improved for older people as they move across hospital settings to discharge home. The project will enable the student to gain skills in hospital ethics procedures, liaison with hospital health information systems, reading and understanding medical records, data collection from medical records, development of a statistical database and cleaning data, data analysis using descriptive and inferential statistical processes, and writing up for publication. It is not expected that students have a pharmacology background to successfully undertake this project.

MULTIPLE SCLEROSIS/NEUROLOGY

170. How do Multiple Sclerosis Risk Genes work? - *also offered as MBSc*

**Supervisors:** A/Prof Helmut Butzkueven and Dr Melissa Gresle

**Project Site:** Department of Medicine, Royal Melbourne Hospital, Royal Parade, Parkville

**Contact:** Helmut Butzkueven E: butz@unimelb.edu.au

**Project Description:** In the last three years, around 30 risk genotypes for MS have been confirmed. Many of these carry small risks (e.g., increasing the risk of getting MS by between 10 and 30%), and many of the risk genotypes are actually fairly common in the non-MS population. One major hypothesis explaining these results is that, in MS patients, the risk genotypes are associated with altered expression of the relevant gene. We are conducting an experiment in which people with early MS and healthy controls are genotyped for the MS risk genotypes and their immune cells are sorted into different subsets (B-cells, T-cells, NK-cells, and monocytes) and their RNA is extracted.

The major aim of this project will be to determine if risk genes alter expression of gene messenger RNA in MS, if this effect does/does not occur in healthy people carrying the same genotype, and, if positive, determine if expression of the relevant protein of interest is also altered in specific immune cell subtypes from patients carrying the risk genotype. We will then progress to genotype-specific functional assessments in human immune cells (functions such as migration, antigen presentation or cytokine production).

We have already identified several potential candidates and will tailor the specific project to the student’s interest. During this project, you will become familiar with MACS and FACS cell sorting, RNA extraction, genotyping, and will be introduced to relevant statistical and bioinformatic techniques. The project is likely to involve short periods of travel to Hobart, Tasmania to work with our collaborating bioinformaticians.

**Feasibility:** The cell collection is well under way so that there will be no delays in relation to data availability or ethics applications.

171. How do relapses relate to progression of disability in multiple sclerosis? - *also offered as MBSc*

**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 disease course of multiple sclerosis (MS) is highly variable and therefore difficult to predict. Information about individual prognosis is invaluable to both clinicians and patients with MS and if known, has the potential to significantly influence treatment decisions. Based on our current knowledge of MS limited prognostication is possible using predictive markers such as age at disease onset, sex, initial symptoms, extent of recovery from first relapse etc.

This project aims at broadening our knowledge of prognostic markers. It will evaluate the relationship between neurological domains affected during relapses and the long-term accumulation of disability. We hypothesise that repeated impacts to certain neurological systems are more likely to result in accelerated accumulation of permanent disability. This project will utilise a large longitudinal collection of data obtained through the international observational database of MS patients - MSBase.

This project would suit people with interest in statistics and health outcome analysis. During the course of the project, you will become familiar with statistical approaches to longitudinal and predictive analyses. You will explore strategies for predictive modeling and for clinical application of the outcomes of your statistical analyses. You will add to the current knowledge about prognostic markers in MS.

172. Predicting treatment response in multiple sclerosis - *also offered as MBSc*

**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. You will become familiar with retrospective evaluation of potential predictive markers, validation of the resulting predictors and planning their clinical implementation.

173. Evaluation of novel treatments for multiple sclerosis - also offered as MBSc

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: Randomised controlled trials (RCT) represent the gold standard for obtaining evidence about treatment efficacy and tolerability. However, they are expensive, time consuming and usually limited by tight selection criteria, which may restrict translation of their outcomes to general populations. Therefore, validation of RCT results in large populations managed in routine clinical practice may be required. For the emerging, more potent treatments for multiple sclerosis (MS), such validation constitutes the opportunity to confirm the outcomes of previous RCTs and at the same time to enhance generalisation of these outcomes to the broad population of patients with MS. This project aims to compare the efficacy and tolerability of a novel agent, Fingolimod, to the more traditional disease modifying agents, interferon beta and glatiramer acetate. It utilises the MSBase - a large international, observational database of MS patients, to construct pseudo-randomised trials. This project aims to validate the outcomes of previous RCTs in a large real world patient sample to determine whether the outcomes of large RCTs apply to a broader MS population.

This project would 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. You will become familiar with propensity estimation and matching procedures and with the construction of pseudo-randomised trials in observational datasets.

NEPHROLOGY

174. 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 scartissue (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 (mouse) models and molecular biology.

175. 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 biopimpedance spectoroscopy 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).


176. Finding genetic mutations in new types of inherited kidney disease: focal segmental glomerulosclerosis – also offered as MBSc

Supervisors: Professor Judy Savage and Dr Yanyan Wang
Project Site: NWAC, Northern Hospital, Epping.
Contact: Professor Judy Savage, T 8344 3260, jsavage@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 Savage 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.

177. Investigating structural co-variance between brain regions in schizophrenia – also offered as MBSc

Supervisors: Dr Paul Klauser (paul.klauser@unimelb.edu.au), Dr Vanessa Cropley (e: vcropley@unimelb.edu.au), A/Prof Alex Fornito E: alex.fornito@monash.edu;
Prof Christos Pantelis (cpant@unimelb.edu.au)

Project Site: Melbourne Neuropsychiatry Centre, 161 Barry Street, Carlton South, The University of Melbourne.

Description of projects: A large body of research has demonstrated that there are reductions in grey matter volume in individuals with schizophrenia. These are most pronounced in select frontal and temporal regions such as the anterior cingulate, medial and inferior frontal cortices, superior temporal gyrus, hippocampus, thalamus and insula. As these regions are involved in a number of higher-order cognitive and behavioural processes, such loss of brain volume may have wide-reaching implications for everyday functioning.

Although the demonstration of volumetric differences in schizophrenia has been informative, it is increasingly recognised that single brain regions do not function in isolation but in an organised fashion. It is also known that communities of brain regions co-vary with other brain regions – a phenomenon called structural covariance. Despite schizophrenia being conceptualised as a disorder of brain connectivity, inter-regional structural covariance networks are not well characterised in individuals with this disorder.

