Basil Hetzel Institute
for Translational Health Research

The Queen Elizabeth Hospital

2017

Honours & Postgraduate Student Research Project Booklet

The Institute

basil hetzel institute for translational health research

TQEH Research Day Award Winners, October 2015

Table of Contents

The Institute

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The Basil Hetzel Institute (BHI) is the productive research arm of The Queen Elizabeth Hospital (TQEH, Central Adelaide Local Health Network) and is located at Woodville South, South Australia. It is headed by Professor Guy Maddern and hosts 19 research groups from the Universities of Adelaide and South Australia as well as the hospital. These groups undertake laboratory, clinical and population studies focusing on the most prevalent diseases/health issues in the regional community. Close links with TQEH clinical departments and shared resources with the universities, along with a $19m purpose-built research facility provides researchers, clinical academics and students with the most modern health and medical research facilities co-located with a hospital currently available in South Australia. Current research areas include cancer, cardiovascular diseases, drug and vaccine development, inflammatory diseases and a range of health services research such as aged care, respiratory medicine, psychiatry and epidemiological studies.

Professor Guy Maddern

http://www.basilhetzelinstitute.com.au/about/research-reports/

Students interested in pursuing Honours, Masters or PhD studies at the BHI are encouraged to contact lead researchers or delegated contacts named within the relevant research groups outlined in this booklet.
http://www.basilhetzelinstitute.com.au/

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Government of South Australia

SA Health

the hospital research foundation
finding cures improving care

The Hospital Research Foundation & TQEH Department Scholarships

POSTGRADUATE DEGREES – MASTERS and PhDs

The Basil Hetzel Institute for Translational Health Research (BHI) is committed to expanding the pool of research scholars at The Queen Elizabeth Hospital. Potential scholars should explore all scholarship opportunities offered by Universities and other sponsors. A number of 12 month Postgraduate Scholarships, funded through The Hospital Research Foundation (THRF) will be available.

Stipend: Equivalent to Australian Postgraduate Award (APA) rate ($26, 288 in 2016; full time candidates are tax free).

Duration: 12 months only (conditions apply). Successful candidates are expected to apply and be awarded other scholarships for the subsequent years of their higher degree.

Number available: Potential exists to award three scholarships.

For more information, including advice to applicants and application forms please go to:
http://www.basilhetzelinstitute.com.au/students/scholarships/postgraduate-scholarships-info2/

HONOURS DEGREES

The BHI offers a number of Honours Scholarships, funded either through The Hospital Research Foundation (THRF) or by individual departments, as outlined below:

Stipend: around $4,000 - $8,000 per annum

Duration: 12 months

Number available: This is dependent on the funding available through The Hospital Research Foundation or through individual departments.

Mid-year commencements, negotiated with a potential supervisor, are permitted.

For more information, including advice to applicants and application forms please go to:
http://www.basilhetzelinstitute.com.au/students/scholarships/honours-scholarship-info2/

Advice for Potential University of Adelaide HDR Candidates

All candidates undertaking a research program at the University of Adelaide are required to participate in the Structured Program. *http://www.adelaide.edu.au/graduatecentre/*

The Structured Program consists of two components:

- **The Core Component** (to be completed within six months of full-time candidature or half-time equivalent); and
- **The Development Component** (extends for the duration of candidature)
  The Development Component focusses on Careers and Research Skills Training (CaRST) and is devised in consultation with the supervisor and tailored to the needs of the individual student. Participation in the CaRST program is compulsory for all new PhD and Master of Philosophy students at the University of Adelaide from 2017. Further information is available at: *http://www.adelaide.edu.au/carst/*

Required Core Component Activities

1. the Graduate Centre's online induction program.
2. the local School/Discipline induction program, including Health, Safety and Welfare training as required
3. the Integrated Bridging Program-Research (international Doctoral students only)
4. introductory training on the Australian Code for the Responsible Conduct of Research
5. introductory training on animal and/or human ethics where applicable
6. reading the University's Research Data and Primary Materials Policy and Guide to Research Data Management and preparing a data-management plan
7. obtaining an Open Research and Contributor ID (ORCID) and registering it with the University
8. undertaking a literature review
9. formulating a research proposal which explicitly considers the ethical, intellectual property, and resource implications of the proposed research (Faculty specific templates are available on the Graduate Centre's web site)
10. presentation of the research proposal at a School seminar program; and
11. Submission of the completed Core Component of the Structured Program form to the Graduate Centre

In addition to completing the required activities detailed above, candidates are expected to become familiar with the Research Student Handbook (produced by the Adelaide Graduate Centre), the Academic Program Rules for their degree, the 'Specifications for Thesis', and the required progress reviews relevant to their candidature: *http://www.adelaide.edu.au/graduatecentre/handbook/05-candidature/06-monitoring-academic-progress/02-milestones/*

Students should consult with the relevant Postgraduate Coordinator regarding regulations governing the use of all departmental resources (e.g. photocopying, placing orders and electronic communications), the role of the postgraduate coordinator and Occupational Health and Safety regulations, policies and procedures.
The current list of Postgraduate Coordinators is available on the Graduate Centre's web site at:
http://www.adelaide.edu.au/graduatecentre/staff/postgraduate-coordinators/pgc-list/#health

Ongoing Commitments for all Postgraduate Students based at the BHI, TQEH

- Attendance at departmental special seminars and BHI Postgraduate Seminars.
- Annual seminar on progress to be given prior to submission of Annual Review of Progress report, and a final seminar to be presented no less than two months prior to the estimated date of submission.
- Any change in status (e.g. full time to part-time or vice versa; leave of absence) to be discussed with the supervisor and Postgraduate Coordinator.

