

Research Honours 2012

School of Medicine

University of Tasmania

The Honours degree provides students with the opportunity to undertake further training in research in biomedical, clinical, 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 medical 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 student's undertaking a major research project, which will involve learning research skills, conducting research on a relevant medical or health area, and completing a thesis detailing and discussing the findings.

The Honours year in School of Medicine (incl Menzies) research programs is available to students completing UTAS degrees such as the B Biotechnology, B Med Res, BSc, MBBS or B Paramedic Prac. Where appropriate, we can also accept students into the Honours program who have completed an equivalent degree from another institution. Students can undertake projects in a broad range of areas including: biochemistry, physiology, anatomy, the pathological sciences, population and public health and paramedic practice depending on their interest And academic background.

All of these can involve research in either the School of Medicine or Menzies Research Institute. The enrolment codes for this course are as follows: course code M4G (Bachelor of Medical Research with Honours) and unit codes CMS405 and CMS406 or course code M4N (Bachelor of Medical Science with Honours), units codes CAM426-429. More information about the course can be found at www.course.utas.edu.au.

The School of Medicine and the Menzies Research Institute offers a broad range of Honours projects. An outline of available projects that the School of Medicine (SoM) are offering in 2012 is contained in this booklet. More information about projects in affiliated centres can be found at the Wicking Dementia Research and Education Centre (www.utas.edu.au/wicking) and the Menzies Research Institute-Tasmania (www.menzies.utas.edu.au)

COURSE OBJECTIVES

Students will undertake a supervised research project with an emphasis on advanced disciplinary knowledge, the use of specialised laboratory, field-work 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 by 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, 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 your thesis.

SCHOLARSHIPS

There are a number of scholarships available to students undertaking research in the School of Medicine and the Menzies Research Institute. Scholarships will be awarded based on academic merit. For more information on availability, eligibility and how to apply go to

<http://www.studentcentre.utas.edu.au/scholarships/>. Please be aware that the CLOSING DATE for applications is October the 31st.

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 do 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 they need to be assured that the appropriate supervision is in place. The Honours committee is comprised of representatives of the School of Medicine and the Menzies Research Institute. Your application will also be judged on your past academic performance.

STUDENT EXPECTATIONS

The course extends from early February to early November (semester 1 commencement) or early June to late July (semester 2 commencement). Attendance requirements will be dictated by the nature of the research 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 accomplish successful completion of the Honours year is a minimum of 40 hours per week equivalent to a standard full-time working week.

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

COURSE CO-ORDINATOR

Dr Sue Pearson: sue.pearson@utas.edu.au
Phone: (03) 6226 4712

Project Title: Characterisation of risk factors for melanoma in the Northern Tasmanian population

Supervisor(s) contact details: Dr Philip Clarke (Dermatologist, Launceston General Hospital); Dr Kathryn Ogden (Research Fellow, UTAS) (Kathryn.Ogden@utas.edu.au)

Research project synopsis

Australia has the highest incidence of skin cancer in the world. Melanoma is not the most common type of skin cancer but it is the most life threatening form of skin cancer. In 2005, there were 10,684 new cases of melanoma, making it overall the fourth most common form of cancer in Australia. Total deaths from melanoma in 2005 were 1,272 making melanoma the ninth most common cause of cancer death. Anecdotally, patients prone to developing melanoma should be easily predicted from demographic and physical characteristics, allowing for a more systematic identification and surveillance of these high risk patients. The honours project will form a component of the larger study whose aims are below. There is capacity for the project to sustain more than one honours student.

Aims and Objectives (Larger study)

- To identify people in Tasmania at high risk of melanoma.
- To provide regular skin inspection and skin imaging for people at high risk of melanoma.
- To reduce the death rate from melanoma by detecting melanoma at an earlier stage.
- To confirm known risk factors for melanoma and to rank them in importance. New risk factors may also be identified.
- Minimise unnecessary mole removal which is a cause of unnecessary anxiety, scarring and expense.
- Education of patients at high risk of melanoma on prevention strategies.

The study will also help to determine the feasibility of whole of population screening for melanoma, which would be a world first. The proposed honours project will use a case control methodology to compare physical and demographic characteristics of patients with a history of melanoma (cases) and age/gender matched controls. In doing so, it will develop a predictive model to assist a targeted screening program.

Location: Launceston Clinical School

Project Title: Farm related deaths in Tasmania over 5 years

Supervisor(s) contact details: Dr Kathryn Ogden, MBBS, FRACGP, MPH Research Fellow Launceston Clinical School (Kathryn.Ogden@utas.edu.au). University Department Rural Health will co-supervise this project (exact personnel to be determined).

Research project synopsis

Agriculture remains a significant industry in Tasmania, and farm related deaths are of significant interest to the community and government. However, accurate information regarding farm related deaths is not readily available due to paucity of information or information of doubtful quality on death certificates, in particular with regards to present occupation. As the ABS mortality data do not have an appropriate and reliable code to identify occupation, and given the relative paucity of circumstances surrounding the death,

the National Coroners Information System provides us with the most valuable resource for determining farm-related deaths in Tasmania.

Aims of the study is to examine the epidemiology of farm deaths in Tasmania over the past 5 years and, ii) to examine the circumstances of farm deaths in Tasmania over the past 5 years.

Methods: The Department of Health and Human Services, Population Health Unit, have approached the University Department of Rural Health to undertake a pilot project looking at the circumstances of farm deaths in Tasmania. The project would involve assisting with the development of an ethics proposal around the collection of this data, the retrospective collection and analysis of data from coronial records. A national survey using similar methodology can be accessed at this link:

<http://pass.org.au/wp-content/uploads/2011/01/Farm-Injury-Related-Deaths-Australia-2003-06.pdf>

Location: Launceston Clinical School

Project Title: A study of the effectiveness of visitor infection control measures at the Launceston General Hospital

Supervisor(s) contact details: Mr Peter Van Winden (Orthopaedic Surgeon, Launceston General Hospital); Dr Kathryn Ogden (Research Fellow, UTAS) (Kathryn.Ogden@utas.edu.au).

Research project synopsis

The student would work with the supervisors and the infection control department at the Launceston General Hospital to design and implement a mixed methodology research project aimed at evaluating current methods for infection control of visitors to the hospital and hospital staff. Research methods utilised will include an examination of existing literature, observation of practices of staff and visitors regarding infection control measures in a variety of settings (eg on the wards, in theatre, cafeteria etc), and interviews with, and surveys of, staff and visitors regarding their understanding and intentions regarding infectious control measures. Both qualitative and quantitative data will be generated. It is intended that this project will provide both locally and externally relevant data.

Aims of the study are to i) to determine the effectiveness of current methods for infection control of visitors at the Launceston General Hospital and ii) to use this and existing evidence to provide recommendations for future infection control methods.

The project will be designed to allow for completion within the timeframe required for an Honours year; there may be some initial planning required late 2010 to allow for the preparation of an ethics application so that the data collection can begin early 2011. However, this will not require the student to be located in Launceston until 2011.

Location: Launceston Clinical School/Launceston General Hospital

Project Title: Management of metabolic syndrome in psychiatric patients on antipsychotic medication

Supervisor(s) contact details: Dr Ben Elijah (Consultant Psychiatrist, LGH) and Dr Kathryn Ogden (Research Fellow, UTAS) (Kathryn.Ogden@utas.edu.au).

Research project synopsis

For reasons of lifestyle and a side effect of medication, psychiatric patients are at particular risk of metabolic syndrome. Dr Ben Elijah from the Launceston General Hospital has worked with leaders in this area in previous positions and would like to determine how best to promote cardiovascular health in the population of psychiatric patients with metabolic syndrome under the care of the psychiatry service at the LGH.

Aims of this study are to: i) undertake a literature review to determine current models of care for psychiatric patients with metabolic syndrome, ii) undertake a retrospective audit aimed at determining current practices regarding the identification and management of metabolic syndrome in patients under the care of the psychiatric service, Launceston General Hospital and iii) evaluate a pilot intervention aimed at better addressing metabolic syndrome in these patients.