The proposed honours project will investigate whether there are differences in the pattern of structural co-variance of brain regions in individuals with established schizophrenia compared to healthy controls and/or between subgroups of individuals with the disorder. This will be done using an imaging approach called ‘voxel-based morphology’, where grey matter volume at each voxel will be compared across the brain and between groups of subjects. The student will be responsible for the pre-processing and statistical analysis of MRI scans that have been collected from the Australian Schizophrenia Research Bank. The student will also be trained in the application of imaging analysis in neuropsychiatry.

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

Supervisors: Dr Chris French, A/ProfAnthony Hannan, Dr Nigel Jones, Prof Terrence O’Brien
Project Site: Melbourne Brain Centre
Contact: Chris French frenchc@unimelb.edu.au
Patterns of brain wave activity have been associated with higher cognitive activity in humans and animals, and 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 in motor 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 behavioral 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.

179. Neurodevelopmental and neuropharmacological mechanisms in mouse models of schizophrenia – also offered as MBSc

Supervisors: Dr Udani Ratnayake and A/Prof Maarten van den Buuse

Project Site: Level 4 and 6, Florey Institute of Neuroscience and Mental Health, Melbourne Brain Centre, The University of Melbourne, Parkville

Contact: Dr Maarten van den Buuse, T: 90356624, E: mvdbuuse@unimelb.edu.au

Project Description: Schizophrenia and depression are devastating chronic mental illnesses which affect a significant proportion of the population. Antipsychotic and antidepressant drugs are available and have efficacy, however many patients are refractory to treatment or experience serious side effects.

The Behavioural Neuroscience Laboratory uses behavioural animal models to study neuropsychopharmacological mechanisms involved in schizophrenia and depression. In rats or mice, behavioural tests are combined with specific neuropharmacological approaches and state-of-the-art automated equipment is used for detailed behavioural analysis. This in vivo work is complemented with receptor autoradiography and molecular studies on gene expression.

Schizophrenia and other mental illnesses are likely to be caused by an interaction of genetic and early neurodevelopmental factors, leading to altered expression of trophic factors in the brain and changes in synaptic density and neuronal activity. We use mice with altered brain expression of trophic factors such as BDNF (brain-derived neurotrophic factors) and Reelin. In these mice we investigate the effects of chronic stress or drugs of abuse (cannabis, methamphetamine) in specific behavioural models to assess neuropharmacological regulation of behavior.

180. Neuropharmacology of animal models of schizophrenia and depression: Role of oestrogen – also offered as MBSc

Supervisors: Dr Rachel Hill, Dr Andrea Gogos, Dr Xin Du and A/Prof Maarten van den Buuse

Project Site: Level 4 and 6, Florey Institute of Neuroscience and Mental Health, Melbourne Brain Centre, The University of Melbourne, Parkville

Contact: Dr Maarten van den Buuse, T: 90356624, E: mvdbuuse@unimelb.edu.au

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There are gender differences in schizophrenia and depression in terms of frequency, age of first onset, symptom severity and treatment response. The reason for this difference is unclear but is believed to be related to a ‘protective’ action of oestrogen and an opposite effect of testosterone. These effects may be mediated during puberty, when the brain undergoes extensive plastic changes and remodelling. This project will investigate the modulatory effect of oestrogen and testosterone on behaviour and adolescent development. The studies will focus on the behavioural and neurochemical effects of dopaminergic and serotonergic drugs in different hormone conditions.

181. Cannabis and methamphetamine as risk factors in schizophrenia – also offered as MBSc

Supervisors: Mr Michael Notaras, Dr Udani Ratnayake, Dr Rachel Hill and A/Prof Maarten van den Buuse

Project Site: Level 4 and 6, Florey Institute of Neuroscience and Mental Health, Melbourne Brain Centre, The University of Melbourne, Parkville

Contact: Dr Maarten van den Buuse, T: 90356624, E: mvdbuuse@unimelb.edu.au

Project Description: Schizophrenia and depression are devastating chronic mental illnesses which affect a significant proportion of the population. Antipsychotic and antidepressant drugs are available and have efficacy, however many patients are refractory to treatment or experience serious side effects. The Behavioural Neuroscience Laboratory uses behavioural animal models to study neuropsychopharmacological mechanisms involved in schizophrenia and depression. In rats or mice, behavioural tests are combined with specific neuropharmacological approaches and state-of-the-art automated equipment is used for detailed behavioural analysis. This in vivo work is complemented with receptor autoradiography and molecular studies on gene expression.

There are gender differences in schizophrenia and depression in terms of frequency, age of first onset, symptom severity and treatment response. The reason for this difference is unclear but is believed to be related to a ‘protective’ action of oestrogen and an opposite effect of testosterone. These effects may be mediated during puberty, when the brain undergoes extensive plastic changes and remodelling. This project will investigate the modulatory effect of oestrogen and testosterone on behaviour and adolescent development. The studies will focus on the behavioural and neurochemical effects of dopaminergic and serotonergic drugs in different hormone conditions.
automated equipment is used for detailed behavioural analysis. This in vivo work is complemented with receptor autoradiography and molecular studies on gene expression. Cannabis and methamphetamine abuse are well-known risk factors in the development of psychosis. However, it is unclear exactly how these drugs cause such effects or interact with neurotrophic factors in the brain. The work in this project will focus on the effects of chronic treatment of young-adult mice with cannabinoid receptor agonists or methamphetamine. This work will be done in mice which carry the most common human polymorphism in the BDNF gene, val66met. Effects of the treatments will be analyzed at the level of behaviour and indices of the activity of brain dopamine and serotonin.

