Basil Hetzel Institute
for Translational Health Research

The Queen Elizabeth Hospital

2019

Honours & Postgraduate Student
Research Project Booklet

TQEH Research Day Award Winners, October 2017
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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. The BHI is headed by Professor Guy Maddern and hosts research groups from the Universities of Adelaide and South Australia as well as TQEH. These groups undertake laboratory, clinical and population studies focusing on the most prevalent diseases/health issues in the 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 disease, drug and vaccine development, inflammatory disease and a range of health services research such as aged care, respiratory medicine, psychiatry and epidemiological studies.

Professor Guy Maddern

Students interested in pursuing Honours, Masters or PhD studies at the BHI are encouraged to contact the lead researchers or delegated contacts named within the relevant research groups outlined in this booklet. More information about many of these groups can be found on the BHI website. [http://www.basilhetzelinstitute.com.au/students/postgraduate-honours-opportunities/](http://www.basilhetzelinstitute.com.au/students/postgraduate-honours-opportunities/)

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The Hospital Research Foundation Scholarships

The Institute (BHI) Policy Committee supports the following Scholarship categories for 2019.
Enquiries to the TQEH Research Secretariat: gwenda.graves@sa.gov.au

1. **12 month THRF Postgraduate Research Scholarship**
   - **Applications:** Open 23 July 2018; close 31 October 2018
   - **Scholarship Value:** RTP Stipend rate for 2019 (expect in vicinity of $28,000)
   - **Number offered:** Variable, depending on funds available
   - **Eligibility:** Open to medical and science students enrolling in 2019 in a research higher degree at a South Australian University and supervised by researcher based at TQEH/BHI. A student can only hold The Hospital Research Foundation Postgraduate Research Scholarship if they do not simultaneously hold another fully funded Postgraduate Research Scholarship
   - **Condition:** 70% of work must be conducted at TQEH/BHI. Students reapplying for continuation of Scholarship funding must demonstrate that they have applied in 2019 for external scholarships for 2020. Continued funding is subject to satisfactory academic progress report and available funds.
   - **Selection:** When assessing a student’s application for The Hospital Research Foundation Postgraduate Research Scholarship the Basil Hetzel Institute (BHI) Scholarship Selection Committee considers academic merit, postgraduate clinical training, where relevant, the quality of the proposed research, the suitability of the intended supervisor and Department, the capacity of the Department to support the student project, suitability of the applicant for research training, publications and highly relevant work experience.

2. **NEW Postgraduate Top up Scholarships (Non-Medical degree background)**
   - **Applications:** Open 23 July 2018; close 31 October 2018; Additional round may be considered
   - **Total Scholarship Value:** Up to $10,000 per year for 3 years (PhD program) or 2 years (Masters)
   - **Number offered:** Variable, depending on funds available
   - **Eligibility:** Non-medical background graduates enrolling in a higher degree in 2019 at BHI who have been awarded a fully funded external scholarship. Subsequent proof of acceptance of external scholarship and enrolment start date required. Reports from referees who know the student’s capacity for training are still required as part of the application submission process. Open to domestic students only.
   - **Condition:** 70% of work must be conducted at TQEH/BHI; continued funding is subject to satisfactory academic progress.

3. **THRF Honours Research Scholarships**
   - **Applications:** Open 23 July 2018; close 22 November 2018
   - **Total Scholarship Value:** $8,000 for the year
   - **Number offered:** Variable, depending on funds available
   - **Eligibility:** Students must be eligible to enrol in an Honours Degree with any University in South Australia. A student can only hold The Hospital Research Foundation Honours Research Scholarship if they do not simultaneously hold another Honours Scholarship.
   - **Condition:** 70% of work must be conducted at TQEH/BHI.
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/](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/](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. 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)
9. presentation of the research proposal at a School seminar program; and
10. Online 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/](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. Upon enrolment, students will be notified as to which Postgraduate Coordinator they have been allocated.

**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 Betty Sallustio; ph +61 8 8222 6510; benedetta.sallustio@sa.gov.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

University of Adelaide Faculty HDR Student Support Officer, Office of Research Development & Research Education
Roy Sneddon; ph +61 8 8313 9996; fhsresed@adelaide.edu.au

CRICOS Provider Number 00123M

University of South Australia

Advice for Potential University of South Australia HDR Candidates

Further information about all higher degrees:
http://unisa.edu.au/research/degrees/

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

CRICOS Provider Number 00121B

Flinders University

Advice for Potential Flinders University HDR Candidates

MASTERS and PHDs
Further information: https://www.flinders.edu.au/study/apply/apply-research-degree

HONOURS
Further information: https://www.flinders.edu.au/study/apply/honours

CRICOS Provider Number 00114A
THEME: CANCER

Liver Metastasis Research Group

Lead Researcher:
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The Liver Metastasis Research Group investigates the molecular and cellular immune mechanisms that determine the capacity of a tissue to resist metastatic invasion. Our goal is to address the urgent medical needs of risk prediction, prevention, early detection, and treatment of liver metastases. Being a small group with a clear translational research focus on the development of predictive and therapeutic biomarkers, we apply a straightforward bed-to-bench-and-back approach to determine the beneficial/detrimental functions of key immune mediators in cancer patients with distinctive disease progression patterns.

Inflammation is the very complex set of immune pathways underlying the normal acute response to injury and infection. However, unresolved chronic inflammation is a key driver of degenerative diseases and cancer. Therefore, protective adjustment of inflammation requires molecular and functional characterisation of the master regulators, which control the delicate balance between health and disease.

Research Projects for Honours or Higher Degree Research Students

The nexus between metabolism, immunity, and liver metastasis (Supervisors: Dr Ehud Hauben and Professor Guy Maddern)
Liver metastasis is the leading cause of cancer-related death in bowel cancer patients. We do not know why in some patients the cancer spreads to the liver while others are cured by surgical removal of the tumour from the bowel. Our hypothesis is that liver resident cells either permit or resist invasion and growth of tumours based on the local capacity to effectively mount a protective immune response.