This project would employ a number of small components including a retrospective audit of current practices, interviews with staff aimed at identifying barriers to care, a literature review of evidence supporting interventions, and an evaluation of a pilot program aimed at improving these patients' cardiovascular risk factors.

The following paper is of relevance for anyone interested:

Lambert, T. J. and J. W. Newcomer (2009). "Are the cardiometabolic complications of schizophrenia still neglected? Barriers to care." *Med J Aust.* **190**(4 Suppl): S39-42

Location: Launceston Clinical School

Project Title: Validation of the Stroke Aphasia Depression Questionnaire (Hospital version) for identification of depression in an elderly non-aphasic patient population

Supervisor(s) contact details: Dr Fiona Bardenhagen (Clinical Neuropsychologist, Launceston General Hospital); Dr Kathryn Ogden (Research Fellow, UTAS) (Kathryn.Ogden@utas.edu.au).

Research project synopsis

The Stroke Aphasia Depression Questionnaire – Hospital version (SADQ-H) was developed for stroke patients with aphasia, however its applicability as a screening tool for mood disorders in other patient groups has not been determined. Dr Bardenhagen is a clinical neuropsychologist who believes that this observational assessment tool could be used successfully in patient groups other than those which it was primarily developed for, especially those elderly patients who would deny depressive symptoms if given a formal self-report mood screen.

The research project will investigate if the SADQ –H has concurrent validity with self-reported, validated measures including the Hospital Anxiety and Depression Scale (HADS) and the Geriatric Depression Scale. Demonstrating its concurrent validity with self-report measure for non-aphasic patients would make it a useful adjunct to self-report mood

measures by rating patients' behaviours with the SADQ-H. It could also provide a useful formalised observational screen that could be done by nurses to identify patients who need further evaluation of mood (this might involve some modification of the form, to allow daily recording of observed behaviours).

Depending on the results, a mood and anxiety screening protocol (using the SADQ-H if it's valid for non-aphasics and other instruments) could be developed. The initial research could lead to further study looking at a trial of implementation of the screen on a general medical ward, comparing the prevalence of detected mood disorders pre and post implementation. This would be beyond the scope of the Honours year however if desired could provide ongoing work which has the potential to lead to a PhD.

Location: Launceston Clinical School/Launceston general Hospital

Project Title: A pilot study to determine the prevalence of thyroid disease in association with iron deficiency among Tasmanian pregnant women

Supervisor(s) contact details: Dr A. Khalafallah; Dr Kathryn Ogden (Kathryn.ogden@utas.edu.au).

Research project synopsis

Background: The incidence of thyroid disease in the northern Tasmanian antenatal population is estimated at about 1% for severe disease and 2-3% for subclinical disease. There is no data available in pregnancy. Furthermore, the current targeted screening based on clinical examination and history is probably insufficient to identify the real incidence of thyroid disease. Predictors for thyroid deficiency are iodine deficiency, anaemia and autoimmune disease.

Patients and methods: This is a prospective observational non-controlled study to be conducted at the Launceston General Hospital (LGH). The trial will be offered to pregnant women who attend for routine antenatal care at the LGH. A representative blood sample of women presenting for antenatal care at the Queen Victoria Outpatient (QVOP) department, upon consent would be tested for TSH, FT4 FT3 and anti TPO antibodies as well as iodine level in urine. Iron studies and a full blood count would also be performed to test for the presence of concomitant iron deficiency anaemia. In addition a detailed questionnaire will be administered to these women to identify women that would have been candidates for thyroid testing based on history and symptoms alone.

Potential benefits: The aim of study is to determine the actual incidence of thyroid disease within the northern Tasmanian obstetric population and its possible association with iron deficiency. This may help the clinicians to early screen and diagnose thyroid disease in pregnancy and hence offer the appropriate treatment. This study will be expected to commence by end of 2010 for a 12 months period.

Location: Launceston Clinical School

Project Title: *H.pylori* issues in refugees – the Launceston experience

Supervisor(s) contact details: Dr Andy Hodson (GP, refugee health specialist, Refugee Health Centre, Launceston); Dr Kathryn Ogden (Research Fellow, UTAS). Contact Kathryn.Ogden@utas.edu.au

Research project synopsis

Background: Since 2007 most newly arrived refugees to northern Tasmania have had a health screening via the Launceston Refugee Primary health care clinic. As part of this screening they have had serological testing for *H.pylori* with eradication therapy prescribed for all testing positive.

Aims:

- 1) *H.pylori* incidence with regard to country of origin / family relationship.
- 2) Reliability of history as a predictor for carriage
- 3) Any correlation with iron status
- 4) Any correlation to vitamin B12 levels
- 5) Compliance / complications of eradication therapy

Methods: retrospective data analysis of consecutive clients at the clinic from 2007 to current. Literature review of current theories of *H.pylori*

Location: Launceston Clinical School

Project Title: Vitamin D issues in refugees – the Launceston experience

Supervisor(s) contact details: Dr Andy Hodson (GP, refugee health specialist, Refugee Health Centre, Launceston); Dr Kathryn Ogden (Research Fellow, UTAS). Contact Kathryn.Ogden@utas.edu.au

Research project synopsis

Background: Since 2007 most newly arrived refugees to northern Tasmania have had a health screening via the Launceston Refugee Primary health care clinic. This has included estimating vitamin d levels, liver function, calcium and phosphate. In addition to these tests done at arrival there is also recording of height / weight . There has been a clinical suspicion of a growth spurt in children in the first few months of arrival. For those with low levels of vitamin d megadose supplementation has been the preferred treatment option. However we are now suspicious that this is not effective.

Aim/s:

- 1) Ascertain if there is any correlation between vitamin D / alkaline phosphatase / Calcium and phosphate levels with reference to country of origin / family relationships / age/ religion.
- 2) See if there is any relationship between arrival height / weight to vitamin d levels and subsequent growth velocity in children <15yo. Iron status is also to be included as a potential confounder
- 3) Examine data to see if megadose strategy is working and raise other treatment options

Methods: retrospective data analysis of consecutive clients at the clinic from 2007 to present. Literature review of current theories on vitamin D metabolism.

Location: Launceston Clinical School

Project Title: A pilot study to determine the prevalence of thyroid disease in association with iron deficiency among Tasmanian pregnant women

Supervisor(s) contact details: Dr A. Khalafallah; Dr Kathryn Ogden
Kathryn.ogden@utas.edu.au ,

Research project synopsis

Background: The incidence of thyroid disease in the northern Tasmanian antenatal population is estimated at about 1% for severe disease and 2-3% for subclinical disease. There is no data available in pregnancy. Furthermore, the current targeted screening based on clinical examination and history is probably insufficient to identify the real incidence of thyroid disease. Predictors for thyroid deficiency are iodine deficiency, anaemia and autoimmune disease.

Patients and methods: This is a prospective observational non-controlled study to be conducted at the Launceston General Hospital (LGH). The trial will be offered to pregnant women who attend for routine antenatal care at the LGH. A representative blood sample of women presenting for antenatal care at the Queen Victoria Outpatient (QVOP) department, upon consent would be tested for TSH, FT4 FT3 and anti TPO antibodies as well as iodine level in urine. Iron studies and a full blood count would also be performed to test for the presence of concomitant iron deficiency anaemia. In addition a detailed questionnaire will be administered to these women to identify women that would have been candidates for thyroid testing based on history and symptoms alone.

Potential benefits: The aim of study is to determine the actual incidence of thyroid disease within the northern Tasmanian obstetric population and its possible association with iron deficiency. This may help the clinicians to early screen and diagnose thyroid disease in pregnancy and hence offer the appropriate treatment. This study will be expected to commence by end of 2010 for a 12 months period.