University of Adelaide Postgraduate Coordinators, The Queen Elizabeth Hospital
Discipline of Medicine: Dr Peter Zalewski; ph +61 8 8222 7344; peter.zalewski@adelaide.edu.au
Discipline of Surgery: Dr Prue Cowled; ph +61 8 8222 7541; prue.cowled@adelaide.edu.au

University of Adelaide Honours Coordinators, The Queen Elizabeth Hospital
School of Medicine: Professor Chris Rayner; ph +61 8 8222 5501; chris.rayner@adelaide.edu.au

Advice for Potential University of South Australia HDR Candidates

Further information about all higher degrees:
http://www.unisa.edu.au/Research-BT/
http://www.unisa.edu.au/Research/Research-degrees/
http://www.unisa.edu.au/Research/Research-degrees/Enquire-about-a-research-degree/

HONOURS
Further information: *http://www.unisa.edu.au/Health-Sciences/Programs-and-Courses/Honours/*

Advice for Potential Flinders University HDR Candidates

MASTERS and PHDs
Further information: *http://www.flinders.edu.au/research-degrees/*

HONOURS
Further information: *http://study.flinders.edu.au/apply/honours/*

THEME: CANCER

Colorectal Cancer Research Group

Lead Researcher:
Professor Tim Price
timothy.price@sa.gov.au

The Colorectal Cancer Research Group moved to new laboratories in the Basil Hetzel Institute in 2009. In 2014, the group incorporated the newly established SAHMRI Colorectal Node, and now works on a comprehensive program in colorectal cancer spanning prevention, biology and treatment. Themes include identification, development and clinical trial of new therapeutic agents for the treatment of colorectal cancer, development of new biomarkers of drug resistance and therapeutic targets, investigating the molecular mechanisms underlying colorectal cancer, and identification of risk factors.

Molecular Oncology Colorectal Cancer

Lead Researcher:
Dr Jennifer Hardingham
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A major focus of our group is the collaborative investigation of novel synthetic inhibitors of aquaporin water channels in preventing tumour angiogenesis and progression in mouse models of colorectal cancer. Another focus is the determination of predictive biomarkers of response to therapeutic agents in metastatic colorectal cancer and the detection of circulating tumour cells (CTC) and circulating DNA mutations as prognostic markers in colorectal cancer.

Front row L-R: Jenny Hardingham PhD, Amanda Townsend MBBS FRACP, Back row: Hilary Dorward BSc (Hons), Tim Price MBBS FRACP DHlthSc, Yoko Tomita MBBS FRACP MSc, inset Eric Smith PhD

Research Projects

Role of aquaporins 1 and 5 in colon cancer growth, angiogenesis and metastasis (Honours or PhD)
Aquaporins (AQPs) are water channel proteins involved in cellular water flux, and implicated in migration, angiogenesis and metastasis in cancer. The drug discovery program in Professor Yool's lab has identified drugs that modulate aquaporin channel activity. We have found that several of these drugs are effective in vitro at reducing migration and invasion of colon cancer cells and preventing angiogenesis (tumour blood vessel formation). We are investigating the efficacy of these drugs in stopping tumour growth and metastasis in a mouse model of human colon cancer. Our hypothesis is that tumour cells that lack AQP1 activity are unable to respond to hypoxia which drives angiogenesis. Techniques include cell culture, CRISPR gene knockout, RT-PCR, western blotting, functional assays of cell proliferation, invasion, migration, and angiogenesis and mouse models of human colon cancer.

Colorectal Cancer Research Group *(continued)*

Molecular Oncology Colorectal Cancer *(continued)*

Genome-wide association studies (Honours or PhD)
We have access to tissue from several large cohorts of colorectal cancer patients from oncology clinical trials. Next generation sequencing platforms will be used in correlative studies to identify biomarkers of resistance to therapeutic agents. Techniques will include DNA and RNA/microRNA isolation from tissue blocks, library preparation, bioinformatics, and statistical analysis.

Investigation of circulating DNA mutations in colorectal cancer (CRC) (Honours or PhD)
Circulating tumour-derived DNA (ctDNA) may be present in plasma samples from patients with CRC, and the concentration level has been inversely correlated with survival outcome. It's thought the ctDNA is derived from circulating tumour cells (CTC) yet there are reports of cases in which ctDNA was detected but no CTC were detectable (Bettegowda et al., 2014), suggesting that tumour DNA could be released from tumour exosomes in the circulation. ctDNA from plasma (liquid biopsy) provides a means to analyse tumour mutations to enable more sensitive disease monitoring. This means that disease recurrence or progression would be detected at an earlier time-point than would be possible with CT/PET imaging. Techniques include DNA isolation from plasma, digital droplet PCR, mutation analysis, statistical survival and correlative analyses.

Western blot analysis (Hilary Dorward)

Colorectal Cancer Research Group *(continued)*

SAHMRI Colorectal Node

Based at the Basil Hetzel Institute, TQEH

Lead Researcher:
Associate Professor Joanne Young
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L-R: Ms Wendy Uylaki and A/Prof Joanne Young

Within the SAHMRI Colorectal Node, the South Australian Young Onset Colorectal Cancer Study (SAYO) is a hospital-based research program for identifying the causes and consequences of colorectal (bowel) cancer in young adults. The program has an ongoing registry for research participants and an associated database, with topics spanning genetics, pathology, and psychosocial aspects of this condition. The group consists of a research fellow, medical oncologist and hospital scientist. In addition, a network of collaborators contribute to research directions, analysis and outcomes of the project.

