RESEARCH HONOURS 2017
DIVISION OF MEDICINE

This booklet contains a list of available research projects for 2017
The Honours degree provides students with the opportunity to undertake further training in research in biomedical sciences, clinical sciences, health services and population health. This is a year-long program of advanced study that includes development of skills in understanding the scientific literature in biomedical and health fields as well as the student’s aptitude in scientific writing and presentation. The critical element of the Honours year across all of our programs is the focus on students undertaking a major research project, which will involve learning research skills, conducting research on a relevant biomedical or health area, and completing a thesis detailing and discussing the findings.

The Honours year in the Division of Medicine research program is available to UTAS students who have completed an undergraduate degree in the BSc, BMedRes, BBiotech, BBiotechMedRes (or similar), three years of the MBBS program or a Bachelor of Paramedic Practice. Students from other institutions can also apply to do the program where they have completed similar degrees. Students can undertake projects in a broad range of areas including: biochemistry, physiology, anatomy, neuroscience, human genetics, microbiology, the pathological sciences, population and public health, clinical trials, and paramedic practice depending on their interest and academic background.

An outline of available projects that the Division of Medicine (DoM) is offering in 2017 is contained in this booklet. If you cannot find a suitable project in here or have a desire to undertake a project in a certain area or with a certain researcher it is worthwhile contacting that researcher to discuss your idea. Often more projects are available but have not been listed. More information about projects in affiliated centres such as the Wicking Dementia Research and Education Centre and Menzies Institute for Medical Research can be found online.

**COURSE OBJECTIVES**

Students will undertake a supervised research project with an emphasis on advanced disciplinary knowledge, the use of specialised laboratory, fieldwork and/or statistical techniques relevant to their chosen research area, planning and conducting a scientific investigation and effective communication of research findings. Students will also gain experience in scientific writing and oral presentations. By the completion of the program students should be able to write a scientific report to a standard acceptable for submission to a peer-reviewed journal, and deliverable at a relevant conference or scientific meeting.

**ACADEMIC REQUIREMENTS**

The compulsory components of the assessment for all Honours programs include a literature review as part of the thesis introduction, two seminar presentations, a thesis and a supervisors’ report. One seminar presentation will be a critical review of a journal article and the second seminar presentation will be from your thesis.

**SCHOLARSHIPS**

There are a number of scholarships available to students undertaking research in the Division of Medicine. Scholarships will be awarded based on academic merit. If you are an MBBS or Paramedic student you can apply directly to the Division of Medicine using the application form available from stephen.richards@utas.edu.au. This form will also be used to assess and approve your Honours application. For more information on availability, eligibility and how to apply for other scholarships including those offered through the Menzies Research Institute Tasmania go to http://www.studentcentre.utas.edu.au/scholarships/.

Please be aware that the CLOSING DATE for non-MBBS applications is October the 31st. (NB For MBBS students the earlier date of 2 Sept 2016 applies, due to forward planning considerations).
YOUR APPLICATION TO DO HONOURS

To apply to do Honours students should have completed three years of a relevant undergraduate degree with a credit average, or equivalent. It is a good idea before you apply to do Honours to identify a project that appeals to you and to make contact and discuss the project with the supervisor. Once you have decided to apply go to ‘Future students’ on the UTAS website for information on the application process.

To be successful in your application to study for Honours you will need to satisfy the Honours committee that you have a suitable project that constitutes the workload of an Honours thesis and that it can be accomplished within the time frame. In addition to this the committee will need to be assured they need to be assured that the appropriate supervision is in place. Your application will also be judged on your past academic performance.

All students need to apply online. If you are an MBBS student undertaking a project in the DoM you should complete the Honours application form that appears on the DoM research website page. Following approval of this application you will be able to enrol in the Bachelor of Medical Science with Honours (M4N). Paramedic students in the Bachelor of Paramedic Practice with Honours (M4P) should also complete this same process. Undergraduate science students can enrol in the Bachelor of Medical Research with Honours (M4G), Bachelor of Biotechnology and Medical Research (K4L) or the Bachelor of Science with Honours (S4E) as appropriate.

STUDENT EXPECTATIONS

The course extends from late February (semester 1 commencement) to late October or mid-July (semester 2 commencement) to March or April the following year. Attendance requirements will be dictated by the nature of the research for example, whether the project is being undertaken within a hospital or within a laboratory. Attendance requirements will be agreed mutually between student and supervisor. There is an expectation despite the nature of the project that the minimum time required to successfully complete the Honours year is a minimum of 40 hours per week equivalent to a standard full-time working week.

The University and the Division of Medicine acknowledges that students are Division in extra-curricular activities and is generally supportive of students’ activities. The Division of Medicine must be confident that these activities do not significantly impact on the students’ ability to complete the requirements of the Honours year.

For additional information regarding Honours contact Dr Steve Richards, the Course Coordinator. Contacts for projects supervised at other centres under Division of Medicine Honours are listed below. Menzies projects are listed separately at: http://www.menzies.utas.edu.au/education/study-at-menzies/phd-and-honours

NB: Below are listed projects available currently (as of August 2017); further projects will be added in Nov 2016. If you are interested in an area of research carried out by a Division of Medicine, Menzies or Wicking researcher that does not appear in this document, it may be worthwhile approaching them directly to see if they are considering supervising Honours projects in 2017.

COURSE COORDINATOR
Dr Steve Richards: Stephen.richards@utas.edu.au
Phone: (03) 6226 2673

ADDITIONAL CONTACTS
Dr Kathryn Ogden: Kathryn.ogden@utas.edu.au
(Launceston) Phone: (03) 6348 8790

Dr Peter Lucas: p.v.lucas@uts.edu.au
(Paramed Pract) Phone: (03) 6226 6952

Dr Anna King: A.E.King@utas.edu.au
(Wicking, lab-based) Phone: (03) 6226 4817

Dr Kaylene Young kayaklene.young@utas.edu.au
(Menzies) Phone: (03) 6226 7745
Clinical & population health-based projects (involving human subjects and/or data)

Project title: Automated control of inspired oxygen therapy in neonates

Supervisor(s) contact details: Prof Peter Dargaville (peter.dargaville@ths.tas.gov.au), Dr Tim Gale (tim.gale@utas.edu.au)

Avoidance of hypoxia (low blood oxygen level), and especially for the preterm neonate, hyperoxia (high blood oxygen level), is fundamental in the delivery of respiratory support to the newborn infant with respiratory insufficiency. Hypoxia in preterm infants is most commonly a consequence of respiratory distress syndrome, and, if not adequately treated, substantially increases the risk of mortality. Conversely, unrestricted and/or inadequately regulated oxygen therapy causes overgrowth of vasculature in the developing retina of the preterm infant. This retinopathy of prematurity (ROP) is a continuing problem in NICUs in the Western world, and is a significant concern in developing and newly industrialised countries.

At present in most NICUs, moment-by-moment changes to FiO$_2$ are under the control of the bedside staff, who make adjustments based on the transcutaneous oxygen saturation level (SpO$_2$). Despite the best efforts of staff at the bedside, neonates on respiratory support spend considerable amounts of time with SpO$_2$ readings outside the desired or target range. A study conducted at RHH in 2012 by UTAS MBBS Honours student Kathleen Lim (the SNOOT study) found that in preterm infants on non-invasive respiratory support, SpO$_2$ was maintained in the target range only 31% of the time.

The data collected in the SNOOT study$^{1-3}$ have aided our efforts to develop an inspired oxygen controller. This is a device that receives transcutaneous oxygen saturation (SpO$_2$) readings from a bedside oximeter, verifies and processes the oximetry data, compares the SpO$_2$ readings with predetermined targets in a control algorithm, and sends signal pulses to a servomotor to automatically turn the FiO$_2$ dial of a gas blender. The control algorithm at the heart of our control device has some unique features that have not been incorporated in FiO$_2$ feedback control systems previously. We believe these additional features will allow more precise targeting of SpO$_2$ in preterm infants receiving oxygen than ever before possible with an automated FiO$_2$ control system. Preliminary studies of 4 h duration under controlled conditions, with a researcher present throughout, have been conducted in 2015 by our current UTAS MBBS Honours student, Gemma Plottier. We have found that in preterm infants our device appears to maintain SpO$_2$ in the target range more effectively than manual control, with few episodes of hypoxia and hyperoxia.

The next stage of development of the oxygen control device is a study (the SANTO-B study) in which automated control will be compared with manual control under standard clinical conditions for 24 h periods, without a member of the research team consistently in attendance. These studies will begin later in 2015, and will continue throughout 2016. The involvement of an MBBS Honours student in this next stage would be a great boost for the project, as has been the case in 2012 and 2015.

Location: School of Medicine, Hobart

Project title: Patient-centred health care: Investigating the views of stakeholder groups.