Location: Launceston Clinical School & Launceston General Hospital

Project title: The impact of high flow nasal cannulae therapy during inpatient stay of infants with bronchiolitis

Supervisor(s) contact details: Dr Sean Beggs (Sean.Beggs@dhhs.tas.gov.au), School of Medicine and Royal Hobart Hospital.

Research project synopsis

To determine whether the introduction of heated humidified high- flow nasal cannulae (HFNC) decreases the length of stay for an infant < 24 months old with bronchiolitis admitted to a general paediatric unit or paediatric intensive care unit.

This study intends to compare the outcomes of infants with bronchiolitis who receive either standard nasal prong oxygen support or HFNC oxygen. To do so a retrospective audit of medical records will be conducted of infants <24months admitted with bronchiolitis during 2008. This data will be compared with infants admitted with bronchiolitis during 2011. The 2011 data will be collected prospectively. The key data sets will include length of stay, nursing observations (heart rates, respiratory rate, oxygen saturations, work of breathing), gestational age, weight, intubation rates, time receiving oxygen, oxygen flow rates, RSV status.

Location: School of Medicine & Royal Hobart Hospital

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: Investigate community and out of hospital management of anaphylaxis to inform best practice guidelines within a multi-disciplinary health care environment

Supervisor(s) contact details: Ms Melanie Blackhall (Melanie.Blackhall@utas.edu.au) & Mr Dale Edwards (Dale.Edwards@utas.edu.au)

Research project synopsis

Currently the first line of community based anaphylaxis treatment is the use of an adrenalin auto-injector device to deliver a lifesaving dose of adrenalin. Current ASCIA best practice guidelines suggest the treatment with adrenalin is the first priority and delaying or withholding adrenalin can result in deterioration and death. The purpose of the project is to investigate management of anaphylaxis in the community and ultimately to provide evidence to support current or future guidelines and clinical practice.

This project will explore the incidence of anaphylaxis presentation to ambulance services, and hospital services within Tasmania, the management provided and the health outcomes resulting from these presentations. This will allow the research team to determine the frequency and appropriateness of Adrenalin auto injecting device – in general population.

There are a number of potential opportunities for honours research within this project(s) including:

- Conduct of a retrospective review of presentations to ambulance services, exploring presentation frequency, management and outcomes
- Conduct of a retrospective review of presentations to hospital emergency departments, exploring referral pathways, presentation frequency, management and outcomes (including hospital length of stay)
- Review of practice guidelines and protocols for the management of community based anaphylaxis presentations.

By identifying best practice pre-clinical and clinical teaching practice will be informed across MBBS and paramedic practice degrees. The project will also inform patient education within clinical environment plus preventative health care and clinical protocols.

Location: School of Medicine, Hobart

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: “Tas+HPV”

Supervisor(s) contact details: Prof Richard Turner (richard.turner@utas.edu.au)/ Dr Maree O’Sullivan (maree.o’sullivan@dhhs.tas.gov.au)

Research project synopsis

This is a cross-sectional study of the 200 or so hiv-positive people in Tasmania. Its principal aim is to document the prevalence of anal and genital dysplasia / neoplasia and the carriage of high-risk (oncogenic) human papilloma virus genotypes. It will also explore the medical and behavioural determinants of these. The role of the student will be to directly deal with subjects for study recruitment, specimen collection and questionnaire administration (at least in Hobart); data analysis and reporting will also be required.

Location: School of Medicine, Hobart

Project Title: Epidemiology of thyroid cancer in Tasmania

Supervisor(s) contact details: Dr Barry Edwards (info@craigow.com.au) /Dr Mary Self (M.B.Self@utas.edu.au)

Research project synopsis

This study will involve a review of hospital/clinic case records and data from the Tasmanian cancer Registry, to determine the incidence of thyroid cancer in Tasmania – with respect to time, place and histological type. Information of treatment outcomes will also be sought.

Location: School of Medicine, Hobart

Project Title: Development of hospital avoidance guidelines and rationale for infectious disease patients

Supervisor(s) contact details: Mr Dale Edwards (Dale.Edwards@utas.edu.au), Dr Richard Bradbury

Research project synopsis

Presentation of uncompromised patients with contagious gastrointestinal and respiratory conditions to hospital has a number of flow on effects including increasing demand on limited emergency department resources; creating a risk of exposure to infection for patients and staff and flow on limitations affecting patient access to emergency department services including ambulance waiting times due to bed block. Infection of patients in the emergency department delays healing and extends bed stays for those patients following admission. The development of a guideline to assess and manage such patients in the out of hospital environment will reduce the risk of cross infection, reduce demand on hospital services, increase available bed spaces and reduce the need for patient isolation in hospital, as well as reducing the impact of ambulance waiting times at hospital.

This project offers a number of opportunities for Honours students, including:

- Conducting a retrospective review of patients presenting to ambulance services with contagious gastrointestinal and respiratory conditions, including the treatment provided and transport (if any).
- Conducting a retrospective assessment of the number of infectious patients with contagious gastrointestinal and respiratory conditions attending emergency departments that do not require hospitalisation and are subsequently discharged.
- Testing a clinical assessment tool to be used to establish the need for transport, versus the suitability for community based management plan (hospital avoidance).

There are additional opportunities for this research team in the development and refinement of the above mentioned clinical assessment tool.

Location: School of Medicine, Hobart

Project Title: Evaluation of the “Docs for a Day” (DFD) program

Supervisor(s) contact details: Dr Stephen Wilkinson (wilko1952@gmail.com) / Emeritus Prof Carey Denholm

Research project synopsis

Since 1996 the Division of Surgery, Royal Hobart Hospital (RHH) has hosted an educational program for grades 5 and 6 school children, called the “Docs for a Day” (DFD) program. DFD provides school children with a 1.5 hours hands-on experience of an acute hospital. The aim is to decrease the anxiety of hospitals (a positive outcome if participants were to present to the hospital later as patients), and to deliver positive health messages including a strong anti-smoking message, and the benefits of a healthy diet, avoidance of sunburn and maintenance of exercise.

To mid 2010, approximately 4000 children have attended the program and the original cohorts are now in their 20s. Anecdotal experience based on posters, letters, project materials, e-mails and teacher feed-back sheets is that the DFD experience has a powerful emotional experience on children. What has not yet been evaluated, however, is: What is

the duration of the emotional experience of children attending DFD? Do later events/experiences re-trigger those emotional feelings? Are health choices later in life influenced by the DFD program? This project aims to answer these questions.

The research student will be involved in the design of a DFD website. Using an online survey accessible from the website previous participants in the DFD program including students, teachers and parents, will be invited to record their experience and the influence it has had on them. Additional components of this honours project will include the analysis of the data providing answers to the three research questions and the formulation of recommendations regarding the continuance of the DFD program, its structure and its exportability to other hospitals in Australia.

From the perspective of the researcher the program is designed to provide experience in reviewing relevant technical literature, designing a computer based research resource, data collection and analysis, report writing and the formulation of logical conclusions and recommendations from work undertaken.

Location: School of Medicine & Royal Hobart Hospital

Project title: Understanding the psycho-socio-biomedical journey of hepatitis C treatment

Supervisor(s) contact details: Dr Kwang Chien Yee (kcyee@utas.edu.au).

Research project synopsis

The number of patients infected with hepatitis C in Australia is about 200,000. In the past decade, the treatment of hepatitis C infection has improved dramatically. With the current treatment, patients with hepatitis C infection have a successful rate of 60-90% in achieving viral clearance. Achieving viral clearance will prevent many complications of chronic liver disease and reduce disease burden in the future. This project aims to understand the psycho-social and biomedical journey of patients undergoing hepatitis C treatment with the aim of developing better model to support hepatitis C treatment in Tasmania. The primary data collection method utilised in this research project is semi-structured interview and health information analysis using clinical process mapping. It is anticipated that this project will interview patients undergoing treatment for hepatitis C, new prescribers of hepatitis C treatment as well as policy makers, allied health professionals and hepatitis C nurse. Students will be provided with education and training in regards to data collection and analysis. The Honours project will form part of this long term research project to investigate an aspect of hepatitis C treatment. Prospective students should discuss with supervisor in regards to which aspect of the research project the students are interested in participating.