Research Projects

Early Onset Colorectal Cancer and Metabolic Syndrome

Our preliminary evidence suggests that the increase in incidence of colorectal (bowel) cancer in young adults may be related to the rising rate of metabolic syndrome components in the young adult population. In this study we will explore the overlap of genetic predispositions to both CRC and diabetes in young adults with pre-malignant polyps, or cancer. We will use pedigree analysis, next generation sequencing of the germline, and detailed epigenetic assays of colorectal tissue to identify markers of risk for CRC in the young adult population. It is our long-term objective to help identify at-risk young individuals in primary healthcare settings.

Medical and Psychosocial Aspects of Colorectal Cancer in Young Adults

Colorectal cancer (CRC or bowel cancer) is a common malignancy of older adults. However, over 1100 Australians under the age of 50 develop CRC each year, and the incidence of young onset disease has been rising in Australia and other Western countries during recent decades. Young adults with CRC suffer significant mortality and morbidity in the most productive time of their life. In this project which would suit a psychology or nursing student, we will undertake a comprehensive study of the medical and psychosocial aspects of having CRC as a young adult. This will include the risk factors such as personal or family history of diabetes, family history of CRC, the diagnostic journey of the patient (since the majority of young patients present late in the course of their disease), and the life impacts post diagnosis on family and relationships, career and education, and physical and mental health.

Liver Metastasis Research Group

Lead Researcher:
Dr Ehud Hauben
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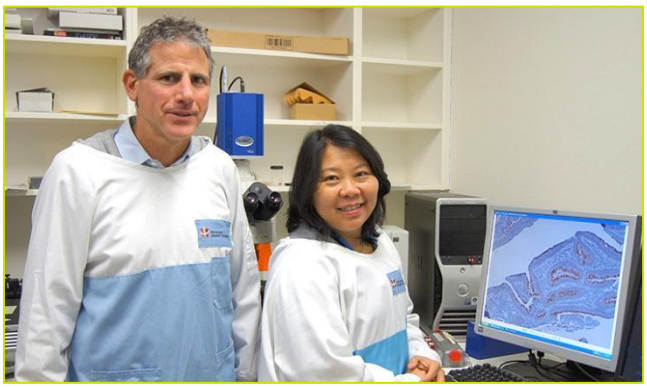

L-R: Dr Ehud Hauben and Dr Chandra Kirana

Liver Metastasis Research Group takes advantage of expertise in cancer research, immunology and cell biology to address the urgent clinical need of early detection, risk prediction and treatment of liver metastases in patients with colorectal cancer. Being a small group with clear translational research focus on development of predictive and therapeutic biomarkers, we apply a straightforward bed-to-bench-and-back approach utilising high-throughput methods for target discovery in cancer patients' blood and tissue samples. Our technology platform includes state of the art proteomic techniques.

Research Projects

- Development of predictive biomarkers of metastatic colorectal cancer
- HLA-G expression in CRC cell lines and clinical samples
- The role of the chemokine receptor system in CRC liver metastasis
- Midkine as candidate biomarker of hepatic metastatic progression

Northern Network Colorectal Surgical Science

Lead Researcher:
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The Northern Network Colorectal Surgical Service (NNCSS) incorporates the colorectal units at the Royal Adelaide, The Queen Elizabeth and Lyell McEwin Hospitals. The NNCSS conducts research assessing the efficacy of new and/or emerging surgical and oncological interventions, novel treatment options, post- operative care, and quality of life improvements for patients with colorectal diseases, such as cancer, haemorrhoidal disease, anal fissure, and pelvic floor disorders.

Students who are interested in pursuing a career in surgical and clinical research are encouraged to contact our team to discuss research opportunities.

Research Projects

- A study of operative costs versus quality outcomes in diverse operative procedures
- The growth of organelles from mesothelioma and pseudomyxoma peritoneii (in conjunction with Dr Dan Worthley, University of Adelaide, based at SAHMRI)
- Psychological impact of surgical treatment of pseudomyxoma peritoneii

Solid Cancer Regulation Research Group

Lead Researcher:
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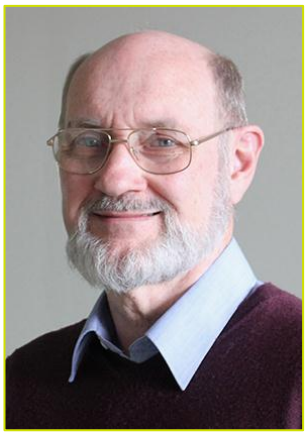

The Solid Cancer Regulation Research Group has a focus on the molecular biology of prostate and oesophageal cancers. The projects offered will use mass spectrometry imaging (MSI) to map molecules in tissue sections. After MSI the slide can be stained or immunostained. The spatial distribution and amount of the molecules can then be aligned with histological features. Dr Johan Gustafsson of the ARC Centre of Excellence in Convergent Bio-Nano Science & Technology (UniSA) will co-supervise these projects, which will be based at the Basil Hetzel Institute and the Future Industries Institute.

Research Projects

Mapping the expression of the androgen receptor (AR) and FKBP5 in oesophageal and prostate cancer tissues

There is a strong association between the expression of these two genes and overall survival, but the current methods for their measurement are subjective and at best semi-quantitative. Two MSI methods to map and quantitate these genes will be assessed. The first will investigate specific antibodies tagged with either photo-cleavable or metal reporters. Following incubation with a tissue section, MSI will be used to measure the reporter distribution. The second will use MSI to identify specific proteolytic peptide products of AR and FKBP5 in MSI spectra from trypsin treated tissue sections. This project may lead to the development of a clinical test to predict survival.