182. Functional disconnections and the pathophysiology of psychosis - also offered as MBSc

Supervisors: Dr Nigel Jones and Prof Terence J O’Brien.
Project Site: Department of Medicine
Contact: Dr Nigel Jones T: 9035 6402 E: njones@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. Identifying substrates for Selenium Binding Protein 1 and their functional consequence in the human brain – also offered as MBSc

Supervisors: Dr Tammie Money, Professor Brian Dean, A/Professor Elizabeth Scarr and Professor Ian Everall
Project Site: Melbourne Brain Centre, Level 4, Royal Melbourne Hospital City Campus, Parkville
Contact: Dr. Tammie Money E: ttmoney@unimelb.edu.au T: 9035 6664

Background: The aim of this project is to identify substrates for selenium binding protein 1 (SELENBP1) in schizophrenia. Previous studies from our laboratory have shown that SELENBP1 gene expression is significantly upregulated in schizophrenia from several studies in both brain and blood (Glatt et al., 2005, Kanazawa et al., 2007). However, it is not clear what is causing this increase. A previous study showed that selenium is bound to SELENBP1 at the Cys57 residue (Raucci et al., 2011), but in vitro studies from our laboratory showed that physiological levels of selenium do not affect the expression of SELENBP1. Therefore, this project will investigate what else binds to SELENBP1 and what the consequence of this interaction is in the human brain.

Aims:

- **To identify substrates for SELENBP1 in the human brain**
  To achieve this aim co-immunoprecipitation will be used to isolate SELENBP1 and attached complexes from postmortem human brain tissue. Following isolation, the complex will be identified using mass spectrometry

- **To determine the involvement of the identified substrates on the expression of SELENBP1 and functional effects on cell health**
  This aim will utilise cell culture to determine the effect of the identified substrate on the level of expression of SELENBP1 and the effect on normal cell function. Cells expressing endogenous SELENBP1 will be grown and exposed to differing levels of the identified substrate. RNA will be extracted and levels of SELENBP1 expression will be measured using quantitative PCR, as well as markers of cell health.

Skills: This project will involve training in postmortem brain tissue handling, protein extraction, co-immunoprecipitation, mass spectrometry, cell culture, quantitative PCR and statistical analysis.
184. Temporal lobe epilepsy, the HPA axis and depression - *also offered as MBSc*

**Supervisor:** Prof Terence O’Brien, Dr Dennis Velakoulis,  
**Project Site:** Department of Psychiatry and Medicine  
**Contact:** Terence O’Brien T: 8344 5490 E: obrientj@unimelb.edu.au  
Dennis Velakoulis T: 9342 8750 E: dennis.velakoulis@mh.org.au

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

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

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

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

185. Does stress contribute to epilepsy? - *also offered as MBSc*

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

- 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.

186. Investigating the stress response in a mouse model of autism

**Supervisors:** Dr Elisa Hill, Assoc. Professor Anthony Hannan.  
**Project Site:** Howard Florey Institute, University of Melbourne  
**Contact:** Dr Elisa Hill Tel: 8344 3261 Email: elhill@unimelb.edu.au,  
Assoc. Prof Anthony Hannan Email: ahann@florey.edu.au

**Aims of Project:** This project will investigate behavioural aspects and markers of stress in the NL3 mouse model of autism using:
- Anxiety and stress paradigms
- Cortisol and c-fos levels with labelling for neuronal markers
- Ultrasonic vocalisation pattern analysis

Autism Spectrum Disorder (ASD) is a prevalent neurological disorder characterised by impairments in social interactions, communication, and repetitive behaviour. NL3 mice express a mutation in the Neurelin-3 gene identified in two brothers with autism and show increased synaptic inhibition in the somatosensory cortex as well as impairments in social behaviour.

In addition to altered sociability, these mice demonstrate an aggressive phenotype and one aim of this project is to investigate possible links with an altered stress response using a cortisol assay for stress. To investigate the possibility that specific neuron types are upregulated in the stress response, a c-fos assay will be carried out following stress (isolation housing and aggression test) with double labelling immunocytochemistry for neuronal subtypes (GAD and neu-N). There is also scope to assess mice for altered communication patterns by recording ultrasonic vocalisation patterns.

**Skills:** Behavioural and animal handling skills. Vocalisation pattern data acquisition and analysis. Cortisol assay for stress and c-fos assay for neuronal activity.
187. Investigating effects of cannabinoids on sensorimotor gating in a mouse model of autism

**Supervisors:** Dr Dan Malone (Monash Institute of Pharmaceutical Sciences) and Dr Elisa L Hill (Dept of Medicine, University of Melbourne).

**Project Site:** Monash Institute of Pharmaceutical Sciences, Royal Pde, Parkville 3050

**Contact:** Dr Elisa Hill Tel: 8344 3261 Email: elhill@unimelb.edu.au  
Dr Dan Malone Tel:99039576 E: Dan.malone@monash.edu

**Aim:** To investigate the effects of pharmacological agents that modulate cannabinoid pathways (CB agonists and antagonists) on sensorimotor gating in a mouse model of autism. Autism Spectrum Disorder (ASD) is a prevalent neurological disorder in which the vast majority of patients show altered sensory perception. ASD patients demonstrate deficits in sensory motor gating compared to controls. NL3 mice express a mutation in the Neuroligin-3 gene identified in two brothers with autism and show increased synaptic inhibition in the somatosensory cortex as well as deficits in social behaviour including decreased sociability and increased aggression. While the NL3 mutation is known to be located at the postsynapse, the increase in frequency of inhibitory synaptic events suggests a change in presynaptic release of neurotransmitter. Cannabinoids serve as retrograde inhibitory messengers (ie they travel in the reverse direction across synapses) in the brain to inhibit neuronal function and transmitter release. A disruption in this pathway could result in increased inhibition as reported in the NL3 mice and contribute to the observed behavioural phenotype.

In this project we aim to use the non-invasive PPI test in the NL3 mouse model of autism to assess for alterations in sensorimotor processing. Based on published data demonstrating altered cortical inhibition in these mice, we will also investigate effects of modulating the inhibitory cannabinoid pathway using pharmacological agents.

**Skills:** Behavioural and animal handling skills. Data acquisition and analysis using the Pre Pulse inhibition test for sensorimotor gating. Evaluation of behavioural effects of cannabinoids in NL3 mice and controls.