Location: School of Medicine & Royal Hobart Hospital

Project title: Understanding the patient's narrative for bowel cancer screening program in Australia to develop patient-centred clinical care indicators

Supervisor(s) contact details: Dr Kwang Chien Yee (kcyee@utas.edu.au).

Research project synopsis

Colonic cancer is one of the most common cancer in Australia and worldwide. It is estimated

that 1 million patients are diagnosed with colonic cancer each year and the incidence will increase by 50% in the next decade. In Australia, 13,000 patients are diagnosed with colonic cancer each year, resulting in 6,000 deaths per year. Many of these cancers are preventable. While there are significant improvement in the treatment of colonic cancer in recent time, prevention of colonic cancer remains the best method to improve mortality and morbidity related to colonic cancer. Australia has adopted two-stage colonic cancer screening program, with faecal occult blood testing as the first step. The second step is delivered through usual care for patients with faecal occult blood test.

While clinical indicators are currently being considered for the bowel cancer screening program, there is little evidence to understand the program from patient's perspective. More importantly, there is a lack patient-derived, patient-centred clinical care indicator development. This program aims to understand patient's expectation for care and therefore derive patient-centred clinical care indicators. The primary data collection method utilised in this research project is semi-structured interview, literature review and health information analysis using clinical process mapping. It is anticipated that this project will interview patients participating in national bowel cancer screening program. The Honours project will form part of this long term research project to investigate bowel cancer screening program from patient's perspective. Prospective students will participate in the process of data collection, analysis and presentation of data.

Location: School of Medicine & Royal Hobart Hospital

Project title: Understanding electrogastrography in health and disease

Supervisor(s) contact details: Dr Kwang Chien Yee Email: kcyee@utas.edu.au.

Research project synopsis

Many patients suffer from gastric motility and contractility problems. The understanding of control of gastric motility and contractility has not been extensive research due to the lack of easily assessable investigations. This project is an exploratory project, aiming to develop an understanding of electrogastrography. This will involve setting up electrogastrography, analysing and interpreting electrogastrography in healthy patients and in patient with diseases. This is an exciting exploratory study, which might achieve an exciting new way of understanding gastric motility and functions. Prospective students will participate in the process of data collection, analysis and presentation of data.

Project title: Using the OSSIE guide to improve quality and safety in Healthcare

Supervisor contact details: Dr Kwang Chien Yee (kcyee@utas.edu.au).

Research project synopsis

Medical errors are common within healthcare delivery. It is estimated that 16.6% of hospital admissions in Australia are associated with adverse events. About half of these cases are preventable. Many cases of medical errors and adverse events are related to clinical communication and clinical handover. Clinical handover is considered a high priority for patient safety improvement in recent years by World Health Organisation and The Australian Commission (the Commission) on Safety and Quality in Health Care.

The Commission has funded various projects around the country, including a major project

in Tasmania, through the Department of Health and Human Services and University of Tasmania. The project aims to produce a standardised operating protocol for clinical handover. This project has formed the basis of the national clinical handover improvement guideline, known as the OSSIE guide. The OSSIE guide has been endorsed by all federal and state health ministers this year as the national framework for clinical handover improvement.

This project will aim to understand the utilisation of OSSIE guide to improve quality and safety in health care. The research methodology is well established and published in the OSSIE guide for clinical handover improvement. Dr. Yee is the primary author of the OSSIE guide. This is a five step clinician engagement guide to improve clinical handover and clinical communication. Students will be involved in the design, data collection, implementation and evaluation of OSSIE guide in various quality and safety improvement initiatives.

Location: School of Medicine & Royal Hobart Hospital

Project Title: Translational Research in Practice: A Case Study

Supervisor(s) contact details: Dr Stella Stevens email: stella.stevens@utas.edu.au, Professor Craig Zimitat email: craig.zimitat@utas.edu.au.

Research project synopsis

Integrating research into routine practice in health care takes too long. Health care improvement initiatives based on research take less time, but are largely top-down driven, and the efforts of clinicians at the workplace receive scant attention from administrators (Greenfield, Nugus et al. 2011). Yet, the evidence we have points to the futility of this approach: without clinician engagement in health care improvement, top down policies, frameworks and targets have little impact (Mountford and Webb 2009).

The School of Medicine has been engaged in developing a multidisciplinary group of clinicians to conduct research into priority areas for health care improvement in their workplaces. They have reviewed the relevant literature, conducted the research using a range of methodologies, and are currently implementing the results of their findings within their health service. Some have published their results and all are evaluating the outcomes of their projects in terms of process and outcomes. Their work is a good example of translational research.

Aims of this study are to: i) produce a case study based on this group of clinicians to improve our understanding of the critical success factors for translational research and, ii) to use the evidence resulting from the case study as preliminary work to underpin a larger study of the barriers to translational research and associated strategies to overcome these.

Location: School of Medicine, Hobart

Project Title: The Pathology of COPD

Supervisor(s) contact details: Dr Richard Wood-Baker (Richard.WoodBaker@utas.edu.au)

Research project synopsis

Background: We recently reported, using immunohistochemical staining of endobronchial biopsies collected at bronchoscopy, that reticular basement membrane (Rbm) in smokers and COPD was extensively fragmented suggesting that smoking is likely to initiate the

transition of airway epithelial cells to a mesenchymal phenotype through a process called epithelial mesenchymal transition (EMT) and resulting Rbm fragmentation and cleft formation.

Aims: To investigate TGF- β , RAGE and transcription factors (phosphorylated SMAD2, 3, 7 and TWIST) that lead to expression of the EMT proteome in smoking and COPD airways.

Methods: To assess the mechanisms driving airway inflammation and remodelling, we will immunostain airway biopsies for expression of RAGE. For TGF β ₁ and transcription factors (SMAD-2, -3, -7 and TWIST) we will use both quantitative immunohistology and quantitative reverse transcription (RT)-PCR (qPCR) for their RNAs extracted from biopsies. We will also use these methods on cell pellets (mainly macrophages) from BAL (bronchoalveolar lavage; essentially airway washings) that have been stored for each individual, and on primary epithelial cells derived from relevant COPD/smoker/control.

The candidate will work within the Respiratory Research Group, and will have the opportunity to work both with lab based researchers, and clinicians from the Royal Hobart Hospital.

Location: Menzies Research Institute & Royal Hobart Hospital

Project Title: Rehabilitation in Chronic Obstructive Pulmonary Disease

Supervisor(s) contact details: Dr Richard Wood-Baker (Richard.WoodBaker@utas.edu.au).

Research project synopsis

Background: As their condition progresses, people with COPD have increased hospitalisation, decreased quality of life and physical activity. Anecdotally, while people wait to attend pulmonary rehabilitation there is limited follow-up and self-management support appears to have been limited. Pulmonary rehabilitation, usually delivered face-to-face in groups, aims to improve the health of those with COPD by encouraging the adoption of self-management and health-related behaviours.

Aims: To investigate the influence of importance and confidence in achieving behavioural change.

Methods: We have data collected from participants who took part in a controlled trial of telephone mentoring in COPD. Behavioural change was moderated by telephone mentoring using action planning methodology. Before and after self-reported outcomes of planned actions will be compared to objective assessments of health-related quality of life, lung function and activity.

The candidate will work within the Respiratory Research Group, and will have the opportunity to work both with lab based researchers, and clinicians from the Royal Hobart Hospital.

Location: Menzies Research Institute/Royal Hobart Hospital

Project Title: The role of Vitamin D in Airway Diseases

Supervisor(s) contact details: Dr Richard Wood-Baker (Richard.WoodBaker@utas.edu.au).