Prediction of response to neo-adjuvant therapy in oesophageal cancer

Radiotherapy and/or chemotherapy are frequently used in the treatment of oesophageal cancer, either before surgery or as palliation to reduce difficulties in swallowing in patients unsuitable for surgery. Over 50% of tumours are resistant to these therapies, which are unpleasant, may have serious side effects, and can result in worse outcomes in non-responders. MSI will be used to discover biomarkers which predict tumour response to radio- and/or chemo-therapy.

Surgical Science Research Group

Lead Researcher:
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The Surgical Evaluation Group has research interests in developing minimally invasive techniques capable of destroying both primary and secondary liver tumours by inserting electrodes into the tumours. A study looking at inoperable colorectal metastatic disease has commenced using this technique together with new hybrid technology. The evidence behind new surgical technologies and its implementation and introduction into the Australian healthcare system is another focus. A further research interest is in the prevention of adhesion formation after abdominal surgery.

Research Projects

- Ablative techniques in tumour treatment
- Health technology assessment in surgery
- Prevention of adhesion formation in abdominal surgery
- Surgical simulation
- Factors in surgical mortality
- Surgical coaching

THEME: CARDIOVASCULAR DISEASES

Cardiovascular Pathophysiology & Therapeutics Group

Lead Researcher:
Professor John D Horowitz
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Our interests are to delineate the pathophysiology of "new" forms of cardiac disease emerging with the ageing of the population and with the obesity epidemic of the 21st century. We wish to link this with the development of appropriate treatments, using a "bench to bedside" approach. Examples include aortic valve disease, stress cardiomyopathy, atrial fibrillation and various forms of angina pectoris.

Research Projects (Honours)

Impact of BNP on stabilization and function of the myocardium (Dr S Liu, Dr Y Chirkov, Prof J Horowitz)
We have recently shown that BNP exerts important anti-inflammatory effects, by stabilizing white blood cells. We wish to determine whether this results in limitation of inflammatory change within the heart, and how this can best be employed clinically.

The heart in stress (Tako-Tsubo) cardiomyopathy (Dr TH Nguyen, Dr A Sverdlov, Prof J Horowitz)
Tako-Tsubo cardiomyopathy (TTC) occurs mainly in ageing women as a dysfunctional, inflammatory response of the heart to adrenaline. We have partially characterised the chemical signal transduction pathway in TTC, and now seek to evaluate potential therapeutic avenues, using cell culture and intact animal models.

Variability in adenosine signalling in human platelets: therapeutic implications (Dr Y Chirkov, Prof J Horowitz)
Adenosine functions both as a coronary vasodilator and inhibitor of platelet aggregation. It partially mediates the effects of the novel anti-aggregatory agent ticagrelor. We wish to determine sources of inter-individual variability in platelet adenosine signalling in patients with ischaemic heart disease and/or diabetes, and to identify means for predicting responsiveness.

Impact of proton pump inhibitor therapy on vascular endothelial function (Dr TH Nguyen, Prof J Horowitz)
Protein pump inhibitors, although used very widely to suppress gastric acid secretion, may not be completely safe for the heart. We will test the hypothesis that these agents increase plasma levels of the nitric oxide synthase inhibitor ADMA, and therefore impair endothelial function. Experiments will include evaluation of vascular endothelial function and also determination of plasma ADMA concentrations.

Clinical Pharmacology Laboratory

Lead Researcher:
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The Clinical Pharmacology Unit at The Queen Elizabeth Hospital is affiliated with the Discipline of Pharmacology at the University of Adelaide. It provides a clinical therapeutic drug monitoring service coupled with an active research program in the areas of heart disease, kidney transplantation and cancer. Since the BHI is the research arm of TQEH, researchers can work closely with the hospital's clinical divisions. This has led to a focus on translational health research, an innovative 'bench to bedside' approach in which scientific discoveries can be quickly translated into improved patient care and treatment.

Research Projects

Metabolic Treatments for Heart Disease
Heart disease is commonly caused by narrowing of the heart's arteries, reducing the availability of oxygen and hence energy. Ischaemic heart disease is associated with angina, poor quality of life and increased risk of myocardial infarction and heart failure. As populations age, more people are diagnosed with ischaemic heart disease and heart failure, and despite current therapies, many continue to experience symptoms and have poor prognoses. Perhexiline is an old drug that is very effective in the treatment of angina, even when other therapies have failed. Recent research indicates that it may also be very effective at treating other forms of heart disease, including heart failure. It has a unique mechanism of action, directly improving energy metabolism in the heart and modulating a major intra-cellular regulatory protein TXNIP, which has been linked to both heart disease and cancer. Clinical use of perhexiline is currently limited by its potential to cause hepatic and neural toxicity. This project will investigate the biochemical mechanisms of action of perehxiline and structurally related compounds, particularly effects on energy metabolism and TXNIP expression in the heart, as a basis for developing new therapies for heart disease.

Individualising Transplantation Therapy
The success of kidney transplantation depends largely on preventing rejection of the new organ, using a combination of immunosuppressant drugs. These drugs have narrow therapeutic indices and can cause renal, gastrointestinal or haematological toxicity. Due to significant variability in their elimination from the body, doses are currently individualised by targeting therapeutic concentrations in blood. Despite this, rejection and toxicity still occur. Our research focuses on understanding immunosuppressant distribution into lymphocytes (the mediators of rejection) and renal tissue (a major site of toxicity), as a means of better predicting individual risk of rejection and damage to the transplanted organ. This project will investigate genetic variability in the pathways of immunosuppressant elimination in both kidney donors and recipients, to determine its impact on intra-renal and intra-lymphocyte exposure to immunosuppressants, and its association with rejection and long-term function of the transplanted kidney.