Supervisors: Dr Kathryn Ogden; Senior Lecturer, Launceston Clinical School Kathryn.Ogden@utas.edu.au; Jenny Barr, Patient Partner Program Development and Strategy Director Jenny.Barr@utas.edu.au.

Project synopsis: Patient-centredness in health care delivery recognises that patients’ values and preferences must be central in the delivery of care, both at the organisational and professional level. The notion of patient-centred care is not a new one with efforts to operationalise and study it dating back to at least as early as 1986. However, 30 years later patient-centred care remains somewhat of an enigma, with “many evangelists but few practitioners”1(p 97757) and ongoing debate and discussion as to the imperative for patient-centred care being taught and practiced and how it can be better achieved.

Through previous work at the Launceston Clinical School we have developed a conceptual map for ‘Patient-Centred Care Requirements.’ It outlines how an operational perspective to patient-centred care can be considered, refocussing attention towards ‘how’ to achieve patient-centred care. Our focus on ‘requirements’ aimed to lead to the complexity of patient-centred care delivery being better understood, thereby informing the definitions of patient-centred care in a more comprehensive way. 123 statements have been generated identifying elements required for patient-centred care.

This project will build on this work by collecting and analysing the views from five different stakeholder groups of each requirement statement regarding their relative importance, feasibility and how well they are achieved. Participants will be recruited from five stakeholder groups: patients and carers; clinicians’ health care managers; peak body representatives; and educators, and asked to rate each of the 123 statements contained in the Patient-Centred Care Conceptual Map on a 5 point likert scale according to importance, feasibility and how well they are achieved. Data will be collected using the CS Global Max online platform (http://www.conceptsyltems.com/software/) and analysed to determine the stakeholder views on the elements of patient-centred care. Data will also be used to develop additional visual tools (pattern matches and go-zones) which will enable its use for education and training in a variety of settings. A further qualitative component may also be possible, but will not be crucial to achieve an honours level project, and can be negotiated depending on feasibility within the 12-month timeframe.

Location: Launceston Clinical School

Associated Scholarship: The successful applicant will be able to apply for an additional scholarship from the Clifford Craig Medical Research Trust.

Reference:
Project Title: Heterologous effect of diphtheria, tetanus, acellular pertussis vaccination on influenza vaccine challenge in the elderly

Supervisor(s) contact details: A/Prof Katie Flanagan (Katie.flanagan@ths.tas.gov.au) Dr Kathryn Ogden (kathryn.ogden@utas.edu.au).

Research Project Synopsis
The world's population is aging, with dramatic rises predicted in the coming decades; thus a healthy aging population is a major public health priority. However, the immune system declines with increasing age leading to increased susceptibility to infectious diseases, and suboptimal responses to vaccination, an ideal tool to prevent infections. Furthermore, it is increasingly acknowledged that childhood vaccines have major immune modulatory effects, beyond the induction of vaccine-specific immunity. Specifically, our previous studies demonstrate diphtheria-tetanus-pertussis (DTP) vaccine causes sex-specific immunosuppression and interferes with subsequent measles vaccine efficacy. However, the non-specific effects of vaccines, and their impact on the immune system of the elderly are an important, but as yet untouched, area of research. In this project will use state-of-the-art immunological tools to interrogate the complex relationship between the immune response to two vaccines recommended in the elderly in Australia, the seasonal influenza vaccine and DTP. This information will be used to provide the much needed evidence based rationale to implement optimal vaccination schedules in this vulnerable group.

Study Aim
Determine the effect of DTP vaccination prior to or co-administered with the influenza vaccine in the elderly on innate immunity.

Methodology
Elderly adults >65 years and healthy adults aged 30-50 years will be will be randomised prospectively into 1 of 3 vaccine groups at enrolment (see diagram below). Vaccines will be administered intramuscularly into the deltoid (different arms when both vaccines are given together).

30mLs venous blood (24mLs in heparin tubes, 2mLs in serum tube, 2mLs in EDTA) will be taken by the research nurse at the LGH Vaccine Trial Centre at the time points in the figure (circles).
The project question will be addressed by culturing whole heparinised blood overnight with a panel of Toll-like receptor (TLR) ligands and whole killed pathogens. Culture supernatants will be collected and stored at -70°C for later multiplex cytokine analysis. The multiplex assays will be done in Melbourne. We anticipate ~150 subjects will be tested in this way.

The student will also help with the recruitment, vaccination and bleeding of study subjects. They will also be trained in sample processing. Serum and plasma will be collected and stored from the remaining blood samples, and then peripheral blood mononuclear cells (PBMC) will be collected following density gradient centrifugation. We will also store PBMC in Trizol for later RNA extraction. Samples will be shipped intermittently to the Dept of Immunology and Pathology, Monash University in Melbourne for further analysis.

**Outcome:** The student will determine if the different vaccine schedules have an impact on innate immunity.

**Location:** Vaccine Trial Laboratory, Launceston General Hospital and Systems Vaccinology Trial Centre, Clifford Craig Medical Research Trust.

**Associated Scholarship:** The successful applicant will be able to apply for an additional scholarship from the Clifford Craig Medical Research Trust.

**References**


**Project Title:** How is chronic kidney disease identified and managed in General Practice? (Students undertaking this project may be eligible for a scholarship aimed at projects undertaken at the Launceston Clinical School and within General Practice)

**Supervisor(s) contact details:** Assoc Prof Jan Radford (Assoc Prof of General Practice, UTAS); Dr Kathryn Ogden (research Fellow, UTAS); Drs Rajesh Raj, Matthew Matthew, and Duncan Cooke (renal physicians, Launceston General Hospital) (J.Radford@utas.edu.au)

**Research project synopsis**
Identifying patients in a general practice population at risk of developing chronic kidney disease (CKD) is an important part of preventative health care, as is optimally managing those with a diagnosis of chronic kidney disease. It is estimated that 10% of all adults presenting to a general practice in Australia have CKD, and 80% have at least one risk factor for CKD. Early
intervention can reduce progression and cardiovascular risk by up to 50%, and may also improve quality of life. This study will contribute to knowledge on how to improve the detection and care of chronic kidney disease patients in general practice.

**Aims and objectives:**

- To determine how practices identify and record which of their patients have CKD and the accuracy of practice datasets.
- To identify factors impacting on the accuracy of a practice database of patients with CKD including opportunities for improving record management.
- To explore factors involved in delivering optimal care to prevent progression of kidney disease and optimal management of established CKD.

**Methodology**

This project will involve the systematic review of general practice patient records and surveys and interviews with a number of participating clinicians and patients. This approach will require an analysis of both qualitative and quantitative data.

**Location:** Launceston Clinical School.

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**Project Title:** How can influenza vaccination of pregnant women be optimally delivered in general practice?

**Supervisor(s) contact details:** Assoc Prof Jan Radford (Assoc Prof of General Practice, UTAS); Dr Kathryn Ogden (Research Fellow, UTAS) (J.Radford@utas.edu.au)

**Research project synopsis**

Vaccinating pregnant women against influenza is now accepted as an important preventative health care activity. Ensuring that all pregnant women in a general practice population are vaccinated against influenza requires a systematic approach. How general practice monitors the delivery of this care has not been fully investigated. This project will contribute to knowledge on how to ensure systematic care is delivered to this potentially vulnerable population.

**Aims and objectives:**

This project aims to determine the prevalence of influenza vaccination among pregnant women within participating general practices and develop strategies for enhancing vaccine coverage, if needed. In order to achieve these outcomes the student will work with supervisors and general practice staff to identify:

- Existing processes for recording both current pregnancy and influenza vaccination status within General Practice, and the accuracy of these processes,
- Factors impacting on the accuracy of coding for pregnancy and influenza vaccination status including whether and how accuracy can be improved through enhanced data management, and
- Barriers to the prescription and uptake of influenza immunisation during pregnancy.

**Methodology**

This will be a mixed methods study involving a systematic review of clinical records and surveys and interviews with participating GPs, other practice staff and patients. Both qualitative and quantitative skills will be developed during the analysis of clinical record data and the development and analysis of survey and interview data.

**Location:** General Practices in the Launceston region and the Launceston Clinical School.
Project Title: How do GPs implement treatment guidelines in patients with a pre-existing condition?

**Supervisor(s) contact details:** Assoc Prof Jan Radford (Assoc Prof of General Practice, UTAS); Dr Kathryn Ogden (Research Fellow, UTAS); contact (J.Radford@utas.edu.au)

**Research project synopsis**
General Practitioners are bombarded with treatment guidelines and recommendations to treat to target for many conditions. This project will look at how a single aspect of an updated guideline is implemented in General Practice, concurrent with ongoing management of patient with pre-existing coronary heart disease. In August of 2012 the Heart Foundation updated their secondary risk prevention guide with a new target for treating elevated low-density lipids (LDL) from 2.0mmol/L to a new target 1.8mmol/L. This project will explore how GPs apply new treatment targets to pre-existing patients.