Research project synopsis

Background: Allergic asthma and chronic obstructive pulmonary disease (COPD) exacerbations peak at different times of the year; asthma in spring/summer and COPD in winter. Vitamin D, a known immunomodulator, also has seasonal variation, and peaks in

summer and drops in winter. The severity of both conditions may be modulated by vitamin D.

Aims: To investigate the role of Vitamin D in asthma and COPD.

Methods: We intend to collect blood for cellular assays and vitamin D levels in summer and winter, and link these to lung function in the subjects. We will examine the cytokine profile of the participants to see whether they are skewed towards Th1 in COPD and Th2 in asthma. Th1 cytokines drive cellular immune responses, whereas Th2 cytokines predominantly drive antibody responses. In addition, we will investigate T regulatory cells in all groups. T regulatory cells are a very small subset of CD4⁺ T cells which are vital in controlling immune responses and regulating resolution of infections. Also, we will culture cells with calcitriol (vitamin D) to see if this modulates the cytokine profile in the different groups. By modulating peoples' vitamin D levels, it may be possible to ameliorate the severity of asthma and COPD.

Location: Menzies Research Institute & Royal Hobart Hospital

Project Title: Interferon-beta, Statins and vitamin D. Do some drugs work by modifying vitamin D synthesis?

Supervisor(s) contact details: Dr Niall Stewart (Niall.Stewart@utas.edu.au).

Research project synopsis

Background: A side effect noted in both Statin and Interferon-beta (IFN β) therapy has been an increase in vitamin D status in recipients. Statin therapy is important in lowering cholesterol and reducing cardiovascular disease risk, whereas IFN β is used in a range of diseases, from cancer to Multiple Sclerosis (MS). Interestingly, the conditions treated with these drugs are less severe in those with naturally high vitamin D levels. In animal models of MS, cancer and cardiovascular disease, vitamin D is protective. It is a powerful modulator of the immune system, and acts as a strong anti-inflammatory. It promotes Interleukin-10 secretion (an immunosuppressive cytokine) and suppresses inflammatory cytokines such as Interferon-gamma (IFN γ). It is possible that some of the benefits associated with Statin and IFN β therapy are due to the concomitant increase in vitamin D. Alternatively, these drugs may not be efficacious in people with low vitamin D.

Project: In this project, the candidate will establish cultures of keratinocytes (the cells associated with the majority of vitamin D synthesis). The keratinocytes will be treated with different Statins and IFN β s, and the production of 7-dehydrocholesterol (the precursor of vitamin D) will be measured by High Pressure Liquid Chromatography (HPLC). In addition, cultures of CD4⁺ T cells will be established. The effect of Statins and IFN β s (with or without added vitamin D) on cytokine production will be analysed. If time permits, T regulatory cell activity will also be analysed, as these cells are important in autoimmune diseases and the inflammatory process.

The candidate will learn cell culture techniques, high pressure liquid chromatography and flow cytometric cell and cytokine analysis. They will work within the Respiratory Research Group, and will have the opportunity to work both with lab based researchers, and clinicians from the Royal Hobart Hospital.

Location: Menzies Research Institute

Project Title: Flow dependence of deadspace – a new more sensitive method for detecting small airway disease

Supervisor(s) contact details: Assoc. Prof. Justin Walls (J.Walls@utas.edu.au) and Assoc. Prof. David Johns, School of Medicine

Research project synopsis

The Tasmanian Longitudinal Health Study (TAHS; formerly called the Tasmanian Asthma Study), has now been running for 40 years. The participation of the Tasmanian community has helped to make TAHS one of the world's largest and longest running studies on respiratory health in the world. The most recent follow-up study of the TAHS has involved contacting all the brothers and sisters who were part of the original study back in 1968, and sending them questionnaires in the mail. This study has been designed to show us the reasons why one brother or sister may develop asthma, but other children in a family may not develop this disease. Studying siblings is a unique way to look at lung diseases, which has not been done anywhere else in the world.

A clinic based follow up is also underway in which respiratory function is determined along with a novel measure of airway health utilizing anatomical dead space. This measure promises to identify airway disease at an early stage and will give insight into the disease process. UTAS staff in partnership with a Swiss Instruments company has developed this new test, which is currently being automated.

Students undertaking this project would join an NHMRC project team evaluating the TAHS data already collected. The focus of the work would be to evaluate the new measure of airway function and to identify risk factors for small airway disease and would have both laboratory and analytical components. This project would be appropriate for students who may wish to continue in post-graduate research with the potential for the preliminary data gathered in this unit to extend into an Honours and PhD topic.

Location: School of Medicine, Hobart

Project title: Towards a better understanding of uraemic molecules

Supervisor(s) contact details: Dr Matthew Jose (Matthew.Jose@utas.edu.au). Menzies Research Institute & RHH Dialysis Unit, Dr Rob Shellie/Dr Emily Hilder, School of Chemistry, UTAS.

Research project synopsis

Measurement of kidney function and adequacy of dialysis have relied on the concentration of small molecules in the serum: urea and creatinine. In CKD, a serum creatinine concentration allows calculation of eGFR, a reasonable measurement of kidney function or glomerular filtration rate. However there is a wide variation on how this relates to symptoms in people with low kidney function. With dialysis, achieving urea clearances above 65% with each dialysis has been determined to be the minimum standard, yet removal above this level does not have any consistent benefit. Urea itself does not cause the toxic effects of uremia, thus removal of it is used as a surrogate for some other, more relevant molecule that is accumulated in kidney disease. Refinements in the dialysis procedure have improved both quality and quantity of life, but this improvement has plateaued in the last 10-years. Over 50% of people still die within 3 years whilst treated with

modern dialysis. Improvements that are theoretically beneficial include longer-hours on dialysis, convective techniques (hemodiafiltration) or the use of high-flux membranes (allowing removal of larger sized molecules). Further improvement in outcomes is critically dependent on our ability to understand more about the toxic molecules that accumulate or are altered in the uraemic state. The aims of this project include:

- Identification of molecules that signal early kidney disease
- Identification of toxic molecules that contribute to symptomatic kidney disease
- Identification of toxic molecules that contribute to premature cardiovascular death
- Identifying better ways of assessing kidney function in a more specific and relevant way with regard to symptoms and cardiovascular disease
- Optimising treatment for the removal of these toxic molecules from people with ESKF through the use of dialysis techniques and 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 & RHH Dialysis Unit.

Research project synopsis

People with chronic kidney disease have low blood levels of vitamin B, C & D. 25-vitamin D is lower than in people without kidney disease, 1,25-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: 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: Brain structure and disruption in a neurofilament knockout mouse model

Supervisor(s) contact details: Dr Matthew Kirkcaldie (Matthew.Kirkcaldie@utas.edu.au).

Research project synopsis

Neurofilament proteins are important structural components of neurons in rodent and human brains, and are implicated in the pathology of diseases such as motor neuron disease and Alzheimer's disease. A line of transgenic mice lacking the neurofilament light (NFL) subunit, the backbone of these filaments, have been used in studies of disease mechanisms. However, no systematic description has ever been published of structural changes in the nervous systems of NFL-knockout mice. Recent data from our lab group has also suggested that other intermediate filament proteins may form alternative assemblies with the other neurofilament proteins as a substitution for NFL, and this may offer important clues to the functional properties of these widely expressed cytoskeletal components.

This project would involve mapping the expression and distribution of NFL and other intermediate filament proteins across the brain and spinal cord of NFL knockout and wildtype mice. If time permits, cell culture studies may also be used to investigate the relationship between NFL and other cytoskeletal proteins. Immunohistochemistry, transmitted light, fluorescence and confocal microscopy will be used for structural studies, and the project will offer a thorough grounding in laboratory neuroanatomy and immunohistochemistry which are an excellent basis for further studies of CNS disease and structure. A successfully completed project will also be written up in a form suitable for publication in a peer-reviewed journal.

Location: School of Medicine, Hobart

Project Title: How is the brain wired together?