Translational Vascular Function Research Collaborative

Clinical Physiology of Vascular Function Research Group

Director and Contact:
Professor John Beltrame
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Staff & students from the Clinical Physiology of Vascular Function Research Group

This clinical research team utilise both invasive and/or non-invasive techniques to identify the presence of vascular dysfunction in patients with vascular symptoms including angina and intermittent claudication. These include the assessment of coronary artery spasm, coronary blood flow, cardiac magnetic resonance imaging, subcutaneous blood flow and endothelial function.

Research Projects

Vasomotor Studies of Patients with Myocardial Infarction and Non-Obstructive Coronary Arteries: Approximately 5-10% of patients who experience a myocardial infarct do not have significant coronary artery disease, prompting the clinical question of what is the underlying mechanism? This study will utilise invasive and non-invasive clinical techniques to elucidate potential mechanisms that may be responsible for the myocardial infarct.

Translational Vascular Function Research Collaborative *(continued)*

HIPER : Healthcare Innovation, Policy and Evaluation Research

Director and Contact:
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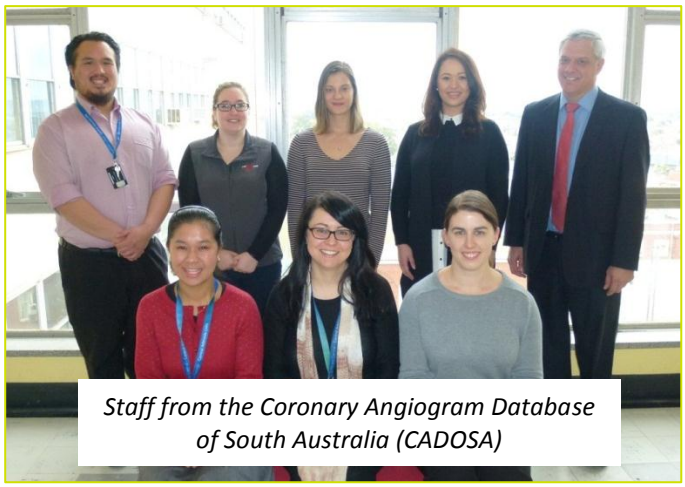

Staff from the Coronary Angiogram Database of South Australia (CADOSA)

HIPER conducts high impact research directly impacting policy and translating into practice, to achieve improved and safer health outcomes, and ultimately maximum value from health delivery systems. Consistent with the changing environment in medical research, this group adopts both a patient and systems-level approach to the advancement of cardiovascular healthcare. The research is based on clinical medicine, epidemiology and statistics, which are combined with a range of methodologies including clinical registries, implementation science, big data analytics and patient reported outcomes.

Research Projects

Coronary Angiogram Database of South Australia (CADOSA) - Improving Health Outcomes in Patients undergoing Coronary Angiography

Coronary angiography is the clinical benchmark technique in the assessment of coronary artery disease with more than 6,000 performed in South Australia each year. Despite its diagnostic benefits in identifying the presence of coronary disease, its benefit to the patient has been less rigorously studied and will be the focus of this project. CADOSA is an internationally renowned clinical registry incorporating global links with organizations including the American College of Cardiology National Cardiovascular Data Registry and the International Consortium of Health Outcomes Measurement (ICHOM).

Cardiac Device Safety and Performance

Implanted cardiac devices such as pacemakers and defibrillators are among the most common and costly procedures performed in Australian hospitals. The research aims to investigate variation in the safety and performance of these devices with a focus on reducing device-related complications and to develop machine learning methods to automate the detection and reporting of adverse events. This research provides the foundation for development in a range of methods and skills to assess and report procedural safety, quality, and patient outcomes; work with both clinical and routinely collected hospital data from multiple Australian hospitals; and the opportunity to collaborate with leading clinical and health services researchers nationally and internationally.

Quality and policy strategies to reduce hospital readmissions and emergency care encounters

One in 5 adults aged ≥18 years have an unanticipated readmission or an emergency department visit within 30-days of hospital discharge which are distressing for patients and costly to the health system. This project aims to evaluate the burden of these hospitalisations among Australian hospitals using linked hospitalisation data. It focuses on the

(1) Frequency, variation and cause of these visits
(2) The associated cost and resource utilization
(3) The evaluation of potential clinical and policy interventions to reduce these hospitalisations. The central goal is to generate research that may inform future policymaking to reduce unanticipated hospitalisations.

Northern Cardiovascular Research Group

Based at the Lyell McEwin Hospital

Lead Researcher:
Associate Professor Margaret Arstall
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The Northern Cardiovascular Research Group

The aim of our research group is to improve treatments and healthcare systems for people with cardiovascular disease in Northern Adelaide. Our research themes include management of coronary heart disease, heart disorders during pregnancy, and heart disease in women. We are a passionate team of clinicians and scientists who have a strong focus on collaborative clinical research in a hospital setting. The diversity of our research interests and methods means that there are many opportunities for students to explore and develop their own research strengths.

Research Projects (Honours)

Validation of a novel method to assess endothelial function

Endothelial function is an important factor to consider when evaluating overall cardiovascular health. Our research group has identified an easy and non-invasive method for assessing endothelial function. This project will involve validating our method in a range of populations and clinical settings.

Pregnancy and heart disease

Traditional risk factors for heart disease include hypertension, diabetes, smoking and obesity. There is clear evidence that pregnancy complications should be counted as equally important risk factors, but they are not routinely considered by clinicians. This project seeks to explore the importance of pregnancy complications in women who present to the Lyell McEwin Hospital with heart disease.