188. How does Age of Illness Onset affect severity and extent of MRI Brain Structural Abnormalities in Schizophrenia

- also offered as MBSc

**Supervisors:** Prof Christos Pantelis, Dr Alex Fornito, Melbourne Neuropsychiatry Centre

**Project Site:** Melbourne Neuropsychiatry Centre, National Neuroscience Facility (NNF), Alan Gilbert Building, Level 3, 161 Barry Street, Carlton South, Vic 3053

**Contact:** Prof Christos Pantelis E: cpant@unimelb.edu.au  
Dr Alex Fornito T: 8344 1876. E: fornitoa@unimelb.edu.au

**Project Description:** Research at the Melbourne Neuropsychiatry Centre has demonstrated that the onset of schizophrenia is characterised by dynamic brain changes that begin prior to illness onset and progress throughout the course of the illness, particularly in frontal and temporal lobe regions. We have also demonstrated that the onset of schizophrenia is associated with pronounced cognitive changes that parallel clinical symptoms, and that these changes indicate that onset of the disease may ‘arrest’ normal brain maturational processes. Given that frontal and temporal brain regions continue to develop into the second and third decades of life, when the onset of schizophrenia is most common, we hypothesise that the timing of illness onset is a critical factor in determining the nature and extent of these brain changes. Specifically, we predict that later illness onset will be associated with relatively preserved neuroanatomy and cognition, due to reduced maturational disruption. By addressing this question the proposed applicant will specifically investigate issues related to normal brain maturation, schizophrenia-specific changes, and the interaction between the two. The research will be conducted using magnetic resonance images already acquired as part of the Australian Schizophrenia Research Bank together with computerised techniques to delineate differences in brain structure and cognition.

189. Stem Cell based modelling of Human Neurological Disorders: Towards Drug Discovery for improved Therapeutics

- also offered as MBSc

**Supervisors:** Assoc. Prof. Jeremy M Crook, Dr Nao Kobayashi, Prof. Stan Skafidas, Prof. Christos Pantelis, Prof. Ian Everall

**Project Site:** Centre for Neural Engineering, Melbourne Neuropsychiatry Centre, and Department of Psychiatry, The University of Melbourne

**Contact:** Prof Jeremy Crook T: 03 9035 3647 E: jcrook@unimelb.edu.au

**Project Description:** Stem cells represent useful tools for modelling development and disease. For example, induced pluripotent stem (iPS) cells carrying or modified to carry defective genes can be investigated in vitro to understand latent molecular mechanisms and disease characteristics. Once characterised, cell lines can be employed for drug screening towards developing novel pharmacological therapies. We have a number of Honours projects available for clinical or science graduates involving human brain derived neural progenitor cells (NPCs) and iPS cells. Disease models of interest include schizophrenia, autism and other disorders of brain development. Successful candidates will have the opportunity to receive training in somatic cell reprogramming for iPS cell derivation, culture and differentiation and will develop experience in methods of RNA interference, and molecular
and functional assays for in vitro characterisation. We anticipate studies will result in better understanding disease aetiology, pathology and the development of new medicines for improved therapeutics.

190. 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.

191. Characterisation of physiological stress responses in patients with depression and epilepsy - also offered as MBSc

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.

192. Is ADAM17 expression decreased in the brains of people with mood disorders?

Supervisors: Andrew Gibbons & Prof Brian Dean
Project Site: Florey Institute for Neuroscience and Mental Health, Parkville
Contact: Dr Andrew Gibbons E: agibbons@unimelb.edu.au; T: 90356746

Project Description: Mood disorders are amongst the most prevalent psychiatric disorders in society. However, the underlying cause of these disorders remains elusive. Clinical studies have reported altered levels of cytokines in the blood of people with major depressive disorder and bipolar disorder. Our group has recently shown that the level of a biologically active, membrane-bound, precursor of the soluble cytokine tumour necrosis factor (tmTNF) is increased in post-mortem cortical tissue from subjects with major depressive disorder and subjects with bipolar disorder. By contrast levels of the soluble TNF cytokine (sTNF) remain unchanged. A possible explanation for this increase in tmTNF is that the expression or activity of ADAM17, a metalloprotease that cleaves tmTNF to release sTNF, is abnormal in the affected cortical regions in people with these disorders.
This project will measure ADAM17 expression in post-mortem cortical tissue from subjects with major depressive disorder, bipolar disorder and control subjects. Western blotting will be used to measure ADAM17 protein levels in the dorsolateral prefrontal cortex and anterior cingulate cortex, two regions of the brain where subjects with mood disorders have increased levels of tmTNF. Data from these findings will be compared with tmTNF levels in this tissue to determine whether the increased levels of tmTNF may be due to a reduction in ADAM17 protein levels. ADAM17 enzyme activity assays will also be used to determine whether ADAM17's ability to cleave tmTNF is affected in individuals with mood disorders.

The techniques students 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
- Immunoprecipitation
- Enzyme activity assays

**193. Investigation of genes that are altered in the brains of people with schizophrenia**

**Supervisors:** Assoc Prof Elizabeth Scarr & Dr Madhara Udawela

**Project Site:** Mental Health Research Institute, Melbourne Brain Centre, Parkville

**Contact:** Madhara Udawela E: mudawela@unimelb.edu.au; T: 90356601

**Project description:** Levels of binding to muscarinic receptors are altered in the brains of people with schizophrenia. Since the development of more selective ligands, all studies report a decrease in the levels of binding to M1/M4 receptors, as shown by levels of [3H]pirenzepine.

In 2002 we showed that it is the M1 receptor that is decreased in the brains of people with schizophrenia. In 2009 we showed that this decrease occurs in a distinct sub-group of people with schizophrenia, who have on average 75% less binding to muscarinic receptors. Work is now undergoing to understand the consequences of this decrease and to identify other neurochemical changes in order to obtain a full picture of the different pathophysiology seen in this group.

Our recent microarray study identified several candidate genes and pathways that are potentially different between the groups, and we are now following these. The follow up studies will be performed using quantitative real-time PCR in the same tissue, to confirm the microarray data. Once confirmed, the study will be extended to other brain regions implicated in schizophrenia to determine the extent of these changes throughout the brain. Next, tissue from subjects with other psychiatric illnesses will be examined to determine the disease specificity of these changes. Finally the pathways will be studied in brains from animals treated with antipsychotic drugs to make sure the alterations to the pathway are not an outcome of the treatment these people received.

This project will employ the following laboratory techniques:
- RNA extraction and cDNA synthesis
- Standard PCR including primer design and optimisation
- Agarose gel electrophoresis and DNA extraction from gel
- Quantitative real-time PCR

**194. Characterising morphological abnormalities of the cerebral cortex in established schizophrenia: A structural MRI study - also offered as MBSc**

**Supervisors:** Dr Cali Bartholomeusz, Dr Sarah Whittle, Prof Christos Pantelis.

**Project Site:** Melbourne Neuropsychiatry Centre, Department of Psychiatry, National Neuroscience facility, Level 2-3 Alan Gilbert Building.