In Australia metastatic colorectal cancer (mCRC) is the second most common cause of cancer-related death. Analysis of the South Australian Clinical Registry for mCRC revealed that 60% of mCRC patients suffer from spread of cancer to their liver.
Early onset of CRC and associated liver metastases in obese individuals is on the rise; however, our understanding of the role of metabolic pathways in regulating hepatic immune functions that allow or prevent liver metastasis remains very limited. Changes in liver composition may promote a favourable environment for tumour survival and growth. Therefore, strategies to limit fatty infiltration of the liver, to maintain hepatic immune function, to reduce damaging inflammatory and fibrotic processes, and to promote specific anti-cancer immune responses, can be developed as preventive therapeutic approaches for mCRC.

The response of liver-resident immune cell subsets to metastatic invasion (Supervisors: Dr Ehud Hauben and Dr Kevin Fenix)
Metastasis is a complex process that relies on interactions between invasive circulating tumour cells and resident stromal cells that constitute the metastatic microenvironment. Tissue resident lymphocyte subsets and peripheral lymphocyte infiltrates can either prevent the metastatic process or support the invasion and growth of disseminated cancer cells. Primary liver cancer is initiated by chronic liver inflammation driven by hepatitis virus B or C infections, alcohol consumption, or non-alcoholic fatty liver disease. However, the link between liver disease and secondary hepatic malignancy remains controversial. The aim of this project is to determine the phenotype and function of T lymphocyte subsets and innate lymphoid cells in primary and secondary hepatic malignancy. Molecular characterisation of the role of specific lymphocyte subsets in liver metastasis can promote development of new strategies for risk prediction and prevention of metastatic progression.

Development of targeted nanoparticles as preventative therapy for liver metastasis (Supervisors: Dr Ehud Hauben and Professor Guy Maddern)
The liver is the most common site for distant metastases from cancers arising in other organs. Secondary liver cancer (SLC) accounts for 95% of all hepatic malignancies, representing the second most common cause of cancer death worldwide (788,000 deaths in 2015). The majority of SLC cases are not amenable to surgical resection, resulting in a 5-year survival rate of about 11% in SLC patients. Healthy liver tissue is capable of activating local immunity against invading metastatic cells, while local immune dysfunction can render liver tissue susceptible to SLC. Nanovectors can be engineered to deliver therapeutic proteins that restore the local immune response against invading tumour cells. In particular, porous silicon nanovectors (pSiNVs), a new addition to the nanoparticle-based drug delivery vehicle field, combine biocompatibility, biodegradability, and high payload capacity. The use of pSiNVs for anticancer drug delivery was shown to overcome some of the challenges of conventional therapy. The aim of this proposal is to complete the preclinical development phase of a selected pSiNV - drug combination that will safely and effectively eliminate and prevent metastatic tumours spread and recurrence, through restoring antitumor immunity and intercepting tumour cell invasion and growth.

Development of predictive biomarkers of response to immunotherapy and radiotherapy in cancer patients (Supervisors: Dr Ehud Hauben and Professor Guy Maddern)
The future of cancer therapy lies in identifying subsets of patients who will benefit from particular therapies, using predictive biomarkers. These technologies offer hope of enhancing the value of cancer medicines and reducing their toxicity, cost and failure rates. Cancer immunotherapy is a therapeutic strategy designed to help the immune system destroy cancer cells, often by eliminating the effect of regulatory mechanisms (immune checkpoints) that control the capacity of our immune cells to attack other cells in our body. Programmed death 1 (PD-1) is a checkpoint protein on immune cells called T cells. Antibodies that block PD-1 protein improve survival in patients with advanced non-small-cell lung cancer (NSCLC). Lung cancer is the leading cause of cancer death: in 2017 there were 9021 deaths caused by lung cancer in Australia (AIHW 2017). This project aims to capitalize on the opportunity to analyze clinical samples from immunotherapy treated lung cancer patients. Our aim is to identify, validate and clinically develop novel biomarkers of response, toxicity and resistance following treatment of cancer patients with immunotherapy alone or combined with radiotherapy.
Solid Tumour Group

Lead Researcher:
Professor Tim Price
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The Solid Tumour Group, incorporating the SAHMRI Colorectal Cancer Node, is headed by Professor Tim Price and works on a comprehensive program in colorectal and breast cancer spanning prevention, development and novel therapies. Themes include identification, development and clinical trial of new therapeutic agents for the treatment of colorectal cancer and breast cancer, development of new biomarkers of drug resistance and therapeutic targets, and mouse models of breast and colon cancer for efficacy testing of new drugs.

We have found that one in five young adults who develop colorectal cancer carries an inherited gene mutation which has predisposed them to this condition. Most of the young adults who carry the mutation have no characteristics which would have triggered genetic testing to be carried out. This suggests that all young patients with colorectal cancer should undergo genetic testing to identify such gene mutations as these may also be carried by other family members. Prevention strategies for colorectal cancer can then be put into place by enrolling family members into surveillance colonoscopy programs.

We have also found that a new type of drug derived from a plant used in herbal medicine has been shown to significantly inhibit the formation of new blood vessel networks (angiogenesis). This process is necessary for the growth and metastasis of solid tumours such as colorectal or breast. We will be testing the efficacy of this new type of drug in animal models of cancer. This work is being done by the Molecular Oncology Group in collaboration with Professor Andrea Yool, Adelaide Medical School.


Research Projects (suitable for Higher Degree Research Students)

Type 2 diabetes and early onset bowel cancer (Supervisor: Professor Tim Price)
Colorectal cancer (CRC) incidence is rising among young adults, at a time when the rate of this condition is declining in the older patients in our population. The reason for the decline in older cases is population screening via stool testing and colonoscopy. However the increase in the younger members of our population is unexplained. Recent work from our South Australian Young Onset CRC study (SAYO) has shown a significant association between young onset colorectal cancer (CRC) and personal and familial risk of type 2 diabetes (T2D). Though diabetes of all types affects 1 in 17 adult Australians (6%), less than 5% have T2D.
This is a highly significant difference. Our finding is novel, and suggests that having a personal or first-degree family history of T2D may potentially identify a subset of young adults at increased risk for CRC. This project will extend our established studies, and allow us to sample different groups across the population of SA including rural and urban patients. It will also investigate a novel mechanistic basis for young onset CRC, and feasibility of discovering blood test markers to identify those young adults at highest risk.