**Aims and objectives:**
- To determine how practices identify and record patients diagnosis of coronary heart disease, and
- To explore the factors involved in modifying practice in order to deliver optimal care as determined by updated guidelines.

**Methodology**
An audit of patient records will be used to identify the study population and determine what proportion have been diagnosed and are being actively managed. Surveys and interview will be conducted with clinicians and patients in order to determine their knowledge of and attitudes towards the implementation of updated guidelines. Both qualitative and quantitative skills will be developed during the analysis of clinical record data and the development and analysis of survey and interview data.

Location: Launceston Clinical School.

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Project Title: Using advanced imaging to gain a better understanding of hand osteoarthritis

**Supervisor(s) contact details:** Dr Dawn Aitken (Senior Research Fellow), Dr Kathryn Squibb (Research Fellow and Radiographer), Prof Graeme Jones (Professor of Rheumatology and Epidemiology and Head of the Musculoskeletal Unit), Contact: dawn.aitken@utas.edu.au or kathryn.squibb@utas.edu.au

**Research project synopsis and aims**
This project aims to gain a better understanding of hand osteoarthritis using advanced imaging modalities including x-ray, MRI, ultrasound, and micro-CT scanning. 200 older Tasmanian’s between the ages of 60 – 90 years were enrolled in the study. They have provided information about hand symptoms, including pain and dysfunction and have undergone extensive scanning including x-ray, MRI, ultrasound, and a new novel micro-CT assessment to assess bone architecture. The aims of this study include:

- To examine the relationship between symptoms and structural abnormalities measured using x-ray, MRI, ultrasound, and micro-CT.
- To explore the association between structural abnormalities measured using each modality including bone marrow lesions, osteophytes (bony growths), joint space narrowing, and inflammation.
Ultimately this project will provide a better understanding of the pathology of hand osteoarthritis and aims to provide insight into the onset and progression of the disease. This work is highly suitable for somebody with an interest or background in musculoskeletal health.

**Project Title: Translational Health Services Research**

The Translational Health Services Research team is interested in many aspects of the experience of people with dementia and their carers over the course of the condition. Our research interests include the challenges of diagnosis, the delivery of clinical care, in the community, hospitals and residential aged care settings. The team investigates ways to meet future workforce needs, which includes delivering and evaluating better education to health professionals, and programs of care to people with dementia and their families. Our work contributes to the understanding of the translation of research into practice. The Understanding Dementia Massive Open Online Course continues to attract large numbers of participants generating a wealth of data about those who participate and use the course content. The research team follow various methodologies to answer research questions of interest including systematic literature reviews, cross sectional, longitudinal and quasi experimental designs, the design and development of new measures, mixed methods and action research.

If you are interested in discussing a project with the Translational Health Services Team please contact Kathleen Doherty on Kathleen.Doherty@utas.edu.au.

**Project Title: Unnecessary variation in hospital length of stay: are we causing more suffering and how do we prevent it?**

**Supervisors’ contact details:** Dr Nicole Hancock, Head of Department of General Medicine, Royal Hobart Hospital (Nicole.Hancock@ths.tas.gov.au) Dr Jim Stankovich, statistician, Health Services Innovation Tasmania, Faculty of Health (Jim.Stankovich@utas.edu.au)

**Research project synopsis:**

Suppose you are admitted to hospital with pneumonia. Ideally, how long you spend in hospital should only depend on how sick you are. But sometimes other factors come into play. For example, there may be no beds free in the "home ward" where pneumonia patients normally go, so you have to go to the cardiology ward instead. This may mean that you wait longer for your doctor or your dietician to see you, or for some blood tests to be completed. Nobody wants to stay in hospital longer than they have to; it is also a waste of money and resources.

As part of a program to improve processes for medical patients at RHH, we are interested in understanding this sort of unwanted variation in length of stay (LOS). Analysing the medical records of 8972 medical patients admitted at RHH over two years, we found that LOS is

- 38% longer for patients who aren't admitted to a home ward (i.e. "outlier" patients), and
- 14% longer for patients admitted on a Friday compared to patients admitted on a Monday.

The aim of the project is to understand more about this variation in LOS when considering outlier patients and those admitted on different days of the week. Are there subgroups of patients that will suffer more than others? Is there a positive or negative correlation between LOS and probability of being readmitted to hospital? Is it possible to change some hospital work practices to improve these patients’ care? Depending on the student's interests
and skills the research will comprise all or some of the following: statistical analysis of quantitative data, reading and interpreting case notes, and observing and speaking with hospital staff.

Location: Medical Sciences Precinct (Hobart), Royal Hobart Hospital

Project title: ASPREE. A double-blind randomised controlled trial of low dose aspirin for primary prevention in the aged

Supervisor contact details: Prof Mark Nelson (mark.nelson@utas.edu.au)

Research project synopsis
ASPREE is a doubleblind randomised placebo-controlled trial that is investigating whether aspirin can prolong good health and maintain independence amongst older people. The study will involve men and women over 70 years of age who are free from cardiovascular disease, or dementia. Already 16,702 participants have been enrolled in this study in Australia, 886 in Hobart, 554 Launceston and 664 in North-West Tasmania. Opportunity now arises with the locking of the baseline data to answer important questions relating to this very large community based cohort.

Project title: ASPREE Healthy Ageing Biobank

Supervisor contact details: Prof Mark Nelson (mark.nelson@utas.edu.au)

Research project synopsis
The ASPREE Healthy Ageing Biobank is an initiative in which blood and urine samples will be collected from healthy participants, aged 70 and over, who have provided consent to participate in the ASPREE Clinical Trial. Participants in the Biobank will be followed for a period of five years, and may then provide a second blood and urine sample at the conclusion of the study. We have 12,200 baseline samples and will likely collect 9000 participant samples at 3 years into the study. Opportunity arises for requesting samples to answer important clinical questions.

Project title: A randomised clinical trial of STAtin therapy for Reducing Events in the Elderly (STAREE)

Supervisor contact details: Prof Mark Nelson (mark.nelson@utas.edu.au)

Research project synopsis
STAREE is a double blind randomised placebo-controlled trial that is investigating whether statins can prolong good health and maintain independence amongst older people. The study will involve men and women over 70 years of age who are free from cardiovascular disease, diabetes or dementia. This study is just starting in Tasmania and the opportunity is to gain experience in the conduct of a large community trial (18,000).

Project Title: Acute pancreatitis admissions in Hobart

Supervisor(s) contact details: Prof Richard Turner (richard.turner@utas.edu.au)

Research project synopsis
A prospective database of acute pancreatitis admissions to the Royal Hobart Hospital (and possibly private hospitals) will be developed. This will consist of: Independent variables that may include the usually obtained parameters from clinical records, as well as a variety of novel anthropometric and nutritional measures that the researcher would obtain by seeing the
patients themselves. Dependent (outcome) variables would include severe acute pancreatitis (including death), a diagnosis of co-existing chronic pancreatitis, length of stay, and other clinical outcomes. Analysis of the data will yield possible determinants of the stated disease outcomes that may ultimately inform evidence-based clinical practice. The database may also lead to other projects derived from longitudinal follow-up of patients.

Location: School of Medicine & Royal Hobart Hospital

**Project title:** Quantifying the mental workload of Simulated Patients in clinical assessments

**Supervisor contact details:** Professor Richard Turner (richard.turner@utas.edu.au) (and Psychologist from Wicking Institute or School of Medicine Psychology Program)

**Brief description:**
While some work has been done to objectively measure the cognitive and perceptual workload of Examiners involved in live clinical assessments such as OSCEs, there is scant information on the impact of such assessments on, and implications for, Simulated Patients (SPs). The consistency and authenticity of this group of people is essential in ensuring valid and reliable assessment.

The project will use one or more validated psychometric tools to quantify the mental workload for SPs in OSCE stations. Analysis of the data will seek determinants of mental workload, with a view to optimising training and working conditions. This will ultimately contribute to the continuous quality improvement of clinical assessment.

**Project Title: Post breast cancer treatment lymphoedema**

**Supervisor(s) contact details:** Dr Barry Edwards (info@craigow.com.au) / Dr Mary Self (M.B.Self@utas.edu.au) / Prof Richard Turner (richard.turner@utas.edu.au)

**Research project synopsis**
This study aims to assess the prevalence and severity of upper limb lymphoedema following treatment for breast cancer, and to seek determinants for this. Women with a previous diagnosis of breast cancer will be recruited to have assessment by volumetric water displacement. Potential determinants will be sought by means of a questionnaire and review of relevant case notes. This study will be of particular interest in terms of assessing the impact of the recent trend to perform sentinel lymph node biopsies rather than axillary clearance.

Location: School of Medicine, Hobart

**Project Title: Kidney health in Indigenous Australians and New Zealanders**

**Supervisor(s) contact details:** Dr Matthew Jose (Matthew.Jose@utas.edu.au). Menzies Research Institute & RHH Dialysis Unit.