Supervisor(s) contact details: Dr Lisa Foa, lisa.foa@utas.edu.au

Research project synopsis

The brain is an incredibly intricate circuit, wired with almost perfect precision. Errors in the circuit wiring can have disastrous implications, potentially causing a variety of developmental disorders including autism, schizophrenia and Fragile X syndrome. The mechanisms that govern how this precise neuronal circuit is wired during embryonic development are only beginning to be understood. One thing we do know, is that calcium is vital to normal neuronal development. However, our understanding of the mechanisms that regulate calcium signaling are poor. In our lab, we study a variety of proteins that we have shown to be necessary for controlling calcium levels within developing neurons (see refs 1 and 2 below), such as Homer, STIM and Orai. STIM and Orai were recently discovered in immune cells, but our work has demonstrated that they are clearly necessary for correct neuronal development. In particular, we have found that they are necessary for axon pathfinding, the process responsible for wiring the brain circuitry as neurons connect with their correct target cells. Our work aims to understand the mechanisms by which proteins

such as STIM, Orai, Homer and related proteins function in developing neurons to control calcium signaling and hence axon pathfinding in the developing nervous system.

Our lab has a number of projects on offer that examine the cell signaling mechanisms that regulate neuronal development. We collaborate closely with other labs in the Menzies that study neuronal degeneration and repair. This is because that many of the signaling mechanisms that control development appear to also be important in the disease process.

Location: Menzies Research Institute

Project title: Strategies to promote regeneration of the diseased or injured nervous system

Supervisor contact details: Dr Tracey Dickson (tracey.dickson@utas.edu.au), Professor James Vickers (james.vickers@utas.edu.au), Dr Roger Chung (roger.chung@utas.edu.au), Professor Adrian West (Adrian.west@utas.edu.au), Associate Professor Inn Chuah, (inn.chuah@utas.edu.au).

The 30-member NeuroRepair Group of which the team leaders are the supervisors listed above is developing multiple routes to understanding the basic mechanisms by which neurons and other neural cells respond to injury and disease and how this understanding can lead to therapeutic strategies to promote regeneration.

At present, our group is conducting major projects looking at strategies to promote regeneration of the diseases or injured nervous system in the following areas:

Neuron/glia cell interactions

Research project synopsis

In a fairly recent shift in understanding, we now know that CNS neurons have the potential to regenerate after injury. It appears a major reason why recovery after injury or disease is unfortunately so limited is that non-neuronal cells in the brain and spinal cord, such as astrocytes, create a non-permissive environment that inhibits new growth from injured neurons. However, this response is complex and we have discovered that as well as producing molecules which inhibit regeneration, astrocytes produce other molecules which are strongly pro-regenerative. In this project we use sophisticated co-culture models of astrocytes and neurons to understand how these cells interact and affect each other's growth following injury. We have also identified a major pro-regenerative molecule produced by astrocytes which we are developing into a family of agents with therapeutic potential for traumatic brain injury.

Determining the cellular mechanisms underlying neurodegenerative disease: Alzheimer's disease, Parkinson's disease and Motor Neurone disease

Research project synopsis

We have developed a range of cell culture models to investigate key cellular processes implicated in the pathogenesis of neurodegenerative diseases, including excitotoxicity and oxidative stress. These studies also focus on potentially neuroprotective changes in nerve cells in response to pathological stimuli. In addition to these cellular models, we have a range of transgenic animals available that are also utilised in our attempts to elucidate key disease mechanisms. We are developing cutting edge technologies that will allow us to image in real-time using two-photon laser scanning microscopy, both in vivo and in vitro, the

neuronal response to some of these insults. In addition, we are developing novel neuronal culture methods, in collaboration with the UTAS chemistry department that will allow us to dissect the role of specific neuronal compartments in these critical responses.

Strategies to promote regeneration of the diseased or injured nervous system: New therapeutic approaches

Research project synopsis

We are examining potential therapeutic agents for significant human neurodegenerative diseases, such as Alzheimer's disease and motor neuron disease. Using transgenic animal models of these disorders, we are conducting trials of several agents and examining their ability to halt disease progression and to slow neuronal loss. We are also examining the mechanism by which these agents act in cell culture models and, in the case of Alzheimer's disease, we are exploring the biochemical and cellular basis by which our agents disrupt the pathological basis of the disease.

Neuronal response to traumatic injury

Research project synopsis

A range of in vitro and in vivo models are being utilised to examine how nerve cells respond to various forms of structural injury. In particular, the NeuroRepair Group has established models that involve focal axonal damage, and we are now seeking to determine the cellular changes that characterise how nerve cells respond to injury and attempt regenerative sprouting. We have developed unique cell culture models to examine the effects of the mechanical forces on axons characteristic of traumatic brain injury. These are being used to explore the cellular basis for the cascade of pathological changes that lead to neuronal disconnection.

Discerning the link between metal-binding and protein aggregation in neurodegenerative diseases

Research project synopsis

A striking feature of many neurodegenerative diseases (such as Alzheimer's disease, Parkinson's disease and motor neuron disease) is the development of abnormal aggregations of proteins within the brain. Intriguingly, the major protein constituents of these aggregates (such as amyloid beta, alpha synuclein, superoxide dismutase) all have the ability to bind metals such as zinc, copper and iron. Furthermore, metal-binding appears to be an important factor leading to protein aggregation. Our group is interested in understanding what regulates the binding of metals to these proteins, and developing therapeutic strategies to alter and/or impair metal binding and prevent subsequent protein aggregation.

How do peripheral organs regulate how the brain responds to injury?

Research project synopsis

A major and essential response to injury to the brain is activation of immune cells. While the brain has local immunological residents, the microglia, a major component of the immune response to brain injury actually comes from outside the brain – through the activation and migration of immune cells from the periphery into the brain. We are interested in understanding how the brain tells the peripheral immune system it is injured, and how the peripheral immune system subsequently regulates the immune response and repair

mechanisms in the brain. Understanding this process of organ-to-organ communication may reveal novel ways to repair the brain following injury by targeting non-brain organs (such as the liver)!

In vivo brain imaging

Research project synopsis

Our research group has recently obtained a 2-photon/confocal imaging microscope that can be used to examine cellular alterations in living tissues. Studies are underway using organotypic brain slices with this microscope to explore how the pathology of Alzheimer's disease develops in relevant transgenic mouse models. These investigations focus on how amyloid plaques form, as well as how the nervous system is affected by these pathological structures. Also, 2-photon laser microscopy is being used to examine the evolution of nervous system pathology in transgenic mouse models relevant to Parkinson's disease, Alzheimer's disease and motor neurone disease, and to examine the dynamic changes in the brain following focal injury.

Location: Menzies Research Institute Tasmania

Project Title: Various research projects in Cystic Fibrosis, lung infections and immunology

Supervisor contact information: Dr Louise Roddam (louise.roddam@utas.edu.au), Dr Margaret Cooley (margaret.cooley@utas.edu.au), Dr Phoebe Griffin (Phoebe.Griffin@utas.edu.au).

Research Overview: 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.

Students working on the projects outlined below will learn a range of molecular techniques (such as host and bacterial gene expression using real-time qPCR, ELISA assays, fluorescent-activated cell sorting etc). They will also have the opportunity to liaise with clinicians involved in patient care.

At present our group are conducting major projects in the following areas:

Infection with *Pseudomonas aeruginosa* and related bacteria is an indirect cause of the development of CF Related Diabetes (CFRD)

Research project synopsis

People with cystic fibrosis are not only susceptible to lung infections, particularly with *Pseudomonas* bacteria, but also have a tendency to develop a type of diabetes that may require insulin injections. We suspect infection with *Pseudomonas* increases the likelihood a CF patient will develop diabetes, because we have shown that *Pseudomonas* has an effect on a mammalian metabolic pathway involved with insulin use. One key component of this

pathway is a transcription factor called PPAR. To test this idea, we will measure the effect of *Pseudomonas* infection on the activity of PPAR and associated genes in the white blood cells present in sputum: if we are correct, then this activity should be reduced. To check that it is specifically *Pseudomonas* that causes this effect, we will also look at sputum from people with other types of lung infection. If our idea is correct, then this will lead to the possibility of using a drug called rosiglitazone, currently used to treat diabetes, to treat CF patients in a way that could reduce the likelihood of diabetes developing, and might also reduce the severity of *Pseudomonas* infections.