**Exploring the association between bowel cancer and type 2 diabetes (Supervisor: Professor Tim Price)**

Colorectal cancer (CRC) incidence is rising among young adults, at a time when the rate of this condition is declining in the older patients in our population. The reason for the decline in older cases is population screening via stool testing and colonoscopy. However the increase in the younger members of our population is unexplained. Recent work from our South Australian Young Onset CRC study (SAYO) has shown a significant association between young onset colorectal cancer (CRC) and personal and familial risk of type 2 diabetes (T2D). Though diabetes of all types affects 1 in 17 adult Australians (6%), less than 5% have T2D. This project will investigate the association between colorectal cancer and type 2 diabetes from the perspective of a cohort of patients with type 2 diabetes assessing their familial risk for type 2 diabetes and personal and familial risk for bowel cancer and polyps. Variables to be assessed include age of onset of type 2 diabetes, number of relatives with type 2 diabetes, inheritance patterns, including parent-of-origin effects, and how these are related to bowel cancer and polyps.

**Investigating the rise in prevalence of appendiceal cancers (Supervisor: Professor Tim Price)**

Appendiceal cancer is a rare malignancy and has the potential to become an aggressive disease. Though rare the incidence of appendiceal cancer is increasing, and this observation is currently unexplained. Primary adenocarcinoma of the appendix is frequently diagnosed incidentally at histologic assessment of the surgical specimen following appendectomy for suspected or diagnosed appendicitis. This project will examine the demographics, medical history such as appendicitis, histology, and potential risk factors of developing appendiceal cancer. Family history of type 2 diabetes will also be explored. The project will involve patient interviews, and statistical analysis of results.

**Genomic and epigenomic germline changes in early onset colorectal cancer (Supervisor: Professor Tim Price)**

Colorectal cancer (CRC) incidence is rising among young adults, at a time when the rate of this condition is declining in the older patients in our population. The increase in the younger members of our population is unexplained. In this project we will look at germline genomic factors for the development of early onset bowel cancer. Procedures include whole exome sequencing (WES) analysis for rare deleterious mutations, and clusters of moderate risk alleles, SNP genotyping of blood DNA from young onset advanced colorectal cancer patients for known monogenic type 2 diabetes predispositions, known common risk loci for type 2 diabetes and CRC, and novel polygenic signatures in CRC-affected young adults. The project will also explore the possibility that epigenetic changes may be associated with bowel cancer in young patients via epigenetic profiling of normal bowel mucosa and blood in young adults with CRC to determine the DNA methylation age of the normal colonic mucosa, whether there are novel epigenetic changes in the germline, and whether any changes are associated with personal or family history of type 2 diabetes.

**Research Projects (suitable for Honours or Higher Degree Research Students)**

**Role of aquaporin 1 in tumour angiogenesis in colon or breast cancer (Supervisors: Dr Jennifer Hardingham, Dr Amanda Townsend & Professor Tim Price)**

Aquaporin (AQP) 1 is a water channel protein 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 several 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 aim to investigate the efficacy of these drugs in inhibiting angiogenesis
in vitro and in halting metastasis in pre-clinical mouse models of human colon or breast cancer. Our hypothesis is that tumour cells that lack AQP1 activity are unable to respond to hypoxia which drives angiogenesis. We will also establish a biobank of organoids cultured from metastatic breast biopsies for research work, in assessing the response to different novel therapeutic drugs in culture, and in characterising the mutational landscape and how that changes with developing resistance. A biobank of metastatic breast organoids is a much needed resource for future research which is currently lacking in this state. Techniques include cell culture, RNAi knockdown, RT-PCR, western blotting, functional assays of cell proliferation, invasion, migration, and angiogenesis and mouse models of human cancer.

**Determination of biomarkers to predict resistance in tumours from patients undergoing anti-angiogenesis therapy (Supervisors: Dr Jennifer Hardingham, Professor Tim Price & Dr Eric Smith)**

MicroRNA (miRNA) is a class of highly conserved, single-stranded, small RNAs that regulate gene expression at the post-transcriptional level by inhibiting the translation of protein from mRNA or by promoting the degradation of mRNA. Several endothelial-specific miRNAs have been implicated in the regulation of different aspects of angiogenesis, including migration and proliferation of endothelial cells. MicroRNA expression analysis will be used in correlative studies on archival tissue to identify biomarkers of resistance to bevacizumab (anti-VEGF monoclonal antibody). Techniques will include DNA and RNA/microRNA isolation from tissue blocks, running microRNA profiles, bioinformatics, and statistical analysis.

**Role of fibroblasts in mediating resistance to therapy (Supervisors: Dr Eric Smith and Dr Jennifer Hardingham)**

Various cell types of mesodermal origin, including fibroblasts, pericytes, immune and endothelial cells, contribute to the stromal compartment of the tumour microenvironment. These cells are recruited and/or locally expanded from resident cells, and typically display activated phenotypes not found in normal tissue from which the tumour originated. These cells contribute to tumour development, progression and resistance to therapy. While the functional heterogeneity and disparate roles and effects of immune and vascular cells have been widely studied, knowledge about other mesenchymal cells including cancer-associated fibroblasts is poorly understood. This project will investigate the role of fibroblasts in mediating responses to colorectal cancer therapies, including radiotherapy, systemic chemotherapy and targeted therapies. It will involve mammalian cell culture including cancer-fibroblast co-culture, PCR, western blot, immunofluorescence, flow cytometry, lentiviral-mediated modulation of gene expression, *in vivo* imaging in mouse models.
The Surgical Evaluation Group has research interests in:
- Evidence based surgical appraisal
- Evaluation of hepatic surgical outcomes
- Minimally invasive surgery
- Development of techniques for liver tumour destruction (particularly minimally invasive techniques capable of destroying both primary and secondary liver tumours by the insertion of electrodes)


Research Projects for Higher Degree Research Students (Supervisor: Professor Guy Maddern)

The Laparoscopic Simulation Skills Program (LSSP)
Current access to surgical simulation training in Australia is limited and the best formal for delivery is yet to be established. Self-directed learning has the potential to limit the costs associated with simulation training, as well as improve access through increased flexibility of training times. The aim of the LSSP is to develop and assess the efficacy and feasibility of a self-directed simulation based training program, and to determine if a period of more formal (supervised) training is required.