**Research project synopsis**
Indigenous people in Australia and New Zealand experience rates of ESKD several times higher than non-indigenous people. Treatment with dialysis or a kidney transplant is becoming increasingly common, but outcomes are still suboptimal. Five years after a kidney transplant, more than half of all kidney transplants in Aboriginal recipients are no longer functioning (compared to only 20% of non-Aboriginal Australians) and nearly 40% of Aboriginal recipients are dead (compared with only 11% of non-Aboriginal Australians). The aims of this project are:
• To examine factors that influence the outcomes of Indigenous people treated with dialysis through the ANZDATA registry
• To examine factors associated with poor outcome in Indigenous kidney transplantation

Location: Menzies Research Institute & Royal Hobart Hospital Dialysis Unit

Project Title: Vitamins & minerals in people with chronic kidney disease

Supervisor(s) contact details: Dr Matthew Jose (Matthew.Jose@utas.edu.au). Menzies Research Institute Tasmania & RHH Dialysis Unit.

Research project synopsis
People with chronic kidney disease have low blood levels of vitamin B, C & D. 25-hydroxy vitamin D is lower than in people without kidney disease, 1,25-hydroxy Vitamin D is low in nearly all people with end-stage kidney disease. Vitamin B & C are water-soluble vitamins that are washed out by the process of dialysis. Despite these low levels, there is very little knowledge about replacement. This project will examine these vitamins in people on dialysis and the effect of vitamin replacement. The aims of this project are to:

• Identify the prevalence of vitamin deficiency in Tasmanians with CKD
• Examine the effects of vitamin replacement

Location: Menzies Research Institute & Royal Hobart Hospital Dialysis Unit

Project Title: Osteoporosis management in the digital age

Supervisor(s) contact details: Dr Kenneth Lee (Kenneth.Lee@utas.edu.au) / Dr Li-Shean Toh (LiShean.Toh@utas.edu.au)

Research project synopsis:
The Internet has rapidly become an invaluable source of health information. Approximately 80% of Australian Internet users utilise the Internet for health-related activities. Similar figures relating to online health information usage is seen in number of countries across the globe. Additionally, the ‘app’ market is rapidly growing, with well over 150,000 health-related apps ranging from simple diary/activity trackers and information references to disease diagnostics, screening, and prevention tools. Surely both patients and health professionals are making use of this abundance of digitally-based support...or are they? Throughout the developed nations, there is a commonality: our populations are ageing. The increase in the elderly population coupled with the association between osteoporosis and fractures makes the condition a significant global health concern. As such the incidence of osteoporotic fractures is predicted to increase, from one in every 8.1 minutes in 2001 to one in every 3.7 minutes in 2021. A prior fragility fracture increases the risk of subsequent fractures, morbidity, and premature death. Economically, the disability due to osteoporosis in Europe is greater than that caused by cancers. In Australia, osteoporosis is one of the national health priority conditions, and it affects 1 in 10 Australians aged 50 years and above. Ignorance about osteoporosis is still common among health professionals, patients, and the public at large. Given the abundance of online and digital resources available, often at low or no cost, it is prudent to explore technological options to more effectively support osteoporosis healthcare delivery and management.

Aim:
To systematically evaluate the global landscape of online and digital resources used in osteoporosis management.

**Methodology:**

The honours student will:

1. Develop a search strategy with assistance from their supervisors and a medical/health research librarian.
2. Learn to register a systematic review protocol.
3. Perform a systematic review in accordance to established guidelines for the conduct of systematic reviews.
4. Report a systematic review following PRISMA guidelines for reporting of systematic reviews.
5. Aim to produce a sound review suitable for publication in a quality peer-reviewed journal – in doing so, the student will gain first-hand insight into the peer-review process.

**Project title: Use of Medical Mobile Applications Among Clinicians**

**Supervisor(s) contact details:** Dr Long Ming (Long.Ming@utas.edu.au), Dr Tabish Zaidi (Tabish.RaziZaidi@utas.edu.au)

**Research project synopsis**

Handheld computers (HHCs) such as smartphones and tablets are providing a variety of drug information (DI) applications to assist clinicians’ decision making in the clinical and hospital setting. However, little is known about the extent of their use among Australian clinicians. The study is aimed to assess the use of electronic DI resources via HHCs by clinicians in Australia. This study also aimed to investigate the clinicians’ perception toward the DI content and functions of mobile medical applications.

**Methods:** A convenience sampling method will be adopted to invite clinicians working in various sectors such as hospitals, and clinics to participate in this online survey. A validated questionnaire will be administered, and data will be summarized and presented using descriptive statistics.

**Potential benefit:** We will understand the type and frequency of DI search among clinicians in Australia. We will uncover features of a good mobile app and provide information for the development of a locally produced DI sources.

This project is suitable for BMedRes, Paramed, BSc students.

**Location:** School of Medicine, Hobart

**Project title: Use of Medical Mobile Applications Among General Public**

**Supervisor(s) contact details:** Dr Long Ming (Long.Ming@utas.edu.au), Dr Tabish Zaidi (Tabish.RaziZaidi@utas.edu.au)

**Research project synopsis**

Due to the wide use and improved functionality of smartphone, e-health apps which are accessible on mobile platforms made mobile health (mHealth) an easy way for general...
public to seek health information. mHealth is a term used to describe mobile computing, medical sensor, and communications technologies for health-care. It is one of the approaches for health care authority to educate general public on healthcare and well-being services. mHealth application has not proven could improve the healthcare services for elderly in United States. mHealth serves a significant purpose in current and future healthcare delivery and yet research on its use among Australian community is scarce. The study is aimed to assess the use of medical mobile applications by general public in Australia. This study also aimed to investigate the public perception toward the drug information content and functions of mobile medical applications.

**Methods:** A convenience sampling method will be adopted to invite Facebook users to participate in this online survey. A validated questionnaire will be administered, and data will be summarized and presented using descriptive statistics.

**Potential benefit:** We will understand the type and frequency of use of medical mobile applications and drug information search among general public.

This project is suitable for BMedRes, Paramed, BSc students.

**Location:** School of Medicine, Hobart

**Project title:** What should I do when my child is sick? Improving the management of common childhood ailments

**Supervisor contact details:** Dr Bonnie Bereznicki (Bonnie.Bereznicki@utas.edu.au)

**Project synopsis:** Parents are understandably concerned when they have a sick child, and often have difficulty assessing the severity of the illness. Furthermore, lower levels of parental knowledge increase the risk of inappropriate medication use and unnecessary contacts with the healthcare system. Recent Australian and Tasmanian hospital statistics indicate that infants and young children are among the highest users of Emergency Departments (EDs), and a high proportion of these presentations are for non-urgent ailments.1-3

Fever, a main indicator of illness, often creates undue anxiety among parents, and can interfere with the parent’s ability to accurately observe the general wellness of their child. Initial research has focused the burden of childhood fever on the Royal Hobart Hospital ED and Australian families. Preliminary findings demonstrate that childhood fever may place an unnecessary burden on the RHH ED, with the majority of presentations not requiring any hospital care. Moreover, the average time spent in the ED for these cases is over an hour longer than the state average for non-admitted ED cases.4 Further findings from a national survey of over 10,000 parents suggests that parental knowledge and fever management practices are far from optimal, with more than 50% of respondents unsure what temperature constitutes a fever, unnecessarily administering medication to reduce unfounded ‘dangers’ of a fever, with one-third reporting that they had previously called an ambulance or taken their children to hospital for a fever.4 The next step in this research will be to investigate how this burden can be reduced through improved parental education, as well as expanding the research to include other areas of child health. Specific projects will be discussed with students upon contact.
References:


A. Lab-based projects (involving humans, animals or in vitro models)

Project Title: Research Projects in Respiratory Environmental Health and the Fetal Origins of Non-Communicable Disease

Supervisor contact details: Assoc Prof. Graeme Zosky (Graeme.Zosky@utas.edu.au), Dr Renee Dwyer (Renee.Dwyer@utas.edu.au), Dr Ling Chen (L.Chen@utas.edu.au)

Location: School of Medicine, UTAS (Medical Sciences Precinct).

Research overview
The environment that we are exposed to has a significant impact on our health. Our response to these exposures is dictated by a range of factors including the nature of the exposure (e.g. acute vs chronic), the timing of the exposure (in utero vs post-natal) and the individual (e.g. age, sex, health status). We have a range of projects that aim to 1) fill the gaps in our understanding of the impact(s) of common environmental exposures on health and 2) identify the mechanisms underpinning epidemiological associations between environmental exposures and health outcomes. Much of our research is focussed on respiratory health, with an emphasis on the effects of maternal exposure on offspring, but we also have parallel research streams exploring metabolic and neurological outcomes.