Vascular Surgery Research Group

Lead Researcher:
Professor Robert Fitridge
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The Vascular Surgery Research Group is studying outcomes of major vascular procedures such as endovascular AAA repair. We are studying the role of frailty on outcomes of interventions. Diabetic foot ulceration is responsible for over 4,000 major amputations in Australia each year. We are keen to examine which factors are critical in determining who which patients with diabetic foot ulcers will need major amputation, and which factors are associated with wound healing. Our group is collaborating with Profs A Cowin (wound healing, UniSA), M Miller (Nutrition, Flinders University) and P Grimshaw.

Research Projects

We will be studying patients with diabetic foot ulceration at our Multi-Disciplinary Diabetic Foot Clinics and also inpatients to the Vascular Unit at RAH. Features of the wounds, patient co-morbidities and patient fitness/ sarcopenia and nutritional status will be analysed. We will also study molecular aspects of wound healing in collaboration with Prof Allison Cowin from UniSA. In addition, we plan to analyse gait in patients with diabetic neuropathy and the effectiveness of off-loading (A/Prof Paul Grimshaw, Engineering, University of Adelaide).

THEME: CHRONIC DISEASE

Stroke Research Programme

Located at the Basil Hetzel Institute, TQEH and SAHMRI

Lead Researchers:

Prof Simon Koblar
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A/Prof Anne Hamilton-Bruce
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The Stroke Research Programme (SRP) is a collaborative between the Central Adelaide Local Health Network (CALHN), Royal Adelaide Hospital and The Queen Elizabeth Hospital (TQEH) and the University of Adelaide via the Schools of Medicine, Medical Science and Molecular and Biomedical Science. The SRP is located at the South Australian Health and Medical Research Institute (SAHMRI) and The Basil Hetzel Institute (BHI) at TQEH. We are also part of the Australian Stroke Genetics Collaboration, a multi-centre study into genetic causes of stroke. The SRP has trained 26 PhD, 3 Masters and 29 Honours students (25 were H1).

Students & staff from the Stroke Research Programme

Research Projects

Dental Pulp Stem Cell (DPSC) Therapy for Stroke (S Koblar)
Our research investigates brain repair following ischaemic stroke using adult human stem cells from teeth (DPSC). We have published that DPSC have therapeutic potential, however, it remains unknown how these stem cells mediate improvement following stroke, and the best treatment paradigm for DPSC administration. We are also investigating how we make these stem cells available at a human-grade for a clinical trial and if there are differences between young and older DPSC for autologous transplantation in humans.

Npas4 and Stroke (contact Dr Fong Chan Choy: fongchan.choy@adelaide.edu.au)
In 2004, we discovered a new brain specific gene encoding a transcription factor (Npas4) that is expressed specifically in the brain and following injury such as stroke. Exciting findings from our recent research demonstrated that Npas4 has a neuroprotective role in ischaemic stroke and, for the first time, that Npas4 is involved in modulating inflammation, an important contributor to the pathogenesis of stroke. In addition, we have shown that Npas4 also has an important role in neurogenesis (generation of new nerves), which is induced by stroke as a compensatory response to repair brain damage. Our laboratory aims to clarify how Npas4 expression modifies the brain's response to stroke and improves neurological outcomes following stroke.

Stroke Research Programme *(continued)*

Proteomics of Stroke and Transient Ischaemic Attack (TIA) (S Koblar)
TIA is a common precursor and warning sign for an imminent ischaemic stroke. Correctly distinguishing TIA from benign mimic conditions such as complicated migraine or focal seizures is clinically problematic. There are currently no biochemical markers for TIA or stroke, making diagnosis of these conditions dependent on expensive and time-consuming imaging. This study explores the human plasma proteome for differentially expressed TIA- or stroke-sensitive plasma proteins that could be used as diagnostic biomarkers.

Animal Assisted Therapy (AAT) for Stroke Victims (A Hamilton-Bruce)
We will examine saliva of both patients and animals for soluble markers for objective assessment of therapy with pets. We link in this collaboration with Dr Susan Hazel, Lecturer in Animal Science, Roseworthy Campus, University of Adelaide.

Clinical Translation of Stroke Treatment (S Koblar)
We partner with the South Australian Academic Health Science and Translational Centre (AHSTC) to continuously enhance translation of research into healthcare. Stroke is an AHSTC priority and we participate in research to improve stroke unit services and expect the opportunity afforded by the opening of the new RAH will assist us to implement clinical translation of stroke research.

http://www.adelaide.edu.au/srp/

The Health Observatory

Located at the Basil Hetzel Institute, TQEH and SAHMRI

Lead Researcher:
Professor Robert Adams
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We conduct population and clinical research studies and examine health services to identify opportunities that lead to more effective health care and management. The aim of this research is to maximise health outcomes.