**Contact details:** Dr Cali Bartholomeusz Ph: 8344 1878, Email: barc@unimelb.edu.au

**Project Description:** An extensive body of neuroimaging literature suggests that schizophrenia patients invariably display significant reductions in grey matter volume of various brain structures. Grey matter regions most commonly found affected are localised to the temporal and frontal cortices. These regions are particularly important for learning, memory and higher-order cognitive functioning. Thus the implications of grey matter loss are wide-reaching and can impact on everyday functioning.

A great deal of research is now beginning to focus on characterising abnormalities in more detail by investigating cortical thickness, surface area and gyrification/folding. Identifying abnormalities in cortical surface characteristics is now possible with the recently developed automated surface-based approaches. By investigating these specific morphological parameters we will better understand the potential origins of brain abnormalities in schizophrenia.

The aim of the proposed study is to characterise morphological cortical abnormalities in schizophrenia by investigating differences in cortical thickness, surface area and degree of gyrification between healthy controls and individuals with established schizophrenia. The student will be responsible for pre-processing MRI scans that have been previously collected and are part of the MNC databank. The student will also be involved in writing scripts for running the multiple automated processing steps using the neuroimaging Freesurfer software program; and data analysis.
195. Investigating antipsychotic drug action on the epidermal growth factor system as a gateway to novel treatment for schizophrenia - also offered as MBSc

Supervisors: Dr Avril Pereira and A/Prof Suresh Sundram

Project Site: Florey Institute of Neuroscience and Mental Health, Melbourne Brain Centre, The University of Melbourne, Parkville

Contact: Dr Avril Pereira T: 9035 6573 E: avril.pereira@unimelb.edu.au

Project Description: Schizophrenia is a devastating disorder that strikes at young people and persists throughout life. Much of this suffering is borne by up to a third of those for whom current treatments are ineffective. For these treatment resistant patients the alternative is the atypical antipsychotic drug (APD) clozapine, however, its use is limited by disabling side effects. Why clozapine is uniquely effective is unknown but may reside in interactions with intracellular signalling cascades that govern gene transcription and neuronal function. In this regard, we have demonstrated in vitro and in vivo that clozapine signals to the MAPK-ERK cascade in cortical neurons differently compared to other APDs. This pathway is central to the regulation of neuronal differentiation, maturation and plasticity, processes disrupted in schizophrenia. We have also determined that the mechanism through which clozapine affects ERK is mediated by the epidermal growth factor (EGF) receptor. Our cellular, animal and clinical data support our hypothesis of EGF system hypofunction in schizophrenia in a sub-type of patients that respond to clozapine via a novel mechanism that augments EGF signalling. This project will characterise how clozapine recruits the EGF receptor to phosphorylate ERK in cortical neurons and delineate the intracellular path through which this transactivation occurs: activation of mediators such as Src kinases, Ca²⁺, Pyk or PKC; activation of a matrix metalloproteinase; or through β-arrestin mediated endocytosis.

Skills: The candidate will receive training in derivation and culture of primary frontal cortical neurons and will use SDS-PAGE, immunoblotting, immunocytochemical, siRNA, RNA extraction, PCR or RT-PCR methods on cortical cells and APD treated mouse prefrontal cortex to study key proteins in the targeted pathway. An understanding of our current thinking on how the brain is disturbed in psychotic disorders will be gained.

NEUROVASCULAR

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

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.

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

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,
**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 of 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.

**OPHTHALMOLOGY**

198. **Project title:** What are the genes affected in structural renal disease and renal complement diseases? – also offered as MBSc

   **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.

199. **Small vessel disease causing stroke and dementia** – also offered as MBSc

   **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).
200. **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 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](http://sc.mdhs.unimelb.edu.au/how-apply)

**PHARMACOGENETICS AND PERSONALISED MEDICINE**

201. **Pharmacogenomics in IBD - also offered as MBSc**

**Supervisors:** Professor Finlay Macrae and Prof Les Sheffield

**Project Site:** Colorectal Medicine and Genetics, The Royal Melbourne Hospital

**Contact:** Prof Finlay Macrae E: finlay.macrae@mh.org.au

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

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

**Supervisors:** Professor Patrick Kwan, Dr Marian Todaro

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

**Contact:** Patrick Kwan, Department of Medicine (RMH) E: patrick.kwan@unimelb.edu.au; Dr Marian Todaro, Department of Neurology E: Marian.Todaro@mh.org.au

**Project Description:** This study is part of a large project aiming to bring personalised medicine into widespread clinical practice (see project numbers 192 and 193). 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 MBSc
Supervisors:  Professor Stan Skafidas and Professor Patrick Kwan
Project Site:  Centre for Neural Engineering, Department of Electrical Engineering
Contact:  Professor Stan Skafidas, Department of Electrical Engineering, E: sskaf@unimelb.edu.au
Supervisors:  Professor Patrick Kwan, Department of Medicine, E: patrick.kwan@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 commercialization 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 MBSc
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 allele in the MDR1A and 3435C allele in MDR1B. The monolayer model of the cell was used to study the effect of polymorphisms on the transport of AEDs. Pgp is an ATP-transporter, and some AEDs have an electrostatic dipole. To elucidate the role of Pgp in the transport of AEDs, we have found that Pgp with 2677T allele had higher transport function of pitting AED from basolateral to apical side than 2677G allele in cell monolayer, 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 association 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

205. A decision support system for implementation of pharmacogenomics in epilepsy treatment - also offered as MBSc
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.

206. Immune self-reactivity triggered by carbamazepine-modified HLA-peptide repertoire - also offered as MBSc
Supervisors:  Professor Patrick Kwan, Professor James McCluskey
Project Site:  Department of Microbiology & Immunology, Department of Medicine (RMH)
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 greatly increased the risk of carbamazepine-induced severe skin reactions in Chinese/South Asians, but little is known about the underlying mechanisms of these associations. Recent research at the Department of Microbiology & Immunology has demonstrated that direct binding of the drug to the HLA molecule led in Chinese/South Asians, but little is known about the underlying mechanisms of these associations. Recent research at the Department of Microbiology & Immunology 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 carbamazepine-HLA-B*15:02 interaction.