Coaching to enhance surgeons’ non-technical skills
The concept of coaching for performance improvement is an accepted and well-established approach in fields such as sports, education, business and music. It has only been much more recently recognised that application of this model of learning, which is grounded in established learning and psychological concepts, may be of particular value when applied in health care settings. This project investigates whether surgical coaching is a potentially valuable tool to enhance surgeons’ non-technical skills and whether it would be beneficial to develop a surgical coaching program for General Surgeons for the purpose of improving their ongoing professional development.

The use of a novel gel to prevent adhesion formation post-abdominal surgery
Postoperative intra-abdominal adhesions are a major cause of morbidity and mortality and a heavy burden to health care resources. In 2016 and 2017, we investigated the effectiveness of novel recombinant human lubricin gel in preventing intra-abdominal adhesion in a rat model. In 2018, further studies will be complete to investigate toxicity and anti-adhesion properties in more significant operations.

Developing novel diagnostic tools and preventative therapies for metastatic colorectal cancer
The majority of colorectal cancer (CRC) related deaths are attributable to liver metastasis—the most critical prognostic factor observed in CRC patients. However, there is no clinical test to predict metastatic risk and allow informed selection of preventive treatment regimes. The translational challenge, therefore, is to validate immune checkpoint biomarkers controlling metastasis. In collaboration with other groups at the BHI, we investigated the prognostic value of candidate protein biomarkers. HLA-G expression by tumour cells is an established mechanism to escape immune-mediated destruction. Our analysis demonstrated that soluble HLA-G is a differential prognostic marker of liver metastasis in CRC patients. We therefore propose that HLA-G secretion by different cell types is predictive of particular prognosis in sequential CRC disease stages. Our proteomic and lipidomic analysis of CRC patients’ tissue and blood samples identified additional proteins and lipids, which are candidate biomarkers of progression to liver metastasis. These candidates are currently being validated in a larger patient cohort.
Cardiovascular Pathophysiology & Therapeutics Group

Lead Researcher:
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The Cardiovascular Pathophysiology and Therapeutics Group reflects the combined interests of members of The Queen Elizabeth Hospital's (TQEH) cardiology and clinical pharmacology groups. This research collaboration has existed for over the past 20 years at TQEH.

We are mainly interested in developing a better understanding of the “new” cardiovascular epidemics of the 21st century, including atrial fibrillation, systolic hypertension, aortic valve disease, stress “Tako-Tsubo” syndrome and metabolic heart disease. We recognise that these conditions are responsible for impaired quality of life, as well as increased mortality rates. Therefore, we consider the development of effective treatment modalities a major priority.


Research Projects (Honours)

Impaired platelet autacoidal signalling in patients with coronary vasospasm (Supervisors: Dr Y Chirkov, Dr TH Nguyen, Professor J Horowitz)

Angina pectoris is a common and debilitating problem in Western society, usually resulting from narrowings of coronary arteries. However, in a substantial minority of patients, spasm of the large or small coronary arteries is the cause of pain. While this condition can be treated symptomatically, there is no available cure, and many patients have poor quality of life because of frequent and recurrent episodes of pain. We are currently evaluating integrity of signalling pathways related to anti-aggregatory autacoids (e.g. nitric oxide and prostacyclin) in coronary spasm patients, with encouraging pilot results. These ongoing studies may lead to the development of better treatments for this condition.
The "Resilient Heart" project: Towards better understanding of anthracycline-induced cardiac injury (Supervisors: Dr S Liu and Professor J Horowitz)
Chemotherapy-induced cardiotoxicity is an emerging cause of heart failure that could add millions more to the healthcare budget. Currently, there are over 400,000 cancer survivors in Australia and that number is expected to continuously increase. Given that virtually all of the drugs concerned are cardiac toxic, this advance has come at the cost of increased risk of symptomatic or fatal heart failure. Doxorubicin, a member of the anthracycline family, is a well-known chemotherapeutic agent which is used in treatment of a wide variety of cancers. The successful use of doxorubicin has been hampered by toxicities such as hematopoietic suppression, nausea, vomiting, extravasation, and alopecia, yet the most feared side-effect is cardiotoxicity. The planned study will utilize technology which is already established in our laboratory study to establish the determinants of extent of toxic effect of doxorubicin compared with those of other more recently developed antineoplastic drugs. The technology will utilize human myocardial cell grown in culture, and will quantitate the transition from complete cell viability through apoptosis to eventual necrosis. The results will help in the development of methods to develop cardiac-safe anticancer therapeutics.

Research Projects (Higher Degree Research students)

Impact of B-type natriuretic peptide (BNP) on stabilisation and function of the myocardium (Supervisors: Dr S Liu, Dr Y Chirkov and Professor J Horowitz)
We have recently shown that BNP exerts important anti-inflammatory effects, by stabilising white blood cells and diminishing superoxide production. We wish to determine whether this results in limitation of inflammatory change within the heart, and whether this anti-inflammatory effect of BNP is lost in acute heart failure.

The heart in stress: tako-tsubo cardiomyopathy (Supervisors: Dr TH Nguyen and Professor J Horowitz)
Tako-Tsubo syndrome (TS) 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 TS, and now seek to evaluate potential therapeutic avenues, using intact animal models, essentially to characterize the impairment in post-receptor signalling.