Respiratory environmental health
The respiratory health effects of iron oxide particles
The particles in the air that we breathe have well-known detrimental impacts on respiratory health. In order to mitigate the health effects of these particles there are National air quality guidelines. However, these guidelines are based almost entirely on particles that are found in urban environments which are primarily derived from combustion (e.g. diesel) sources. This ignores that fact that a large proportion of the population lives in environments where the primary source of particles is geogenic (earth-derived). We have a wealth of data demonstrating that geogenic particles have a detrimental impact on respiratory health and that the iron content of the particles is a critical determinant of the response. We have a range of projects examining how iron oxide particles impact on the respiratory response to infection and how different cell types within the lung orchestrate the response to these particles.

Health effects of the Hazelwood coal fire
In February-March 2014 an open-pit brown coalmine fire burned for six weeks adjacent to the town of Morwell, Victoria. Environmental sampling in the Latrobe Valley during the fire clearly demonstrated high levels of exposure to the smoke from this fire in the community. The recent Hazelwood Mine Fire Inquiry Report identified a suite of pollutants associated with the fire emissions including carbon monoxide, particulate matter, nitrogen dioxide, sulphur dioxide, polycyclic aromatic hydrocarbons (PAHs), volatile organic compounds, dioxins and furans, and heavy metals. Each of these pollutants has been linked to adverse health effects. In particular, there is significant concern regarding the health impact(s) on children born to mothers who were exposed to the emissions. We are currently running a series of mechanistic and toxicological lab based studies, to complement a large epidemiological study, into the respiratory health effects of these particles and the physico-chemical characteristics of the particles that are the most detrimental to lung health.

Fetal origins of non-communicable disease
Chronic lung disease
For many years we have been interested in the effect(s) of maternal environmental exposures on fetal lung development and how this influences the susceptibility to lung disease later in life. For example, we have shown that arsenic contamination of drinking water impairs lung development, airway growth and exacerbates the response to respiratory viral infection. Similarly, we have been instrumental in demonstrating the importance of vitamin D for normal lung development which has inspired public interest in this area. We have a large biobank of tissue samples from our mouse model studies on these issues and are keen to further explore
the mechanisms linking maternal exposure with the susceptibility to chronic lung disease in
these samples.

*Maternal vitamin D deficiency*
As outlined above, we have a biobank of lung samples associated with maternal vitamin D
deficiency. In addition to these lung samples we have brain, liver, vascular and placental tissue
which means we have the opportunity to assess the impact of *in utero* vitamin D deficiency on
a range of organs. In some of these studies we have also exposed mice to high and low fat
diets which allows us the opportunity to assess how maternal exposure interacts with post-
natal metabolic disease. This work has broad implications for public health.

*Projects*
Honours projects can be negotiated within the scope of the research program outlined above.
Contact Assoc Prof Zosky to discuss.

**Project Title:** Epigenetic Determinants of Radiation Response in Prostate Cancer

**Supervisor contact details:** Dr Kate Brettingham-Moore ([Kate.Brettingham-
Moore@utas.edu.au](mailto:Kate.Brettingham-Moore@utas.edu.au))

**Research project synopsis**
Tumour recurrence is a significant problem following radiotherapy for prostate cancer patients.
In terms of this resistance to treatment, little is known regarding epigenetic alterations caused
by radiotherapy or how this may contribute to resistant subclones responsible for disease
recurrence. Histone proteins may play a role as radioprotectors, with condensed chromatin
scavenging free radicals and protecting DNA from damage. Recent evidence has
demonstrated epigenetic modifying agents capable of DNA methyltransferase and histone
deacetylase inhibition can radiosensitise cells indicating a functional role for the epigenome in
response to this therapy. The epigenetic regulation of response to radiotherapy is key to
understanding the stable marks imparted to the subpopulation of cells that survive treatment.

Preliminary RNA-seq data has revealed that the catalytic subunit of the polycomb repressive
complex, EZH2 and DNA methyltransferase 1 are up-regulated in radiation resistant prostate
cancer cells. This suggests that the resistant cells may form heterochromatin protect
themselves from further DNA damage. This epigenetic change requires further investigation
and molecular characterisation. In addition, the basal chromatin structure and the role this
plays in determining outcome remains to be elucidated. The question also remains as to
whether the basal chromatin state may be predictive of response to radiotherapy. The aim of
this project is to determine the differences in epigenetic marks between cells which respond
well to radiotherapy and those that are resistant. This project will profile a number of epigenetic
markers pre and post-radiotherapy in LNCaP, 22Rv1 and PC-3 prostate cancer cell lines.

Location: School of Medicine and Menzies Institute for Medical Research

**Project Title:** Building tools to control the mind

**Supervisor contact details:** Dr. John Y. Lin ([john.lin@utas.edu.au](mailto:john.lin@utas.edu.au)), Assoc Professor Lisa
Foa ([lisa.foa@utas.edu.au](mailto:lisa.foa@utas.edu.au))

The activities of individual and/or ensembles of neurons in the brain control the behaviour of
higher level organisms from the flatworms to human. The ability to precisely manipulate
the cellular activities or signalling pathways used by neurons in both space and time can reveal
how cellular activity is related to the behaviour of awake animals – providing insights into the
functioning of the mind. The goal of the project is to build protein-based tools that can be used
to precisely manipulate cellular activities with light. This can ultimately be used to manipulate
cellular activity in selective neurons and control the behaviours of laboratory animals. Why use light instead of pharmacological agents? It is totally exogenous from the brain, easy to manipulate precisely within the tissue and have minimal side effects. It also does not cost a lot of money and you cannot spill it on the bench. What are the cellular activities that we are interested in manipulating with light? We are interested in vesicular synaptic release and G-protein coupled receptor pathways such as Gαi, Gαs, Gαq, phospholipase C, protein kinase C and adenylate cyclase (you can take your pick), which are known to be associated with the chemical communication between neurons and modulate behavioural outcomes.

The activities involved in the project: reading, designing your proteins, PCR and DNA gels, molecular cloning, cell culture, microscope work, electrophysiology, breaking things (both intentional and unintentional), building things, biochemical and biophysical characterisation and some thinking would be good.

What is the expected outcome: You will learn something about molecular biology, biochemistry, biophysics, optics, electronics and graduate with an experience of doing a different kind of scientific project.

Project Title: DIY microscope system to illuminate subcellular compartments

Supervisor contact details: Dr. John Y. Lin (john.lin@utas.edu.au), Dr Robert Gasperini (robert.gasperini@utas.edu.au)

Microscopes are essential parts of life science research. Most researchers use one but not many of them know how to build one. For this reason they can be very expensive and can cost more than your house. What is a microscope really? There are lenses to collect and focus light, a light source that provide light, and a light capturing device for making the image (sometimes these are your eyes, sometimes these is a camera). If it is a fluorescence microscope, you need filters to select for the right wavelengths of light and a strong light source to provide the excitation wavelength. Is it possible to build one or modify an existing one at lower cost? It won’t be fancy but it is possible. Can you make one with laser and epifluorescence capacity? This is harder but doable. Are you up for a challenge to do a DIY project that is a little different from your regular biomedical research? The goal is to build or modify an existing microscope that will let us do epifluorescence imaging and also incorporate a dual mirror galvanometer and/or DMD/DLP (digital mirror device / digital light projection) system that gives us the capacity to spatially and temporally control the illumination to a small part of field of view. We will then incorporate this system to selectively manipulate light-responsive proteins in the cells expressing protein-based tools to control cellular response in subcellular location. The goal will be to incorporate this microscope system with the current research in the laboratory to modulate cellular activities in subcellular region. If successful, we will test several of our existing tools to see whether we can limit the manipulation of cellular activities within specific cellular compartments.

The activities involved in the project: reading, learning about optics, building things on a breadboard, optic alignment, laser alignment, writing (or finding existing) computer codes, electronics and cell culture.

What is the expected outcome: You will learn a lot about optics and why off-the-shelf microscope cost so much. If the project is going really well we will get to do some really cool validation and testings in real cells. You will also learn about cell biology and when you complete the project.
Research Projects available in Molecular Neurobiology

Supervisor contact details: Assoc Prof. Lisa Foa (lisa.foa@utas.edu.au), Dr John Lin, (john.lin@utas.edu.au), Professor David Small (d.h.small@utas.edu.au), Dr Kaylene Young Kaylene.young@utas.edu.au

Location: School of Medicine, UTAS and the Menzies Research Institute Tasmania.

How does calcium control the wiring of our brain?
Supervisors: Lisa Foa and Robert Gasperini

Research project synopsis
We all walk around with super-plastic computers inside our skulls, called a brain. The brain is better, faster than a computer though. It can learn with experience, change in response to our environment, our diet, our life. Incredibly, the basic circuitry of our brain is laid down during embryonic and early life. We have very little understanding of how this process occurs during normal development, yet understanding such developmental processes is vital, not only for understanding the developmental disorders of the brain, such as autism, but also for understanding how we might re-connect the circuitry of the brain and spinal cord after trauma.