Can pharmacological agents correct the decreased levels of PON2 enzyme present in CF cells?

Research project synopsis

Cystic fibrosis (CF) is the most common life-limiting, autosomal recessively inherited disease in Caucasian populations. It has a burden of disease (disability-adjusted life years) in people under the age of 35 that is comparable to leukaemia or rheumatoid arthritis. Chronic respiratory tract infection, particularly with *Pseudomonas aeruginosa* is a major cause of morbidity and mortality in CF, and most CF patients take daily antibiotics that partly control but never clear the infection. An important contributor to the virulence and antibiotic resistance of *P. aeruginosa* is the process of bacterial quorum sensing (QS), or population-wide coordination of gene expression. The major bacterial QS molecule can also affect function of human cells by inhibiting the PPAR γ transcription factor, an important regulator of inflammation that is already expressed at lower than normal levels in CFTR $^-$ cells, probably as a consequence of the defect in CFTR. Humans and mice can inactivate 3OC₁₂HSL and related QS signals by means of paraoxonases (PONs), a family of lactonase enzymes of which one, PON2, is expressed in lung epithelium. We have discovered that PON2 is also expressed at lower than normal levels in the CFTR $^-$ human bronchial epithelial cell line and that 3OC₁₂HSL can inhibit induction of PON2 expression in these cells, while upregulating its expression in CFTR $^+$ cells. We have also identified a putative PPAR response element (PPRE) in the promoter of PON2, suggesting a causal link between reduced expression of PPAR γ and PON2 in CF. Projects are available to explore this increased susceptibility to infection in CF patients in relation to PON2 gene expression and to determine the effect of pharmacological agents that may promote PON2 activity in patients.

Does the ability of the quorum sensing (QS) molecule to bind to PPARs correlate with its immunomodulatory capacity

Research project synopsis

We have demonstrated that the bacterial QS signal molecule we work with can bind to PPAR gamma (a mammalian transcription factor), which as suggested in the outline for Project 2, could have implications for the development of diabetes in people infected with *P. aeruginosa*. We also know that the molecule is immunomodulatory, and can modify the immune response in humans and mice in a way that tends to prolong the infection. We wish to determine whether the ability of the QS molecule to bind to PPARs correlates with its immunomodulatory capacity, and if not, what other targets it might interact with. We already know, for example, that PPAR can modulate inflammatory signaling by bacterial LPS. To pursue this project, we will use a fluorescent reporter system to detect binding of QS molecules to PPARs, and will test a range of structural analogues of the QS molecules that have been provided by our collaborator, Professor Paul Williams, in Nottingham, UK. This

project will involve transfection and treatment of a range of cell lines, both “normal” and cystic fibrosis cell lines, and evaluation of PPAR-mediated gene expression by real-time PCR.

Location: Menzies Research Institute Tasmania

Project Title: Protozoa as Eukaryotic Virulence Models

Supervisor(s) contact details: Richard Bradbury (Richard.Bradbury@utas.edu.au)

Research project synopsis

Pseudomonas aeruginosa is a common cause of infections in patients with burns, cancer, cystic fibrosis and those in intensive care units. The organism is thought to interact with the cells of amoebae in a very similar way to that in which it interacts with mammal cells. The mechanism by which *P. aeruginosa* infects amoebae is not completely understood. Without knowing what virulence mechanisms are used by *P. aeruginosa* to infect amoebae, it is difficult to determine what results mean when they test bacteria from human infections for virulence.

This project will involve testing axenic broth cultures of *Acanthamoeba* species and *Dictyostelium discoideum* in a 24 well plate assay in co-culture with multiple laboratory, clinical, nosocomial and environmental isolates of *P. aeruginosa*. Analysis will be performed by direct microscopy of co-culture solutions over time, flow cytometry to determine changes in numbers of amoebae present, bacterial culture for bacterial colony counts over time and spectrophotometry to determine changes in absorbance at differing wavelengths relevant to bacteria/amoebae growth, development and death. These experiments will be used to develop an optimal “gold standard” axenic broth co-culture virulence assay.

The newly developed gold standard method will then be employed in further co-culture experiments using *P. aeruginosa* virulence knock-out mutants from established bacterial strain libraries. The results of this second group of experiments will be used to confirm determine the mechanisms by which *P. aeruginosa* kills *D. discoideum* and confirm existing knowledge about *P. aeruginosa* virulence interactions with *Acanthamoeba* species.

Location: School of Medicine, Hobart

Project Title: Genetic determinants of Giant Cell Arteritis

Supervisor(s) contact details: Dr Barry Edwards (info@craigow.com.au) / Prof David Mackie (Perth)

Research project synopsis

Giant cell or temporal arteritis (GCA) is one of the few true ophthalmic emergencies. It is fairly common in elderly people and is characterised by inflammation of the medium and large arteries of the head and neck. The onset of GCA is usually insidious, however if untreated irreversible complete visual loss occurs. A definitive diagnosis of GCA is made by temporal artery biopsy and histological examination. Despite much work, the underlying pathogenesis of GCA is poorly understood. This project will use archived diagnostic tissue to investigate the molecular aetiology of GCA. We will use the power of high-resolution genetic mapping and expression profiles to identify molecular associations with this important disease. Specifically, this study will investigate the association of specific DNA variants and cellular RNA expression. More specifically it aims to show that constitutional genetic risk

factors exist and are important in the development of GCA, and to identify molecular risk factors by the recruitment and analysis of cases which have histologically confirmed GCA.

Location: School of Medicine, Hobart

Project Title: Epigenetic regulation of gene expression in the immune system

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

Research project synopsis

Orchestration of an immune response is dependent on the rapid expression of a range of immune genes in response to an invading pathogen. Our investigation of one of these genes, the cytokine GM-CSF, has identified a series of epigenetic tags which mark this gene in immune cells, allowing it to be switched on rapidly when required. These tags are not associated with the gene in cell types in which it is not expressed. Aberrant expression of GM-CSF is associated with many immune diseases including asthma, arthritis and also certain leukaemias, and it is likely changes to these epigenetic tags may contribute to aberrant GM-CSF expression in these diseases. Our current research is aimed at: i) identifying how these tags are established during the differentiation of haemopoietic cells; and ii) determining whether these tags also mark other cytokine genes and contribute to their regulation in the immune system.

Research projects in this area involve a range of molecular and cell biology techniques including culturing immune cell lines, isolating murine immune cells and analysing the chromatin structure and expression of immune genes using real-time PCR based assays.

Location: Menzies Research Institute Tasmania

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

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

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: i) identify those genes controlled by RUNX1; and ii) 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: Menzies Research Institute Tasmania

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

A potential prostate cancer susceptibility gene was recently identified through the Tasmanian Prostate Cancer Genetics Study at the MRI. Analysis of the genetic sequence of this gene suggests it is likely to be subject to epigenetic regulation. Our work suggests differences in the methylation of this gene correlate with its activity within prostate cancer cell lines and the tumorigenic nature of these cell lines. While progress to date on this work is currently being prepared for publication, there is considerable scope to further explore the mechanisms involved in the regulation of the ITGA2 methylation in prostate cancer cell lines. Techniques utilised in this work include cell culture, cloning, gene expression analysis and PCR based techniques to determine methylation.