Defects in physiological regulation of platelet aggregation: implications in the setting of potential coronary stenting (Supervisors: Dr Y Chirkov and Professor J Horowitz)
We are studying regulation of blood clot formation in patients with different cardiac conditions. Blood clots cause heart attacks and strokes. Clot formation can be prevented with special medications (e.g.clopidogrel or ticagrelor), which are used clinically to prevent thrombosis. Our research aims to identify a reason for the frequently occurring less-than-expected response to these medications. We are focusing on platelets because the starting point for blood clot is platelet aggregation. Autacoids, naturally occurring within the organism (e.g. nitric oxide and prostacyclin) and which are supposed to control the normal function of platelets, stop working properly in patients with cardiovascular diseases. It turns out that the platelet adenylate cyclase system is particularly important in predicting responses to clopidogrel and related drugs, implying that defective adenylate cyclase signalling may be the basis for poor patient responses to this class of drugs. We are trying to work out what is going wrong with this regulation and how it could be restored.
Clinical Pharmacology Research Group

Lead Researcher:
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The Basil Hetzel Institute for Translational Health Research offers a range of postgraduate and honours training opportunities each year for PhD, Masters and Honours students. Being part of The Queen Elizabeth Hospital, researchers can work closely with the hospital’s clinical divisions, and 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. The Clinical Pharmacology Unit is affiliated with the Discipline of Pharmacology of 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. Through research in these fields we strive to provide a better understanding of drug action, metabolism and disposition in patients with varied genetic makeup in order to better use and tailor medications to each individual, and to develop new therapies.  

Research Projects (Higher Degree Research Students)  
Honours projects are also available with this group. Please contact the lead researcher for more information.

Metabolic treatments for heart disease and cancer
Altered cellular energy metabolism is an underlying feature of both heart disease and cancer. In heart disease, maladaptive changes in energy utilisation and storage contribute to a decline in myocardial function and structural remodelling. In cancer cells, changes in energy utilisation allow increased cell survival, replication and metastasis. In addition, a number of cancer chemotherapy agents cause myocardial damage. Therefore, it is possible that myocardial metabolic agents designed for treatment of heart disease, may also be useful adjunct therapy in cancer. PhD and honours projects are available in two broad research areas:

1. Investigating the efficacy of new myocardial metabolic agents in the treatment of heart failure and ischaemic heart disease.

2. Developing new therapies for chemotherapy-induced myocardial toxicity in cancer patients.
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. Projects are available in two broad areas of research:

1. To investigate genetic variability in the pathways of immunosuppressant elimination in both kidney donors and recipients, to determine its impact on intra-renal and intralymphocyte exposure to immunosuppressants, and its association with rejection and long-term function of the transplanted kidney.

2. To investigate how pregnancy alters the pharmacokinetics of immunosuppressants in renal transplant recipients, and to develop biomarkers that may be used in conjunction with standard monitoring to minimise the risk of nephrotoxicity and graft loss during pregnancy.
The Translational Vascular Function Research Collaborative undertakes basic, clinical and epidemiological studies into cardiovascular disorders with the objective of improving the health outcomes of these patients. Currently the group focuses upon coronary heart disease and peripheral artery disease, although many principles are applicable to other vascular disorders. We aim to conduct interdisciplinary research using a collaborative approach, with results being directly integrated into clinical practice.

The research group includes both physicians and medical scientists located at the Basil Hetzel Institute, and the University of Adelaide's medical school and teaching hospitals. The integrative nature of the group provides a unique opportunity to ensure that innovations are translated from bench to bedside to health outcome, as well as the reverse.


Research Projects (Honours Students)

Coronary Angiogram Database of South Australia (CADOSA): Improving health outcomes in patients undergoing coronary angiography (Supervisors: Professor John Beltrame and Dr Rosanna Tavella)
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).

Vasomotor studies of patients with myocardial infarction and non-obstructive coronary arteries (MINOCA) (Supervisors: Professor John Beltrame and Dr Rosanna Tavella)
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 project will utilise invasive and non-invasive clinical techniques to elucidate potential mechanisms that may be responsible for the myocardial infarct.
Molecular Physiology of Vascular Function Research Group

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The objectives of our research group are to identify and investigate mechanisms and therapies for vasomotor disorders. The research involves investigation of vasospasm of large or small vessels and mechanisms contributing to vasodilatory septic shock. The research team is involved in both preclinical, basic research, and translational research using a three-pronged approach, which includes:

- Clinical characterization of vasomotor disorders
- Discovery of underlying molecular mechanisms
- Exploring novel therapies in basic & clinical studies

Research Projects (Honours and/or Higher Degree Research Students)

- Heterogeneity in vascular tone and blood pressure regulation: exploring intrinsic and extrinsic variability
- Exploring strategies to reduce vasopressor insensitivity in health and disease
- Beyond receptor internalisation, exploring novel regulators of vasopressor sensitivity in blood vessels
THEME: CHRONIC DISEASE

The Health Observatory
Located at the Basil Hetzel Institute, TQEH and SAHMRI

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The Health Observatory is a specialist population research centre conducting a number of large scale representative population studies on health surveillance of chronic disease and related factors. The ultimate focus of the observatory is to contribute to positive ageing by improving population health across the life span. The work involves the tracking of population health to identify gaps/targets that can be better addressed through prevention strategies and/or better management of chronic conditions and conditions associated with ageing.


Research Projects (Higher Degree Research Students)

Sleep medicine and sleep health
The MAILES Sleep Study is one the largest and most detailed population-based studies of sleep in men in the world, including using home-based full sleep studies and extensive biomedical and psychosocial measures. This ongoing project, involving collaboration with researchers across the University of Adelaide, Flinders University and Sydney University, has current National Health and Medical Research Council (NHMRC) funding to collect follow-up data to examine the longitudinal effects of sleep disorders and sleep disturbance in men on health outcomes, links to other diseases and ways to improve service delivery.

Some current projects include: the relationships between sleep disturbance, inflammation and chronic pain; the influence of dietary patterns on sleep apnea; the longitudinal effects of sleep apnea on health, and which moderating factors (e.g. obesity, diet, stress) influence these effects; and more.