Research Projects

Sleep medicine
Examines health outcomes, links to other diseases and ways to improve service delivery

Simulation modelling and systems design
Used to predict the implications of making significant changes to the existing healthcare system, such as with Transforming Health. A simple example created by one of our partners can be seen at: *http://youtu.be/P45WgRlc2sI*

Musculo-skeletal medicine
A wide range of observational and clinical intervention studies in gout, giant cell arteritis and osteoarthritis.
http://www.basilhetzelinstitute.com.au/research/research-theme/chronic-disease/the-health-observatory/

THEME: CLINICAL SCIENCES, HEALTH SERVICES & POPULATION HEALTH

Intensive Care Medicine

Lead Researcher:
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Research in the Department of Intensive Care Medicine at The Queen Elizabeth Hospital focuses on:

- Improving patient safety and outcomes
- Answering pragmatic, relevant clinical questions that are of importance to the clinicians who provide patient care
- Advancements in the delivery of more efficient and effective treatments in the ICU that will not only benefit patients but also decrease costs, preserve resources and increase access to scarce critical care beds
- Statistical analysis of short and long-term outcomes relating to Intensive Care

Research activities conducted within the department are a combination of:

- Investigator-initiated studies, including those by advanced trainees as part of the course requirements of the College of Intensive Care Medicine, and intensive care nurses
- Investigator-initiated studies conducted under the auspices of the Australian and New Zealand Intensive Care Society Clinical Trials Group
- Industry-sponsored clinical trials

Research Projects

The areas of research available for student projects include:

- Sepsis studies
- Observational surveys
- Patient safety
- Nutrition studies
- Outcome studies
- Statistical method reviews
- Pharmacokinetic studies

Psychiatry: Translational Mind and Brain Centre

Director and Contact (based at University of Adelaide / RAH Frome road)**:**
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The Translational Mind and Brain Centre in the Discipline of Psychiatry aims to fill the gap existing between clinical practice and advancement of Neuroscience research in Psychiatry. Our concept builds on an integrated model between basic science, improved diagnostics and novel treatments of Psychiatric Disorders. Research in this centre identifies clinical problems that are taken to the bench-site in a circular process feeding back into clinical practice. We also focus on basic Neuroscience projects that have a clear translational application in clinical practice and on basic science research.
For further details see: *http://health.adelaide.edu.au/psychiatry/research_centres/translational/*

Biomarkers and Pharmacogenetics Research Group

Lead Researcher (TQEH and RAH):
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The Biomarker and Pharmacogenetic Research Group has a clinical orientation towards identifying biological markers relevant to psychiatric disorders and pharmacoresponse with an emphasis on mood disorders, cognitive function, and psychosis. The specific emphasis has been developed in this research group by studying the pharmacogenetic response to antidepressants as well as to electroconvulsive therapies in treatment resistant depression, pharmacogenetics of response to lithium treatment in bipolar disorder and an extensive biomarker project in clozapine treated patients is under way.
http://health.adelaide.edu.au/psychiatry/research/biomarkers_rg/

Research Projects

- Pharmacogenetics of antidepressant treatment response in major depression
- Prediction of treatment response to neurostimulation (e.g., ECT, TMS)
- Pharmacogenetics of Clozapine in Psychosis
- Biomarkers to describe cognitive and emotional phenotypes of depression and psychosis

Psychiatry: Translational Mind and Brain Centre *(continued)*

Epidemiology and Health Services Research Group

Lead Researcher:
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The aim of this research group is to understand health care needs of people with mental health issues and to evaluate effectiveness and accessibility of services in addressing needs. This includes identifying predictors that can help understand successes and failures of health service interventions. The research group aims to develop evidence based service delivery approaches that can address unmet needs in a cost-effective, equitable and easily accessible manner. A focus of this group is on exploring the health service needs and evaluations for patients diagnosed with schizophrenia receiving
http://health.adelaide.edu.au/psychiatry/research/epidemiology_rg/

Research Projects

Chronic Psychosis: Morbidity, Morality and Service use in South Australia
This study uses data linkage of existing information in public clinical services to provide a detailed understanding of treatment processes and outcomes in those with chronic psychosis treated with oral clozapine in comparison to long acting injectable (depot) antipsychotics. Goals include: The identification of local predictors of outcomes in chronic psychosis to inform the early safe use of clozapine over depot medication, the identification of optimal broad physical health monitoring protocols to reduce morbidity and mortality, the development of interventions designed to optimise the management of chronic psychosis that can be directly translated and implemented in local depot and clozapine clinics.

Trajectory Modelling Research Group

Lead Researchers:
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Current diagnostic categories in mental illness are based largely on common symptomatology rather than an understanding of the underlying mechanisms of brain, cognitive and general day-to-day function. Illness and functional trajectories describe patterns of illness and impairment in individuals over time. This research group will apply probabilistic and growth mixture multivariate modelling techniques to various measures of patient history to identify and predict specific illness and functional trajectories in mood and psychotic disorders.

Research Projects

Psychosis trajectory research project
Analysis of existing clinical data of patients with first episode psychosis and their long-term clinical trajectory over time.

Mood disorder trajectory research project
Analysis of existing clinical follow-up data on the relationship between clinical treatment outcomes and long-term functioning in daily life. *http://health.adelaide.edu.au/psychiatry/research_centres/translational/*

Rheumatology Research Group

Lead Researcher:
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Research Projects

The epidemiology of Polymyalgia Rheumatica

Polymyalgia rheumatica (PMR) is an inflammatory syndrome with pain or stiffness, usually in the neck, shoulders, upper arms, and hips, but which may occur all over the body. The aim of this project is to perform a systematic review of the epidemiology of PMR and to determine the epidemiology, clinical features and management of PMR in Australia, using available Australian General Practice Data.

Healthcare utilization in patients with chronic musculoskeletal disorders

The North West Adelaide Health Study (NWAHS) is a representative biomedical population cohort study of approximately 4000 adults aged 18 years and over recruited from the northern and western regions of Adelaide. The study was designed to assess the prevalence of priority conditions and to inform policy decisions about health care provision in South Australia, and NWAHS Stage 2 data collection specifically focused on information relating to musculoskeletal conditions. The aim of this project is to determine healthcare utilization in patients with chronic musculoskeletal conditions, using NWAHS data integrated with Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) data.