The precise connectivity of the human nervous system develops as young developing neurons send out processes, or axons, to connect with their target cells. At the distal tip of extending axons are growth cones (pictured), dynamic motile structures, which guide the developing axons. In this process, known as axon guidance the growth cones navigate the embryonic milieu, detecting, interpreting and responding to a multitude of guidance cues. Aberrant axon guidance is thought to be an important causative factor in several neurodevelopmental disorders such as autism and mental retardation syndromes. Deciphering the molecular mechanisms that regulate axon guidance will improve our understanding of these disorders. It is also hoped that an improved understanding of axon guidance will advance the cause of neuronal regeneration after injury.

Calcium signalling is known to be vital for growth cone navigation. Too much or too little calcium can cause growth cone collapse. However the molecular mechanisms that regulate calcium signalling are unclear. We have several projects in our laboratory that examine which proteins function to control calcium signaling in the growth cone and, importantly, how those calcium signals control the growth cone cytoskeleton. Because controlling the cytoskeleton means controlling growth cone navigation and hence wiring of the brain. Our work centres around live-cell imaging to determine what controls growth cone navigation. We use growth cones from sensory neurons in vitro, where we examine growth cone navigation in response to traditional and novel guidance cues; we use in vivo imaging to examine growth cone navigation as they grow through the cellular milieu of the embryonic zebrafish. We can image calcium signaling in real time and manipulate the activity of the neurons using light (in collaboration with Dr John Lin). Through our work we are deciphering new mechanisms of calcium regulation, and uncovering novel signaling mechanisms that control growth cone navigation in the developing nervous system.

How is gene transcription regulated in neurons?
Supervisors: Lisa Foa, Robert Gasperini and Adele Holloway

Research project synopsis
Gene regulation is a fundamental aspect of normal growth and differentiation of all cells. Mechanisms of neural development are crucially dependent on the orchestrated expression of genes in a timely and coordinated fashion. Errors in gene transcription are a feature of a number of neurodevelopmental syndromes such as autism and increasingly the role of
transcription is being recognized in diseases such as depression. However, our knowledge of the mechanisms that regulate gene transcription within neurons is very limited.

This project aims to examine the role of a protein family known as Homer in the regulation of gene transcription in neurons. Certain calcium signals are known to activate gene transcription in neurons and we hypothesize that Homer proteins integrate these calcium signals, regulating their transmission to the nucleus. We have found that Homer can modulate the activity of an important transcription factor known as NFAT. This project involves examining the interaction between Homer, calcium and NFAT. Several students could work on this project since there are multiple aspects of the project, including protein structure studies, live cell imaging and gene transcription assays. Studies will include methods for molecular biology, tissue culture, live cell imaging and protein biochemistry.

What can we do about Neuropathy?
Supervisors: Dino Premilovac, Lisa Foa and Robert Gasperini

Research project synopsis
One of the major complications of long term diabetes is peripheral neuropathy – nerve damage. There is currently no treatment for neuropathy, which affects more than 50% of all those with diabetes. Diabetic neuropathy occurs particularly in the skin, where nerve fibres retract into the dermis leading to either a loss of touch sensation, loss of thermal sensation, or hyper-sensation resulting in chronic pain, or a combination of these defects. It is also believed to be one of the triggers for the formation of ulcers (and detection of ulcers by those affected due to lack of sensation) and is the leading cause of amputation and hospitalisation among those with diabetes.

In humans, type 2 diabetes takes decades to develop and peripheral neuropathy is usually present at the end of the disease process resulting primarily in response to chronic hyperglycaemia. Due to the long timeframe, it is difficult and time-consuming to fully reproduce the disease progression in lab animals without the use of pharmacologic agents. The first aim of this project will be develop a new animal model diabetic neuropathy. Our aim is to better understand the process of the disease and the to use this model to test novel therapeutics. Our work on growth cone navigation in vitro has led to the discovery of a novel signaling system that may enhance neuronal regeneration after a neuropathy. One of the most important things with regeneration is that the axons grow back to the correct sites, rather than inappropriately branching or sprouting. Such inappropriate sprouting can cause allodynia, which is a painful response to a stimuli that shouldn't normally hurt (like a light touch hurts sunburnt skin). Our ultimate aim is to establish a model where we can guide regenerating axons back to their correct location in the skin, re-connecting functionally, thereby reducing pain.

How do oligodendroglial cells replenish their ER calcium stores?
Supervisors: Kaylene Young, Rob Gasperini and Lisa Foa

Research project synopsis
Oligodendrocyte progenitor cells (OPCs) are the largest proliferating cell population in the adult brain, comprising ~5% of all brain cells. The function of these cells is to generate new oligodendrocytes in the normal brain, and contribute to remyelination in response to a demyelinating disease such as multiple sclerosis. It was recently discovered that neurons form synapses onto OPCs, and that neuronal activity can influence OPC behaviour. But how this occurs is largely unknown. As neuronal activity has been shown to evoke a calcium signal within OPCs, we hypothesise that calcium signalling directs OPC behaviour, and will be reliant on calcium release from the endoplasmic reticulum (ER).

We will examine OPCs and oligodendrocytes in vitro and in vivo to determine which components of the calcium-induced calcium release pathway are active in each cell type, their
sub-cellular localisation, and whether their manipulation can prevent or promote oligodendrocyte differentiation. This project aims to determine the mechanism by which calcium signalling is regulated within OPCs.

Project Title: Regulation of gene expression by the RUNX1 transcription factor

Supervisor(s) contact details: Dr Adele Holloway (a.f.holloway@utas.edu.au)

Research project synopsis
A significant proportion of leukaemias contain genetic lesions that generate altered forms of a protein called RUNX1 (or AML1). RUNX1 controls the expression of genes involved in blood cell growth and it is proposed the abnormal forms of RUNX1 drive aberrant gene expression leading to the development of leukaemia. Our work suggests the abnormal RUNX1 proteins act by generating epigenetic changes within cells and we are focussed on characterising these epigenetic changes. The characterisation of these epigenetic changes is of great interest because while genetic lesions that cause cancer are currently not reversible, epigenetic changes can potentially be reversed by pharmacological intervention, providing promise for the treatment of these leukaemias as well as other cancers caused by epigenetic changes. Our current research therefore aims to:

- Investigate how the altered forms of RUNX1 found in leukaemic cells direct epigenetic changes to these genes.

Research projects in this area involve a range of molecular and cell biology techniques investigating putative RUNX1 target genes we have identified following microarray analysis of cells in which RUNX1 was disrupted. Techniques will include cell culture, cloning gene promoters into reporter plasmids and monitoring reporter activity and analysing the chromatin structure and expression of immune genes using real-time PCR based assays.

Location: School of Medicine

Project Title: Regulation of gene expression in Prostate cancer

Supervisor(s) contact details: Dr Adele Holloway (a.f.holloway@utas.edu.au) and Dr Jo Dickinson (Jo.Dickinson@utas.edu.au)

Research project synopsis
Prostate cancer diagnoses continue to rise rapidly in Australia, but of most concern is our current inability to distinguish aggressive tumours with propensity to metastasize from more indolent disease. We thus urgently require a better understanding of the underlying drivers of this disease, and particularly the factors and mechanisms that drive the transition to more aggressive tumours with a propensity to spread. These factors may represent biomarkers and potential therapeutic targets in prostate cancer progression. Integrins are cell surface receptors that play important roles in cell proliferation, differentiation, survival and migration, and thus play a key role in cancer development and progression. Our current research therefore aims to:

- Investigate the transcriptional and epigenetic regulators of integrins in normal cells, and
- Determine how expression of integrins is altered in prostate cancer cells.

Techniques utilised in this work include cell culture, cloning, gene expression analysis and PCR based techniques to determine methylation.

Location: School of Medicine and Menzies Research Institute Tasmania

Project Title: Genetic Determinants of Radiation Response in Prostate Cancer
Supervisor(s) contact details: Dr Jo Dickinson (Jo.Dickinson@utas.edu.au), Dr Kate Brettingham-Moore (Kate.Brettingham-Moore@utas.edu.au), Dr Adele Holloway (a.f.holloway@utas.edu.au), Dr Jac Charlesworth (Jac.Charlesworth@utas.edu.au) and Dr Jim Stankovich (Jim.Stankovich@utas.edu.au)

Research project synopsis
Currently patients presenting with locally advanced prostate cancer are provided with a number of treatment options including brachytherapy, prostatectomy, High Intensity Focused Ultrasound, hormone therapy and radiotherapy. External beam radiotherapy (RT) is commonly used in combination with hormone therapy as an alternative to or in combination with surgical resection of the tumour. The biochemical failure rate of RT for prostate cancer patients is around 40-50% within 5 years of treatment. Thus a significant proportion of patients derive no survival benefit from this treatment yet are exposed to the significant toxic treatment side-effects. Thus there is an important need to identify patients unlikely to benefit from RT to help direct them towards alternate and ultimately more successful treatment options.