Other projects involve analyses of a Sleep Health Foundation funded on-line study of sleep, to investigate relationships between insomnia phenotypes and help seeking behaviours and outcomes in addition to social patterns of sleep.

Chronic disease and population health
The North West Adelaide Health Study (NWAHS) is a major South Australian chronic disease cohort study of over 4000 adults that has been in operation since 1999. NWAHS was formulated to provide much needed and unique representative, longitudinal data on chronic conditions and health-related risk factors in South Australia. The study's focus is on chronic conditions (including bio-medically measured diabetes, asthma, chronic obstructive pulmonary disease, kidney health, sleep disorders and self-reported doctor-diagnosed arthritis, osteoporosis, cancer, mental health and cardiovascular disease), and modifiable health-related risk factors (such as smoking, alcohol, physical activity, overweight/obesity, cholesterol and blood pressure).
These variables are examined in relation to the demographic and socio-economic characteristics of participants (such as income, education, work, occupation, country of birth, and marital status). The study also collects information from participants about their health care service utilisation and medications, and links this information with data received from Medicare and the Pharmaceutical Benefits Scheme. Data are also linked to SA-NT Datalink for hospital inpatient and outpatient data as well as the National Death Registry (including deaths related to cancer).

A number of projects are available examining the longitudinal time course of health and chronic conditions.

**Simulation modelling and systems design**

Used to predict the implications of making significant changes to the existing health care system, such as with transforming health. The essence of this work is that health service redesign should be tested as rigorously as new treatments or medicines. This advocates acceleration of the redesign of care delivery to patients through well-controlled experiments. Unfortunately, the health service cannot wait until everything is in place and working properly before changes are made. Modelling and simulation makes coordinating this challenge possible. Simulation modelling provides a mechanism to better understand the flow of patients through the system, before changes are made. Currently available projects include looking at: management of acute and chronic patients at the Queen Elizabeth Hospital (funded by the Hospital Research Foundation), expansion and reconfiguration of emergency services at different hospitals, intensive care units, and cardiac care.

A simple visual example created by one of our partners can be seen at: [youtu.be/P45WgRlc2sI](https://youtu.be/P45WgRlc2sI)

**Musculo-skeletal medicine (Supervisor Professor Catherine Hill, email: catherine.hill@sa.gov.au)**

A wide range of human clinical intervention studies in gout, giant cell arteritis and osteoarthritis are ongoing.

In addition, NWAHS has the largest and most comprehensive data on musculoskeletal pain and disability and its impact in Australia. Data analysis is ongoing to support planning of services for musculoskeletal conditions as part of the health reform agenda. International collaborations exist looking at comparisons across countries of foot pain and associated disability.
Health Performance and Policy Research Unit

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The Health Performance and Policy Research (HPPR) Unit assesses important end results of healthcare such as effectiveness, safety, quality, and costs. Combining clinical medicine and data science, our goal is to generate research that informs clinical and policy strategies to improve the quality of care provided by Australian hospitals. [http://www.basilhetzelinstitute.com.au/research/research-theme/clinical-sciences-health-services-population-health/health-performance-policy-research-unit/](http://www.basilhetzelinstitute.com.au/research/research-theme/clinical-sciences-health-services-population-health/health-performance-policy-research-unit/)

Research Projects

Cardiovascular Epidemiology
HPPR holds over a decade of cardiovascular data collected from all public and most private hospitals in Australia and New Zealand. There are unique opportunities for Honours or PhD candidates interested in publishing nation-wide studies of cardiovascular epidemiology for a range of common cardiovascular conditions and procedures such as heart attacks, heart failure, peripheral vascular disease and stroke. Students are supported by senior statisticians and clinicians. This project is ideally suited to students with a background in epidemiology or statistics wishing to apply their knowledge and publish research output. Formal training can be provided for interested students without prior experience.

Cardiac Procedural Safety and Outcomes
Cardiac procedures are among the most common, risky and costly procedures performed in Australian hospitals. The research aims to investigate variation in the safety and outcomes of these procedures with a focus on developing better ways to rapidly identify 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.

Strategies to reduce unanticipated hospital readmissions
Hospital readmissions are common, distressing for patients and costly to the health system. Many readmissions are also preventable. 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 utilisation (3) The evaluation of potential clinical and policy interventions to reduce these hospitalisations. The central goal is to generate research that may inform future policy making to reduce unanticipated hospitalisations.

Avoidable Healthcare Expenditure associated with hospitalisations
In Australia, an estimated $59 billion (or about $2,542 per person) was spent on hospital care in 2013-14 with this cost rising by 4.2% each year - a rate that is considerably faster than inflation. Minimising avoidable healthcare expenditure is thus highly desirable. This project, in collaboration with health economists, will examine avoidable healthcare expenditure associated with hospitalisations and emergency care presentations. This project is ideally suited to students with an interest or background in health sciences, health economics, commerce or social sciences.
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/

Psychiatric and Medical Co-morbidities Research Group
Associate Professor Oliver Schubert, Dr Scott Clark, Professor Bernhard Baune

Lead Researcher:
Associate Professor Oliver Schubert
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The Psychiatric and Medical Co-morbidity Research Group is built around the idea that physical and brain processes are interrelated in a bidirectional way. For example, heart disease is more frequently associated with depression and vice versa. Moreover, individuals with psychiatric disorders have a 25-30 years decreased life-expectancy than the general population due to a high degree of medical comorbidity. The group uses a range of methods providing for investigations of the molecular, functional, clinical, and epidemiological characteristics of psychiatric-medical co-morbidity.

Research Projects (Honours and/or Higher Degree Research Students)

The clinical and cognitive effects of Hepatitis C Virus (HCV) treatment with a DAA medication in people with severe and enduring mental illness
This is a placebo controlled multicentre study in collaboration with the Department of Medicine (Professor Mark Boyd), investigating the effects of a direct acting antiviral (DAA) drug for HCV on psychiatric symptoms and cognitive function in people with severe and enduring mental illness.