Development of a glucocorticoid impact questionnaire

Glucocorticoids (GC) are a class of steroid hormones with immunosuppressive and anti-inflammatory effects. However, they are also associated with a number of side effects. While the treating clinician may focus on the most clinically serious GC related adverse effects, such as an increased risk of cardiovascular disease, diabetes and bone density loss, little is known about the patient perspective of the impact of GC treatment. The aim of this project is to develop a question to measure the impact of GC treatment from a patient perspective. These types of patient reported outcome measures (PROM) are a new era in clinical research which will enable more patient-centred treatment decisions.

THEME: DRUG & VACCINE DEVELOPMENT

Therapeutics Research Centre

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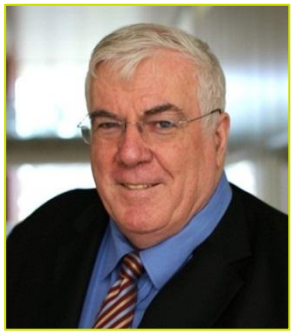

The Therapeutics Research Centre (TRC) is headed by Professor Michael Roberts, an NHMRC Senior Principal Research Fellow. Professor Roberts has a joint appointment between the University of South Australia and the University of Queensland. Staff at the TRC have active research interests covering a spectrum of therapeutics from the chemistry of drugs (including drug design and natural products), the effects drugs have on the body (pharmacology and toxicology) and the effects the body has on drugs (pharmacokinetics and drug delivery) through to how drugs can be best used to treat disease (topical drug delivery and quality use of medicines) for patients. Current special interest areas include defining drug disposition and effects by *in vitro* and *in vivo* (including patient) bioimaging using confocal and multiphoton reflectance, fluorescence and Raman spectroscopy.

Research Projects (Honours, Masters & PhD students – enrolled through School of Pharmacy at UniSA)

Specific targeting of nanosystems by cutaneous delivery (M Roberts, L MacKenzie)
The skin is a major site for the delivery of drugs, cosmetics and increasingly for vaccine, diagnostic and systemic delivery. It is a heterogeneous organ, with several delivery routes and target sites that can be targeted for desirable pharmacological and immune responses. A key challenge is to deliver sufficient quantities of these agents to achieve the desired responses. This project seeks to study the feasibility of using nanosystems to meet these needs, noting also the need to define their safety profiles. A major component of this work is also concerned with the evaluation of nanotechnology products applied to the skin.

Targeted drug delivery by topical application (M Roberts, L MacKenzie)
The aim of this project is to understand how the different chemical structures of drugs, the ingredients in their formulations, the blood flow under the skin and the way in which they are applied combine to determine how deep a drug will penetrate. The outcomes of this work will help us in designing optimal therapeutic formulations for the future and also in minimising the risk of penetrations for materials required to stay on the surface.

The efficacy of silver nanoparticle wound therapies (M Roberts, A Holmes)
This project will establish an in vitro burn wound model utilising ex vivo human skin to investigate the localisation and efficacy of novel and conventional silver nanoparticle therapies. The project incorporates techniques such as multiphoton microscopy, fluorescence lifetime imaging, immunohistochemistry, dermatoming, cell culturing, cryosectioning and nanoparticle characterisation within formulations in order to develop and optimise novel burn wound formulations that incorporate a range of antimicrobial metallic nanoparticles.

Virology Group

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The Virology Group at the Basil Hetzel Institute has a primary interest in the development of novel vaccine strategies for hepatitis C virus (HCV) and human immunodeficiency virus (HIV). The laboratory is staffed by two post-doctoral researchers and two PhD students. We have recognised expertise in novel DNA vaccines and have used these vaccines to elicit humoral and cell mediated immunity to HCV and HIV in vaccinated animals, including a large animal model. The proposed projects will build on and extend this expertise.

Research Projects (Honours)

A chimeric HIV/MLV to assess neutralising antibody to HIV

Our laboratory has developed several innovative vaccines to elicit cellular and humoral immunity to target HIV. We now plan to develop a novel strategy to elicit neutralising antibodies (NAb) to the HIV envelope (Env) protein. However, analysis of HIV NAb is normally dependent on the culture of live HIV which poses certain risks. Thus, the project will generate a replication defective chimeric virus comprising the murine leukemia virus (MLV) capsid pseudotyped with the HIV Env (gp120). This chimera binds to the CD4 molecule resulting in membrane fusion and expression of GFP. Initially, the project will use cell lines to generate chimeras which express two different Env strains, and expanded to develop chimeras able to express any Env strain, by transfecting MLV capsid-positive cells with a plasmid encoding gp120. The HIV/MLV chimeras can then be used in a classical assay to assess NAb raised in response to vaccination.

A strategy to increase the in vivo delivery of DNA vaccines

We patented a novel DNA vaccine that is more effective than canonical DNA vaccines. This vaccine elicited robust immune responses to HIV & HCV, and protected mice against challenge with EcoHIV, a chimeric HIV. A DNA vaccine developed elsewhere protected mice against challenge with Zika virus. Thus, modern DNA vaccines have great potential but ~95% of injected DNA remains extracellular and their efficacy could be improved by increasing intracellular uptake. In this project, a model DNA vaccine encoding GFP & luciferase (LUC) will be used to form a complex with DNA-binding proteins or peptides with cell penetrating properties. DNA binding will be confirmed by gel retardation, and uptake and subsequent expression of GFP in cultured cells analysed by flow cytometry. To determine if the DNA/protein complex delivers DNA more effectively *in vivo*, LUC expression in vaccinated mice will be analysed in the whole body imager.

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