**This project is also listed under Epilepsy and Neuropharmacology and Innate Immunity and Host Defence**

### 207. HLA and its association with skin rashes and drug induced hepatitis: The role of pharmacogenomics to predict anti-epileptic drug side-effect - also offered as MBSc

**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 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 MBSc

**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 pharmacogenomics 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 cerebrovascular ischaemic events.
209. A Pharmacogenomics study of the teratogenicity valproate based on the prospective Australian Register for Anti-epileptic Drugs in Pregnancy - also offered as MBSc

Supervisors:  Professor Terence O’Brien, Professor Frank Vajda and Dr Slave Petrovski - Epilepsy and Neuropharmacology Group, The Department of Medicine: The Royal Melbourne Hospital.

Project Site:  The Department of Medicine (RMH)

Contacts:  Terence O’Brien  T: 8344 5479  E: obrientj@unimelb.edu.au;  Frank Vajda  E: vajda@netspace.net.au;  Slave Petrovski E: slavep@unimelb.edu.au

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

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

**POPULATION HEALTH**

210. Key strategies for engaging users of Social Networking Sites for health promotion - also offered as MBSc

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 MBSc

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 MBSc
   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 MBSc
   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 MBSc
   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 MBSc
   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 MBSc
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 MBSc
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 MBSc
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 development 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 MBSc
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 MBSc**

**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. **Assessment of antenatal and postnatal care for HIV positive pregnant women in Papua New Guinea – also offered as MBSc**

**Supervisor:** Dr Megan Lim  
**Project Site:** Burnet Institute  
**Contact:** E: lim@burnet.edu.au  
**Telephone:** 8506 2403

**Project description** Women in PNG are 80 times more likely to die in childbirth than women in Australia. Furthermore, the prevalence of HIV in PNG is high; around 2% of pregnant women are HIV-positive. There are effective methods for preventing mother to child transmission of HIV (PMTCT), however, in PNG many of these interventions may not be effectively delivered or taken up. The extent to which these interventions are delivered is not well understood, due to poor-quality data collection.  

This study will work to improve data collection systems for an antenatal service in the highlands of Papua New Guinea, and determine the level of uptake and effectiveness of important PMTCT interventions.

222. **Understanding sex work in Vanuatu – also offered as MBSc**

**Supervisor:**  
**Project Site:** Burnet Institute  
**Contact:** E: carolinevg@burnet.edu.au  
**Telephone:** 9282 2243

**Project description** The prevalence of STIs, particularly chlamydia, in Pacific Island Countries and Territories (PICTs) are among the highest in the world. The asymptomatic nature of many STIs, particularly chlamydia and gonorrhoea, makes their public health control problematic, particularly in settings that have limited access to technologically advanced diagnostic procedures. Populations most vulnerable to STIs in the region include young people, female sex workers (FSW), men who have sex with men (MSM), injecting drug users, seafarers, uniformed services and prisoners, however there is an absence of reliable epidemiological information about these groups. In 2011, the Burnet Institute conducted a study with sex workers and MSM to estimate the prevalence of STIs in these populations, and also to investigate risk behaviours and other characteristics associated with STIs. This project will utilize data collected in the Vanuatu Integrated Bio-Behavioural Survey and conduct a more detailed investigation into sex work in Vanuatu.

223. **How does binge drinking impact on health-related behaviours among ex-prisoners in Fiji? – also offered as MBSc**

**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 MBSc**  
Supervisor: Dr Mark Stoove, 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. **Sex, drugs and rock’n’roll: Young people and risk behaviours in a survey at the Big Day Out music festival - also offered as MBSc**  
Note: This project is only available for mid-year enrolment. Please check the website for mid year enrolments.  
Supervisor: Professor Margaret Hellard, Head, Centre for Population Health, Burnet Institute  
Project Site: Burnet Institute  
Contact: Hellard@burnet.edu.au  

**Project Description:** Sexually transmitted infections (STI) are on the rise among young Victorians. Since 2005, we have surveyed over 9,000 people aged between 16 and 29 years of age at Melbourne’s Big Day Out about sexual risk behaviour and drug use. Questions have covered participant’s sexual histories, condom use, knowledge and perceptions of STIs, and STI testing histories. We ask about alcohol and other drug use, and other risks and behaviours such as diet and exercise, contact with police, mental health, and smoking. The Big Day Out festival also gives us an excellent opportunity to inform this population group about sexual health and behaviour that may place them at risk of sexually transmitted infections. Showbags containing safer sex and other harm reduction information are distributed to survey participants and other Big Day Out patrons.

In this project the student will manage and organise recruitment of participants at the Big Day Out. They will then use the data collected to investigate patterns of sexual risk behaviours, knowledge, and attitudes. This will involve quantitative analysis of the relationship between variables such as condom use, number of sexual partners, drug and alcohol use, and perceptions of risk. These findings, in the context of current public health measures, will be used to advise on the design of future sexual health promotion campaigns.

226. **Low income as a barrier to opioid substitution therapy - also offered as MBSc**  
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

227. Improving the health of newborn babies: investigating the role of proteoglycans in causing abnormal growth problems in pregnancies from women with diabetes – also offered as MBSc

Supervisors: A/Prof Joanne Said and Ms Tilini Gunatillake
Project Site: Centre for Health Research and Education, NorthWest Academic Centre, Sunshine Hospital, St Albans
Contact: E: jsaid@unimelb.edu.au or t.gunatillake@student.unimelb.edu.au

Project description: As more and more younger women are developing Type 2 diabetes, we are seeing an increasing number of pregnancies in women with this condition. Type 2 diabetes has significant effects on the pregnancy and leads to an increased risk of stillbirth, fetal abnormalities and problems with growth of the baby. Proteoglycans are important molecules located within the placenta which have a variety of functions. High glucose levels, such as those seen in diabetes, can alter the structure of the glycosaminoglycan side chains of proteoglycans and hence affect their function. The aim of this study will be to extract proteoglycans and glycosaminoglycans from placenta obtained from women with diabetes complicating their pregnancies as well as control (uncomplicated pregnancies) and compare differences in the function of the glycosaminoglycans.