The effects of iron deficiency and its treatment on mental health outcomes in pregnant mothers and their children
This collaborative study (Associate Professor Bernhard Froessler, Department of Acute Care Medicine) investigating the role of iron deficiency and its treatment on mental health outcomes such as depression, anxiety, and neurocognition in pregnant women. Longitudinal assessments of mothers and babies have been conducted during pregnancy and in the first postpartum year.
Biophenotypes for Personalised Psychiatry
Dr Scott Clark, Associate Professor Oliver Schubert, Professor Bernhard Baune

Lead Researcher:
Dr Scott Clark
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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 (Honours and/or Higher Degree Research Students)

Multimodal prediction of the first psychotic episode
This study uses multimodal clinical, imaging and blood based biomarker data to predict the first psychotic episode with novel Bayesian, Machine Learning and trajectory modelling techniques in national and international cohorts of patients assessed at clinical high risk of psychosis.

Prediction of outcomes and treatment response in chronic psychosis
This study uses multimodal clinical and blood based biomarker data to predict medication response, cognition and outcomes in chronic psychosis with novel Bayesian and Machine Learning and trajectory Modelling techniques in a large locally recruited sample of patients treated with depot antipsychotics or clozapine.

Prediction of outcomes and treatment response in mood disorders
This study uses multimodal clinical and blood based biomarker data to predict medication response, cognition and outcomes in chronic psychosis with novel Bayesian and Machine Learning and trajectory modelling techniques in a large locally recruited sample of patients treated and has a specific focus on response to lithium in bipolar disorder.

Cognition and Functioning in Psychiatry Research Group
Dr Scott Clark, Associate Professor Oliver Schubert, Dr Catherine Toben, Dr Catharine Jawahar, Professor Bernhard Baune

Lead Researcher:
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This research group investigates neuropsychological factors that influence the practical capacity of individuals with psychiatric disorders such as depression, anxiety or psychosis to function and perform on a daily basis. The research group undertakes projects that explore cognitive function, emotion and behaviour in psychiatric disorders with or without medical comorbidity. Another major focus of the group is the study of psychiatric interventions on neuropsychological measures of cognition and mood.
Research Projects (Honours and/or Higher Degree Research Students)

The Cognitive Function and Mood Study (CoFaMS)
This study investigates the effects of depression and anxiety on a person's mental status and cognitive capacity by analysing psychological, and functional genetic differences in a healthy cohort and those suffering from mood and anxiety disorders.

Cognitive and Functional Assessment of Psychosis Staging Study (CoFAPSS)
In current clinical practice it is impossible to predict the individual course of psychotic illness or treatment response. This longitudinal study assesses patients at different stages of psychotic illness to develop accurate biomarkers of risk profile, transition between disease stages and potential for functional recovery.
Rheumatology Research Group

Lead Researcher:
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Musculoskeletal conditions/rheumatic diseases are the most common chronic conditions in Australia, affecting a large sector of the population leading to chronic pain, disability, reduced quality of life, and in many cases, shortened life span. Disability associated with musculoskeletal diseases is universal across both developing and developed countries and monetary costs are high with respect to lost earnings, as well as direct health care costs.

The Australian Institute of Health and Welfare (AIHW) estimates that 28% of Australians have arthritis and other musculoskeletal conditions, with an estimated health care expenditure of $5.7 billion in 2008-09. The Rheumatology Department strives to augment its clinical rheumatology services with research programs into the epidemiology, causation and complications of rheumatic diseases (bedside to bench), coupled with the evaluation of new generations of pharmaceutical agents for the treatment of arthritis (bench to bedside). These rheumatic diseases include Sjögren's syndrome, giant cell arteritis, polymyalgia rheumatica, osteoarthritis, scleroderma, rheumatoid arthritis, ankylosing spondylitis, gout, and fibromyalgia.

Head of Department, Professor Catherine Hill, is both an epidemiologist and Rheumatologist. She is a Chief Investigator of the North West Adelaide Study (NWAHS), a longitudinal population health study, Chair of the Australian Rheumatology Association Database (ARAD), a longitudinal database of primarily Rheumatoid Arthritis patients, and a Chief Investigator of the Australian Arthritis and Autoimmune Biobank Collaborative (A3BC), a national, longitudinal biobank established in 2018.


Research Projects (Honours Students)

The relationship between socioeconomic status and medication use in rheumatoid arthritis patients
(Supervisors: Professor Catherine Hill, Dr Rachel Black and Sue Lester)

Different drugs are used in the treatment of rheumatoid arthritis (RA). Some are used to slow or stop the course of the disease and to inhibit structural damage (disease-modifying antirheumatic drugs, DMARDS). Others, such as non-steroidal anti-inflammatory drugs (NSAIDs) are used primarily to ease the symptoms of RA. Adjunct treatments, which should be used sparingly because they are associated with significant side effects, include glucocorticoids (steroids), which provide rapid control of disease activity, and flares, and opioids to manage pain. Effective treatment in RA with the DMARDs should negate the need for ongoing glucocorticoid or opioid use. In Australia, PBS funding of medications should ideally lead to equitable use of medications across groups of differing socioeconomic status (SES). However, other components of SES such as health literacy and lifestyle factors may mean that this is not the case.