Location: Menzies Research Institute Tasmania

Project Title: Inherited determinants of epigenetic alterations and their role in prostate cancer

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

Research project synopsis

It is well established that family history of disease is a strong risk factor for prostate cancer, which indicates that inherited determinants of disease risk play an important role in this cancer. Genome-wide association studies (GWAS) have identified over 40 prostate cancer susceptibility variants associated risk of developing disease. However, many of these DNA sequence variants are not associated with the coding-regions of genes, and the mechanisms of association of these sequence changes with disease are therefore unclear. It is likely that a proportion of these inherited DNA sequence changes in non-coding regions of the genome seed epigenetic changes, resulting in altered expression of associated genes and contributing to the development and progression of cancer. The overall objective of this study is to identify the DNA sequence changes in non-coding regions of the genome which contribute to prostate cancer susceptibility by initiating epigenetic changes (or epimutations) and gene silencing. We will utilise samples collected in the Tasmanian Familial Prostate Cancer Genetics Study, to identify epimutations resulting from underlying inherited genetic alterations that predispose individual to the development of prostate cancer.

Location: 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: Menzies Research Institute Tasmania

Project Title: Efficacy of various embalming fluids on the long term preservation of human cadavers

Supervisor(s) contact details: Dr Anne-Marie Williams (AnneMarie.Williams@utas.edu.au), Dr Jamie Chapman (Jamie.Chapman@utas.edu.au), School of Medicine, UTAS, Ph (03) 6226 2916.

Research project synopsis

Dissection of human cadavers remains a valuable tool in the anatomical education of medical and medical research students. A student's ability to learn through dissection is often influenced by their experience within the dissection lab; not only through the interaction with peers, but through the interaction, however positive or negative, with the cadaver itself.

This project attempts to determine the effectiveness of the current embalming methods in the School of Medicine in the adequate preservation of human cadavers for teaching purposes. Specifically, the project will look at the histological and gross anatomical structure of the cadavers over time and determine the quality and safety of the specimens that eventually are used by medical and medical research students for dissection.

Additionally, alternative methods for body preservation may be investigated to determine their efficacy in comparison to the current methods used in the School.

Location: School of Medicine, Hobart

Project Title: Inspired oxygen control in preterm infants on nasal continuous positive airway pressure.

Supervisor contact details: Associate Professor Peter Dargaville
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The automated and feedback-controlled regulation of fraction of inspired oxygen (FiO₂) is a goal of respiratory intensive care at any age, but in particular within the realm of the newborn intensive care unit (NICU). 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 patient 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 FiO₂ are under the control of the bedside staff, who make adjustments based on the partial pressure of oxygen in arterial blood (PaO₂), or, more usually, the transcutaneous oxygen saturation level (SpO₂). Despite the best efforts of staff at the bedside, neonates on respiratory support spend considerable amounts of time with SpO₂ readings (and therefore PaO₂ levels) outside the desired or target range. In addition, particularly in NICUs where nursing staff time is divided between a number of patients, very significant changes in SpO₂ may go unnoticed and uncorrected for some time, leading to risk of hypoxia or hyperoxia. We have developed an **inspired oxygen controller** that receives transcutaneous oxygen saturation (SpO₂) readings from a bedside oximeter, verifies and processes the oximetry data, compares the SpO₂ readings with predetermined targets in a control algorithm, and sends signal pulses to a servomotor to automatically turn the FiO₂ dial of a gas blender. At the heart of our control device is the software program which directs adjustment of FiO₂ according to SpO₂ values. Within it is a core algorithm performs a “state” and “trend” analysis of second by second SpO₂ readings, and makes FiO₂ adjustments accordingly, in a very similar manner to a previously validated and tested algorithm.

Our control software has, in addition, several unique features which to our knowledge have never previously been incorporated in FiO₂ feedback control systems: The capacity to **“learn” the response of an individual patient** to FiO₂ adjustments, and thus fine tune the response made to a change in SpO₂. This key feature is known as adaptive logic. This software design element gives our system the potential to overcome a key deficiency of any basic FiO₂ control algorithm, and that is the variable response of individual infants to FiO₂ adjustments, and the changing response of an individual over time, in particular as lung disease evolves or resolves. These idiosyncrasies are well known to trained NICU nursing staff, who use their own form of “adaptive logic” to control FiO₂ as best they can in each patient. The capacity to **predict SpO₂ changes** with apnoea (detected via the input of a

signal from a Draeger monitor or Graseby capsule), and with bradycardia (detected from the oximeter output or Draeger monitor). If either (or both) of these physiological disturbances are detected, the sensitivity of the core algorithm to SpO₂ changes is heightened and the response time shortened.

We believe these additional features will allow more precise targeting of SpO₂ in preterm infants receiving oxygen than ever before possible with an automated FiO₂ control system. The next phase for development of the FiO₂ controller is preliminary testing in the NPICU at RHH. A proposal for this work has been developed, and a submission to the Human Ethics Committee will be made in the next month. The project will be ready to begin in late 2010. The preliminary studies will be as follows:

Non-randomised purposive sample (n=20) of preterm infants on nasal continuous positive airway pressure. Time periods of 4 hours (phase I) or 24 hours (phase II) of FiO₂ control, flanked by time periods of standard manual control. During phase I, an investigator (Honours student) present at the bedside at all times, with the intention of monitoring the FiO₂ adjustments made by the control device, and over-riding the set FiO₂ value if the infant's condition dictates.

The following statistical comparisons will be made (phases I and II): i) time spent in normoxic, hyperoxic and hypoxic ranges of SpO₂, and number of lengthy episodes of hyperoxia and hypoxia, ii) number of automated FiO₂ adjustments made during the automatic FiO₂ control period, and iii) number of manual FiO₂ adjustments made during the manual control period.

The results of this study will be publishable in a reputable medical journal, and will also serve as preliminary data for larger scale trials of the device.

Location: Menzies Research Institute & Royal Hobart Hospital

Project Title: Biomarkers to identify intensive care patients who are at risk of neuropsychological damage

Supervisor(s) contact details: Dr Lindsay Edwards; l.m.edwards@utas.edu.au. x2677

Research project synopsis

A substantial fraction of Tasmanians who have spent more than two days in intensive care at the RHH have later developed neuropsychological problems. These problems have a substantial impact on these former patients' quality of life. There is currently no way of identifying these patients early, before neurological damage has occurred. This recently-funded project will use metabolic profiling (metabolomics) to develop a new clinical tool for identifying patients who are at risk during their stay in ICU.

The primary outcome of this project will be a set of biomarkers (small molecules in urine, serum or CSF) that can distinguish those patients who will suffer adverse neuropsychological effects, with an additional analysis to determine biomarkers associated with increased mortality. These candidate biomarkers can either be employed immediately in ICU, or be carried forward into a larger clinical trial to confirm their efficacy. Furthermore, identification of biomarkers is a critical step in understanding the mechanism of damage and thus guiding treatment.

The student that participates in this project will learn a range of useful and transferrable techniques, will be responsible for gathering and analyzing plasma from ICU patients, and will play a pivotal role in the project.

Location: Menzies Research Institute

Project Title: Systems Biology of Alpha-Synuclein

Supervisor(s) contact details: Dr Lindsay Edwards; l.m.edwards@utas.edu.au /x2677

Research project synopsis

Alpha-synuclein is a molecular chaperone that is believed to play a pivotal role in the pathogenesis of Parkinson's Disease and Dementia. In collaboration with Dr Tracey Dickson, we recently showed (using a newly-developed metabolomics platform) that alpha-synuclein plays an important role in maintaining healthy mitochondrial function in cortical neurons.

We are now extending this project to study the role of alpha-synuclein in the brains of living mice, using an integrated systems biology approach. We are using metabolomics, proteomics and computational simulations (in collaboration with colleagues at the University of Iceland Centre for Systems Biology) to study the brains of transgenic mice either lacking alpha-synuclein or whose gene for alpha-synuclein has been replaced with a mutated version that is known to predispose humans to Parkinson's Disease. This study truly embraces a systems approach to the study of neurobiology, by combining genetics, proteomics and metabolomics with computation and simulation.

The student that participates in this project will learn a broad range of techniques, from animal handling to systems biology. Some familiarity with basic programming and decent mathematics will be an advantage.

Location: Menzies Research Institute