This project is being run by an established pregnancy research group. The methodologies are established within our laboratories at the newly built Centre for Health Research and Education, located at Sunshine Hospital, St Albans. As the second largest maternity hospital in Victoria, we have unprecedented access to the patients required to undertake this study. You will have an exciting opportunity to be a part of this dynamic clinical research team comprising obstetricians, haematologists, placental researchers and biochemists.

Techniques: Recruitment of patients, sample collection, HPLC, protein electrophoresis, Real time PCR.

228. Understanding changes in haemostasis during pregnancy and pregnancy complications – also offered as MBSc

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.

229. Multiple serum markers and mid trimester uterine artery Doppler in the prediction of pre-eclampsia - also offered as MBSc

Supervisor: Dr Padma Murthi, Dr Fabricio Costa
Project Site: Pregnancy Research Centre, Royal Women’s Hospital
Contact: Padma Murthi E: padma@unimelb.edu.au

Project Description: No single biomarker already tested has been shown to have sufficient clinical value in the prediction of pre-eclampsia in isolation. Instead, their value seems to be in increasing the predictive value of panels of tests which include other clinical measurements. The aim of this project is to examine the combination of maternal risk factors, mean arterial blood pressure, and uterine artery Doppler, together with novel biomarkers in the prediction of pre-eclampsia. This project would suit a biomedical graduate with an interest in clinical medicine and there will be opportunity for laboratory work. The techniques involved will include learning how to analyse clinical data and perform laboratory assays on serum for biomarkers.

230. Stem cells and their Potential to Treat Clinically Important Disorders of Pregnancy - also offered as MBSc

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.

### 231. Stem Cell Microvesicle Repair of the Damaged Endothelium in Preeclampsia. - also offered as MBSc

**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.

### 232. Pregnancy hormones and their receptors in trophoblast function - also offered as MBSc

**Supervisors:** Dr Padma Murthi, Dr Penny Sheehan and Dr Rosemary Keogh

**Project Site:** Pregnancy Research Centre, Royal Women’s Hospital

**Contact:** Dr Padma Murthi E: padma@unimelb.edu.au or Dr Rosemary Keogh E: rosemary.keogh@thewomens.org.au

**Project Description:** Progesterone (PG) and human chorionic gonadotropin hormone (hCG) are critical for the establishment and for the maintenance of pregnancy. The genomic actions of PG and hCG are mediated by their intracellular receptors. The project will investigate PG and hCG-mediated and signaling pathways that are critical for successful placental cell proliferation, differentiation, and angiogenesis that are important for decidualization. The project will also identify regulators of pregnancy hormone expression in trophoblast cells.

**Techniques:** Cellular and molecular biological techniques including cell culture, functional cell assays (proliferation, differentiation, network formation) real time PCR and RNAi.

### 233. Transcriptional regulation of placental angiogenesis in complicated pregnancies - also offered as MBSc

**Supervisors:** Dr Padma Murthi, Dr Rosemary Keogh

**Project site:** Pregnancy Research Centre, Royal Women’s Hospital

**Contact:** Dr Padma Murthi E: padma@unimelb.edu.au

**Project Description:** In pregnancies complicated by gestational hypertension the feto-placental vasculature is affected by altered expression of several pro-inflammatory cytokines and angiogenic molecules leading to aberrant placental angiogenesis. The molecular mechanisms governing placental angiogenesis are unknown. The project will identify the transcriptional profile of placental endothelial cells and their influence on placental endothelial functions.

**Techniques:** Tissue culture, ligand binding assays, functional cell based assays, protein and molecular biology.

### 234. How do hormones work: investigating new steroid receptors

**Supervisors:** Dr. Penelope Sheehan and Dr. Padma Murthi

**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 parturition1. Yet, in humans, maternal serum progesterone concentrations do not significantly decrease at labour onset2, suggesting a change at the receptor level. However detailed knowledge of intracellular and molecular mechanisms are unknown. We have identified two new receptors capable of binding progesterone which may help improve our understanding of progesterone action. The pregnane X receptor (PXR) is a nuclear receptor which is able to regulate gene transcription. The endogenous ligand with the highest affinity for the PXR is the progesterone metabolite, 5βDHP. Progesterone receptor membrane components 1 and 2 (PGRMC1, PGRMC2) are also putative progesterone receptors. Detailed study of the pathways affected by these receptors using myometrial
explant cultures and gene silencing techniques may provide new therapeutic targets for treatment of preterm birth and also for induction of labour in postdates pregnancy.

This project will build on previous Pregnancy Research Centre findings identifying changes in expression of these two new receptors in association with human labour at term in myometrium. The methodologies are established within our laboratories at The Royal Women’s Hospital.

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

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

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### 235. Phytophenols as therapeutic agents in the management of preterm birth

**Supervisors:** Dr. Martha Lappas and Dr. Ratana Lim  
**Project Site:** Department of Obstetrics & Gynaecology, University of Melbourne located at the Mercy Hospital for Women  
**Contact:** Dr Martha Lappas T: 8458 4370 E: mlappas@unimelb.edu.au

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

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

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### 236. The effect of maternal diabetes on placental function: implications for fetal growth and development

**Supervisors:** Dr. Martha Lappas and Dr. Ratana Lim  
**Project Site:** Department of Obstetrics & Gynaecology, University of Melbourne located at the Mercy Hospital for Women  
**Contact:** Dr Martha Lappas T: 8458 4370 E: mlappas@unimelb.edu.au

**Project Description:** Diabetes in pregnancy is a major health issue globally, affecting up to 14% of all pregnancies. Under diabetic conditions, the placenta undergoes structural and functional changes, which disrupts normal fetal programming. This results in a critically adverse fetal environment, enhancing susceptibility to a number of chronic diseases including obesity, diabetes, cardiovascular disease and certain cancers later in life. We hypothesise that exposure to a diabetic environment disrupts the function of the mitochondria in the placenta leading to the overproduction of reactive oxygen species, which is responsible for cellular and metabolic damage and poor fetal outcome. Thus, the aim of this study is to characterise the effect of diabetes on the function of mitochondrial in human placenta.