It is hypothesised that the variation observed in response to radiotherapy for prostate cancer patients is arises as a result of inherent differences in the function of key genes. The advent of Next Generation Sequencing of the transcriptome permits the mapping of these changes. This has significant benefits in terms of developing clinically relevant predictors as not only can differences in gene expression levels be detected, mutations within those transcribed sequences and genetic rearrangements can also be detected. One of the most frequently observed genetic re-arrangements (approximately 15-80%) prostate tumours is the TMPRSS2-ERG re-arrangement leading to the induction of ERG expression. The overall objective of this proposal is to investigate whether the presence of this re-arrangement is associated with clinical features of disease including radiation response in prostate cancer patients.

Location: School of Medicine and Menzies Research Institute Tasmania

Project title: Pseudomonas aeruginosa in cystic fibrosis

Supervisor(s) contact details: Dr Louise Roddam (louise.roddam@utas.edu.au) and Dr Mark Ambrose (mark.ambrose@utas.edu.au)

Note that Honours students undertaking the projects are eligible for the Dr Leon Wescombe Honours Scholarship. See more information at http://www.studentcentre.utas.edu.au/scholarships/AwardDetails.aspx?AwardId=2228

Cystic fibrosis (CF) is an inherited life-shortening condition that mainly affects the patient’s lungs and is especially prevalent in the Tasmanian population. A frequent complication associated with the disorder is that the lungs of CF patients are often colonised by a bacteria (Pseudomonas aeruginosa) which results in serious lung damage, frequent hospitalisation and more severe disease that significantly shorten life expectancy. This colonisation occurs generally around the age of five years and despite daily antibiotic therapy can’t be eradicated. Once infected, patients experience regular episodes of worsening disease (exacerbations) that accelerate lung damage and decrease lung function, ultimately causing mortality.

Project One: Development and testing a new antimicrobial therapy
We have developed a novel anti-Pseudomonal strategy and initial data demonstrate that it decreases bacterial virulence gene expression, increases bacterial susceptibility to tobramycin (an antibiotic commonly used in the management of CF lung infections) and prevents bacterial modulation of human cell inflammatory and stress response pathways. This therapy will be further explored for safety and efficacy in this project.

Project Two: Studies on mutagenesis in P. aeruginosa

P. aeruginosa is able to survive antibiotic treatment in part at least because it develops resistance through mutation. The precise nature of those mechanism(s) responsible for
generating antibiotic resistance mutations in this organism is not completely understood, however. In this project, we will explore mutagenesis in stationary-phase cells and biofilms of *P. aeruginosa*.

Students working on these projects will learn a range of cellular and molecular techniques (real-time qPCR, cell culture, mutation-detection and biofilm assays, enzyme activity assays, animal handling and intubation, data analysis etc.).

**Project Title: Carbohydrate metabolism in embryonic stem cells**

**Supervisor(s) contact details:** Dr Joy Rathjen (School of Medicine), joy.rathjen@utas.edu.au; Associate Professor Nuri Guven (School of Pharmacy)

**Research project synopsis**

There are many strands of evidence that suggest that nutrients, and specifically amino acids, play regulatory roles in embryonic stem (ES) cells and their differentiation. We have shown that l-proline induces the differentiation of mouse ES cells into a second pluripotent cell population, early primitive ectoderm-like (EPL) cells. In this differentiation process l-proline is taken up by the cell through the system A neutral amino acid transporter, SNAT2, and metabolised by proline dehydrogenase to form reactive oxygen species (ROS) and Δ1-pyrroline-5-carboxylate (P5C). We have shown that pluripotent cells differ in the way l-proline metabolic genes are expressed and we propose that these changes predict the flux of metabolites through the pathway.

There is evidence that other pathways could also be differentially regulated in these cells, most prominently the oxidative phosphorylation and glycolytic pathways, and the use of glucose by pluripotent cells. In this project a broad range of techniques will be used to analyse the way naïve and primed ES cells and EPL cells metabolise glucose and to determine if shifts in pathway use occur with lineage development. Specifically, you will use bioinformatics to look at the expression of genes required for each pathway in the cell and find evidence of differential pathway use and potential pathway regulators. Bioinformatic information on gene expression will be validated with qPCR and western blot. You will use standard metabolic assays to determine the fate of glucose in the cell, and flow cytometry to determine mitochondrial activity. The results will give us an appreciation of how dynamic carbohydrate use is in the pluripotent lineage.

**Project title: Enhancing neurogenesis to promote recovery following traumatic brain injury**

**Supervisor contact details:** Dr Nicole Bye (nicole.bye@utas.edu.au)

**Brief project description:**

Traumatic brain injury (TBI) is a devastating condition that constitutes a major health and socio-economic burden world-wide. In Australia, hospital admissions for TBI are in the order of 150/100,000 population, with a total lifetime cost per patient estimated at $4.8 million. Many neuroprotective strategies have been employed to try to improve outcome, with little success.

Recent research has shown that limited regenerative responses can take place in the adult brain after trauma. One potentially important regenerative process is neurogenesis: the production of new neurons from neural stem/progenitor cells that reside in specific brain regions. While neurogenesis is stimulated after TBI, most of the new neurons die shortly after generation, presumably due to the pathological environment in which they were formed.

The brain’s inflammatory response following injury is likely responsible for both stimulating neurogenesis and ultimately killing the new cells. Neuroinflammation involves activation of CNS microglia and astrocytes and infiltration of immune cells, with subsequent expression of
numerous cytokines and growth factors. With this project, we will identify cellular and molecular components of neuroinflammation that are responsible for mediating neurogenesis, through treating mice subjected to TBI with anti-inflammatory compounds targeting specific glial populations, or with selected growth factors to augment beneficial inflammatory factors. These studies will also identify whether manipulating inflammation to enhance neurogenesis can promote recovery following TBI.

One of the following two topics is to be offered as an Honours research project in 2017 – Dr Ronan O’Toole

**Project title: Tuberculosis**

**Supervisor contact details:** Dr. Ronan O’Toole (Breathe Well CRE, School of Medicine, University of Tasmania). Email: ronan.otoole@utas.edu.au

Tuberculosis (TB) is the leading cause of death in humans worldwide from bacterial infection. In 2013 alone, 9 million people developed TB and 1.5 million died from the disease. In Australia, there were in 1,263 new cases of TB in 2013. Deficiencies exist with respect to the clinical tools available for tuberculosis prevention, diagnosis and treatment. In terms of diagnosis, there is still an over reliance on culture-dependent techniques for both epidemiological typing and drug-susceptibility testing. As the *Mycobacterium tuberculosis* complex consists of slow-growing mycobacteria, *in vitro* cultivation remains a primary rate-limiting step in achieving a laboratory-confirmed diagnosis. Accurate and rapid detection of TB are needed for informed selection of the appropriate treatment regimen, and minimisation of further transmission of the disease. This project topic will focus on the functional characterisation of *M. tuberculosis* complex isolates using next generation sequencing (NGS) data, and on relating mycobacterial genomic variations to TB disease phenotypes.

**Project title: Chronic Obstructive Pulmonary Disease**

**Supervisor contact details:** Dr. Ronan O’Toole (Breathe Well CRE, School of Medicine, University of Tasmania). Email: ronan.otoole@utas.edu.au

Chronic obstructive pulmonary disease (COPD) is emerging as the third largest cause of human mortality worldwide after heart disease and stroke. It kills over 3 million people worldwide each year according to the World Health Organisation (WHO). Lung Foundation Australia has estimated that 1.45 million people in Australia suffer from Chronic Obstructive Pulmonary Disease (COPD) which is now the country’s second leading cause of avoidable hospital admission. There is currently no cure for COPD. The main treatments focus on alleviating symptoms and reducing “infective” exacerbation rates, which are of microbial aetiology. A meta-analysis identified an increased risk of pneumonia in COPD patients with inhaled corticosteroid use. Antibiotic use in exacerbated COPD cases to treat bacterial infections does not reduce hospital stay length or mortality in non-ICU patients, and has a statistically-significant higher risk of adverse events. This project topic will focus on the further development of an innovative class of anti-infective molecule that selectively inhibits infection of the lower respiratory tract by key bacterial drivers of acute exacerbations, *Streptococcus pneumoniae* and *Haemophilus influenzae*.

**Project Title: Next-generation sequencing to map epigenetic profiles in the brain**

**Supervisors:** Dr Phillippa Taberlay, Dr Adele Woodhouse.
Every single cell of the human body contains the same genetic sequence we inherited from our parents; yet, our skin and brain, for example, are remarkably different tissues due to the precision of epigenetic patterning (e.g. DNA methylation and histone modifications) during development and maintained throughout our lifetime. Our ability to map epigenetic marks across entire genomes occurred only relatively recently, since next-generation sequencing technologies became accessible ~5 years ago. The analysis of 'big data' from these studies has created a vast amount of new knowledge about epigenetic patterning, functions and mechanisms; however, these studies have, and are still, largely conducted on samples comprised of multiple cell types (e.g. whole brain, whole blood). We still have little insight into the depth and breadth of differences between individual cell types.