**Techniques:** Tissue culture, mitochondrial cell isolation, PCR-based analysis, Western blotting and ELISA

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### 237. The endothelial-trophoblast interaction during pregnancy

**Supervisor:** Dr Rosemary Keogh and Dr Padma Murthi  
**Project Site:** Pregnancy Research Centre, Royal Women’s Hospital  
**Contact:** Rosemary Keogh T: 8345 3749; E: rosemary.keogh@thewomens.org.au

**Project Description:** There is a dynamic interaction between cells of maternal vessels and trophoblast cells of the placenta during early human pregnancy. The trophoblast cells invade into the uterine maternal vessels and remodel them to facilitate increased blood flow to the placenta to enable the fetus to grow and develop normally. When this is disrupted, serious complications arise which jeopardize the successful outcome of the pregnancy. This project will focus on the interactions between the endothelial cells of maternal vessels and trophoblast cells. In particular, the regulation of trophoblast cell adhesion and migration by endothelial cells will be examined with a focus on a role for cytokines.

**Techniques:** Cell culture, protein arrays, Western blotting, ELISA, real time migration and adhesion assays, microscopy.
238. Developing a new lab-on-a-chip model for studying cell invasion

Supervisors: Dr Rosemary Keogh
Project site: Pregnancy Research Centre, Royal Women’s Hospital
Contact: Rosemary Keogh T: 8345 3749; E: rosemary.keogh@thewomens.org.au

Project Description: This project will develop and test a novel and innovative approach to investigating cell invasion using nanotechnology. Known as lab-on-a-chip (LOC), this technology offers a powerful alternative to current cell culture and animal model systems. LOCs consist of small plastic or glass devices that contain micro-channels and chambers in which cells can be grown and manipulated. Cell growth, concentration gradients, extracellular matrix components and cell-cell interactions can be controlled on a nano-scale which more accurately reflects the in vivo microenvironment of cells and tissues.

Using LOC prototypes, this project will look at the movement of invasive cells through a blood vessel wall into the extracellular matrix. The aims will be to establish a model blood vessel in prototype LOCs, optimize conditions for cell invasion through a blood vessel wall and use the model to study factors that control cell invasion.

Techniques: Cell culture, labelling and tracking cells in real time, fluorescent imaging, time lapse microscopy and cell invasion and migration assays.
2013/14 KEY DATES

Aug-November 2013: Contact potential supervisors to discuss Honours projects (Step 1)
30 August 2013: Open date to register online application
Mid September 2013: Open date to lodge project preferences through HATS
15 November 2013: Closing date to register online application (Step 2)
29 November 2013: Closing date to lodge project preferences through HATS (Step 3)
3rd wk December 2013: First round of offer letters sent by mail to students
6 January 2014: Closing date for acceptance/rejection by students of First Round offers
10 January 2014: Second round of selection and mailing of offer letters begins
26 January 2014: Deadline for Late Applications
10/17 February 2014 (TBC): Honours 2014 Program commences / RMH Academic Centre 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

COURSE WORK

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 24 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

Course Codes:
Bachelor of Biomedicine (Honours) – BH-BMED
Bachelor of Science (Honours) – BH-SCI
RMH Academic Centre Enrolling Unit is: Department of Medicine (RMH)

2013 APPLICATION FOR HONOURS IN THE FACULTY OF MEDICINE, DENTISTRY & HEALTH SCIENCES (FMDHS)

If you wish to be considered for Honours in 2014, and you would like to undertake your project and coursework with the Royal Melbourne Hospital Academic Centre, Faculty of Medicine and Dentistry Sciences or affiliated institute with the enrolling unit being 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 2014.

STEP 2: Lodge an online application
Mid September 2013: Honours Applications OPENS to register for HATS
Lodge an online application between Friday 30 August to Friday 15 November 2013: 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
It is essential you carry out Step 2 BEFORE you carry out Step 3. Note the closing date for Step 2 is 15 November 2013.

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.

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. [http://sc.mdhs.unimelb.edu.au/how-apply](http://sc.mdhs.unimelb.edu.au/how-apply)

**HATS will open mid September 2013 and will close at 5pm on Friday 29 November 2013.**

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.

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 29 November 2013**. 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 of selection in mid January.

**Note:** The Department of Medicine (RMH) is the enrolling unit for the RMH Academic Centre 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 (MC-BMEDSC)
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:

Major Research Project  (Literature Review, Thesis, & Ora Presentations)  125 points
Core Discipline subject  (Introduction to Biomedical Research BIOM40001)  12.5
Discipline Subjects    37.5 points
Professional Skills    25 points

MAJOR RESEARCH PROJECT: 125 points.
A literature review of up to 4,000 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 15,000 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 MSc in the 2014 Honours Project List Handbook: For further details on the project please contact the supervisor listed in the handbook.

HOW TO APPLY FOR MBiomedSc

Course Code MC-BMEDSC

1. Applications for the Masters are made directly via the University online application system from September. Timely applications close on 30 November. 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, you must lodge an online application to the Melbourne Graduate School of Science (who are handling the admission process for Melbourne School of Medicine during transition to 2014).
   http://graduate.science.unimelb.edu.au/apply.php
   You will be required to nominate a Department, Supervisor and Project.

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

Local students applying for the Masters may be eligible for financial support


ENQUIRIES

Masters Admission Administration
Melbourne Graduate School of Science
David Caro Building (Building 192)
Tel: 61 3 8344 6128
Admissions gradscience-apps@unimelb.edu.au
Coursework Team graduate-science@unimelb.edu.au

MMS Masters Coordinator
Prof Lea Delbridge
Department of Physiology
lmd@unimelb.edu.au

RMH Academic Centre Honours/MBSc Coordinators:
– Dr Chris French  E: frenchc@unimelb.edu.au,
– A/Professor Caroline Marshall  E: Caroline.Marshall@mh.org.au

RMH Academic Centre Honours/MBSc Administrator: Mary Ljubanovic  E: mlju@unimelb.edu.au
Faculty of Science MSc (BHS) Coordinator: Professor Lea Delbridge  E: lmd@unimelb.edu.au

RMH ACADEMIC CENTRE DEPARTMENT LINKS:

RMH Academic Centre: 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.obsgyn.unimelb.edu.au/