We have developed a method to look at epigenetic marks in specific cell types. This project will use our expertise in DNA methylation (whole-genome bisulphite sequencing), histone modifications (chromatin immunoprecipitation sequencing) and nucleosome occupancy and methylome sequencing to map epigenetic marks in specific cell types from the brain.
Wicking Centre Honours Projects

The Wicking Dementia Research and Education Centre has a variety of projects ranging from stem cells and primary culture through to live imaging in the brains of transgenic mice and human cohort studies. A sample of projects are listed here but for more information about potential projects and supervisors within the Wicking group please contact: James Vickers James.Vickers@utas.edu.au; Anna King: a.e.king@utas.edu.au; Tony Cook Anthony.cook@utas.edu.au; Alison Canty Alison.Canty@utas.edu.au; Matthew Kirkcaldie Matthew.Kirkcaldie@utas.edu.au; Adele Woodhouse Adele.Woodhouse@utas.edu.au or Jenna Ziebell Jenna.Ziebell@utas.edu.au;

Project 1: CRISPR/Cas genome engineering of human induced pluripotent stem (iPS) cells to investigate brain and eye diseases

Supervisors: Dr Tony Cook, Assoc Prof Alex Hewitt, Dr Anna King

Background: CRISPR/Cas-based technology is being heralded as a relatively straightforward technology for introduction or correction of genetic mutations in mammalian cells. We utilize CRISPR/Cas technology along-side a boutique collection of patient-specific induced pluripotent stem cell lines to investigate diseases affecting the brain and the eye, including dementia, Alzheimer’s disease, glaucoma, Usher syndrome, and Batten disease. We are keen to hear from prospective students passionate about using stem cells, genomics or gene editing approaches to develop novel treatment strategies for such diseases.

As an example honours project, you will use a boutique iPSC line generated from a Batten disease patient, in combination with established pluripotent stem cell lines to generate multiple isogenic cell lines using CRISPR/Cas technology, by either introducing common CLN3 mutations or in the case of patient cell lines, by correcting the disease-causing mutation. By comparing neurons derived from these isogenic iPSC lines, you will quantify CLN3-specific changes in lysosome number, size and function in neurons, that will provide a unique, relevant and specific platform for testing new therapies for Batten disease.

Other projects are also available for 2017, and can be discussed with the project supervisors.

Techniques to be used will include:

Cell culture, including differentiation of pluripotent stem cell lines to neurons and genetic manipulation using CRISPR/Cas.

PCR-based genotyping
Quantitative RT-PCR
Immunofluorescence and confocal microscopy, and image analysis

Contact: Dr Tony Cook Anthony.cook@utas.edu.au
Wicking Dementia Research and Education Centre

Project 2: Epigenetic machinery and mark alterations in transgenic AD mice

Supervisors: Dr Adele Woodhouse, Dr Phillippa Taberlay

There is increasing interest in the role of epigenetic changes in Alzheimer’s disease (AD) (Lunnon et al., 2014, Nat Neurosci, De Jager et al., 2014, Nat Neurosci), including post-translational histone modifications (Narayan et al., 2015, Neurobiol Dis; Gjoneska et al., 2015, Nature). These modifications include post-translational modifications of histone
proteins that are “written”, “read” and “erased” across DNA by epigenetic modifier complexes such as histone deacetylases (HDACs). Our preliminary data in transgenic AD mice indicate that enhancer (H3K4me1, H3K27Ac) and promoter marks (H3K4me3, H3K27me3) are lost from regulatory regions of key risk factor genes for sporadic AD. Several studies have also shown cognitive benefits of HDAC inhibitor treatment in transgenic AD mice (eg. Klein et al., 2015 Neurobiol Aging). However, little is known about the expression of HDACs and histone marks in specific cell types in AD.

This project will use immunohistochemistry to determine the global alterations in histone marks and HDACs that occur in AD resistant interneurons and AD susceptible pyramidal neurons in 3, 6, 12 and 18 month old AD mice and wild-type controls. Immunohistochemistry will also allow us to assess any changes in the localization of histone marks/HDACs in specific cell types as well as in relation to beta-amyloid plaque pathology. For more information contact Adele Woodhouse Adele.Woodhouse@utas.edu.au

**Project 3: Axon Degeneration in a model of Dementia**

**Supervisors:** Alison Canty, Anna King, James Vickers

This project will explore morphological changes of axons in the aged cerebral cortex in a mouse model of dementia. You will use brain tissue harvested from aged transgenic mice carrying the APP-PS1 mutation, which results in the deposition of amyloid plaques in the brain as a model of dementia, crossed with a Thy1-YFP line which has sub-populations of fluorescently labelled excitatory neurons in the brain. The primary objective will be to define axonal changes within, close to and far from plaques including synaptic rearrangements. Scientific techniques involved will include but not be limited to tissue handling and sectioning, immunohistochemistry, advanced microscopy and qualitative and quantitative image analysis. For more information contact Alison Canty Alison.Canty@utas.edu.au or Anna King a.e.king@utas.edu.au

**Project 4: Honours project in Axon Maintenance**

**Supervisors:** Dr Anna King, Prof. James Vickers

The axon is a neuronal structure that is essential for conduction of the action potential. However, few people are aware that the axon can constitute up to 99.9% of the neuronal volume and can transverse through a number of different environments in order to reach its targets. This makes axons incredibly vulnerable in disease and injury. Axons are dynamic structures capable of interacting with their external environment, of rapidly transporting components along their length and of rapid structural plasticity through modulation of their cytoskeleton. Axon can also synthesize proteins and can generate their own self-destruction programme.

Our ongoing research programme investigates both the normal functions of axons as well as mechanisms by which axons degenerate in neurodegenerative disease and traumatic brain injury. These projects use a number of innovative techniques including microfluidic compartmented cell culture techniques, live cell imaging both in vitro and in vivo, retinal models of axon degeneration, in vitro and in vivo viral transduction, electron microscopy, neuronal tracing and transgenic animal models of disease and injury as well as standard techniques such as immunohistochemistry, qPCR and Western blot.
Project 5: Honours project in Frontotemporal dementia

Supervisors: Dr Anna King, Prof. James Vickers

Frontotemporal dementia (FTD) and motor neuron disease are neurodegenerative diseases of ageing linked by a common pathological hallmark, the aggregation of a protein called TDP-43. A small number of cases are caused by mutations in the gene encoding TDP-43 however the majority of cases are sporadic or driven by mutations in other genes such as progranulin, raising the question “what drives TDP-43 pathology”? This project will investigate the factors that contribute to altered TDP-43 expression, localization and aggregation including (but not limited to), gene mutations, oxidative stress, proteasome inhibition, defective nuclear/cyttoplasmic transport, cell stressors, traumatic injury, excitotoxicity, inflammation, axonal transport alterations and other pathogenic proteins. This project will utilize both in vitro and in vivo techniques including cell separation, molecular and biochemical techniques, primary cell culture models, microfluidic technology, viral transduction, live cell imaging and mouse models. You will work amongst a team of researchers and students with expertise in neuroscience research and a focus on dementia. For more information on projects working on FTD contact Anna King a.e.king@utas.edu.au

Project 6: Does plasticity drive the pathology of Alzheimer’s disease?

Supervisor: Dr Matthew Kirkcaldie, School of Medicine

Although deposits of amyloid beta peptide are widely considered to drive the cell damage and death which results in the irreversible cognitive decline of Alzheimer’s disease, the underlying cause of these deposits remains a mystery. Recent understanding of the glymphatic system, which clears amyloid beta and other waste materials from the extracellular space of the brain, gives some understanding of why an individual may be unaffected for 60 years before the rapid accumulation which triggers dementia. This leaves the question of how and why the amyloid beta which overwhelms drainage, is produced.

A clue comes from the areas which fail first: brain regions of high cellular turnover, and those involved in the daily creation and revision of memory. Amyloid beta has been linked to processes of synaptic plasticity, and it is possible that areas in which the structure of connections is continuously changing, will produce the greatest excess and overwhelm the clearance system first. Areas such as the cerebellum, the thalamus and even the primary sensory and motor cortex are almost untouched by pathology, because they do not remain plastic in late adulthood.

This project will use a mouse model of Alzheimer’s disease pathology, the APP/PS1 mouse, and measure levels of plasticity-related proteins and RNA in the cortex, olfactory bulb and hippocampus, for comparison to measures of amyloid beta, both by ELISA and by automated measurement of pathology staining using advanced image processing software developed by our lab. A group of these mice will also have whiskers plucked under anaesthesia, to cause more plasticity in half the cortex, and the effect on the plasticity markers and pathology will be assessed.