The aim of this project is to determine the relationship between different types of medication use, pain, function and SES in RA. Data will be obtained from the Australian Rheumatology Association Database (ARAD), which is a longitudinal database with over 3000 RA patients. Socioeconomic status will be estimated using SEIFA (Socio-Economic Indexes for Areas) indexes developed by the Australian Bureau of Statistics.
The association between dietary patterns and prevalence and incidence of joint pain in the North West Adelaide Health Study (Supervisors: Dr Courtney Davis, Sue Lester, Professor Catherine Hill)

The relationship between diet and arthritis has not been well explored, particularly osteoarthritis. Both rheumatoid and osteoarthritis are associated with joint pain secondary to inflammation, which may be influenced by a number of dietary components such as long chain omega-3 fatty acids, antioxidant vitamins such as vitamin E and C, and polyphenols, including flavonoid antioxidants. Using data collected from the North West Adelaide Health Study, we would like to explore the relationship between prevalence and incidence of joint pain, and dietary patterns. We will be investigating three dietary patterns: a Mediterranean dietary pattern, an anti-inflammatory dietary pattern, and a general healthy eating dietary pattern based on dietary guidelines. A dietary pattern score will be developed from food frequency questionnaire data to establish compliance with each dietary pattern, and scores will be assessed for a cross-sectional, and longitudinal, relationship with joint pain. The results will add to our understanding of the relationship between nutrition and arthritis, enabling clinicians to tailor their advice around eating to patients and the general public.
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 are enrolled through the School of Pharmacy and Medical Sciences at the University of South Australia)

**Which barriers work to prevent dermal exposure of pesticides? (Honours project with Dr Amy Holmes)**

In many countries, particularly poorer countries, there is a severe problem with chronic poisoning from dermal exposure to toxins during and after the spraying of pesticides on to crops. Currently personal protective equipment (PPE) such as gloves are assessed using the BS EN 374-2:2014 standard that measures the time taken for a compound to penetrate the material called ‘permeation breakthrough’. Depending on the lag time of the compound permeating the material the PPE is then categorised into the degree of protection afforded (‘not recommended<splash protection<medium protection<high protection’). What is missing is the link between the ‘permeation breakthrough’ of the PPE and the subsequent penetration across the stratum corneum (outer layer of the skin) resulting in systemic exposure through dermal exposure. It is likely that commonly used PPE such as nitrile gloves, neoprene gloves and clothing significantly occlude the skin causing hydration of the skin. When the skin is excessively hydrated and the corneocytes of the stratum corneum are swollen a penetration enhancement effect may be elicited enhancing the permeation of toxic compounds across the skin. This study will investigate the efficacy of barrier materials designed to prevent the ingress of a series of pesticides (either radio-labelled compounds or ones we already have LC-MS methods established for) into ex vivo human skin. The student will develop skills in a number of key areas that include human tissue preparation, analytical chemistry and regulatory toxicology.

**Honours scholarships available**

Previous Honours students studying with Dr Amy Holmes have been successful in securing a scholarships and travel grants from a range of sources, some of which are specific to the project. Scholarship sources include NHMRC Translational Australian Clinical Toxicology network, The Hospital Research Foundation and Medical Advances without Animals Trust.
Specific targeting of nanosystems by cutaneous delivery (Supervisors: 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 studies 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 (Supervisors: M Roberts, L MacKenzie)
This project aims 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. Results from this work will help us design optimal therapeutic formulations for the future and minimise the risk of penetrations for materials required to stay on the surface.

The efficacy of silver nanoparticle wound therapies (Supervisors: 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.

Students with specific interests in alternative projects are encouraged to contact Dr Lorraine MacKenzie to discuss potential projects.
Virology Group

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Our group has developed a number of experimental vaccines for hepatitis C virus, HIV and Zika virus, and is constantly improving these vaccines with an aim to examine the safety and immunogenicity of an effective vaccine in clinical trials.


Research Projects (Honours)

Expanding the cell mediated immune responses to HIV (Supervisor: Dr Branka Grubor-Bauk)
We have developed a novel HIV vaccine which encodes the conserved capsid protein, Gag. Vaccination of mice with this cytolytic DNA vaccine results in a robust cell mediated immune response to Gag as determined by enzyme linked immunospot (ELISpot) assay and by intracellular cytokine staining (ICS). This immune response provides a considerable level of protection against challenge with EcoHIV, a chimeric virus in which the HIV envelope proteins (Env) have been substituted with the Env proteins from murine leukaemia virus. Challenge of vaccinated mice results in a significantly reduced viral load relative to unvaccinated controls. We now wish to introduce a number of additional HIV proteins into the vaccine, because one of the most effective experimental HIV vaccines included Gag, rev, nef, tat in the vaccine. Thus this project will involve DNA cloning, sequencing and protein expression, prior to vaccination of mice and analysis of the efficacy of the modified vaccine, as assessed by EcoHIV challenge.

A multigenotypic, multiantigenic cytolytic DNA vaccine for HCV (Supervisor: Dr Danushka Wijesundara)
A vaccine designed to induce cell mediated immunity (CMI) to HCV has the potential to protect against infection. However, as the nucleotide sequence of the HCV genome varies by 35% between different genotypes, the production of a universal HCV vaccine represents a major challenge. A convenient way to overcome this difficulty is to generate a cocktail of DNA vaccines which will elicit CMI to each of the genotypes included in the cocktail. However, although we have developed such a cocktail, we have been unable to examine its immunogenicity because the reagents necessary to establish ELISpot and ICS are unavailable for genotypes 2 and 4. Thus this project will generate DNA expression vectors for HCV genotype 2a and 4a non-structural (NS) proteins NS3 and NS5B, express and purify these proteins from mammalian cells, then establish ELISpot and ICS to examine the immune response in animals vaccinated with the cocktail or the individual genotype vaccine.
THEME: INFLAMMATORY DISEASE

ENT Surgery

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The Department of Otolaryngology, Head and Neck Surgery at The Queen Elizabeth Hospital is committed to excellence in translational research and education. Research in our department is focused mainly on understanding the pathogenesis of chronic rhinosinusitis (CRS), using a multidisciplinary approach, aimed at identifying new diagnostic/prognostic markers and treatment strategies to the benefit of our patients. Research projects cover all aspects of rhinological research from pathophysiological aspects of CRS to the identification and validation of new treatment strategies in vitro and in vivo, bringing research from bench to bedside.


Research Projects (Honours Students)

A new treatment for invasive *P. aeruginosa* wound infections (Supervisors: Prof PJ Wormald, A/Prof S Vreugde, A/Prof A Psaltis)

*P. aeruginosa* is an opportunistic pathogen frequently responsible for severe infections in chronic wounds, lungs and sinuses. With the emerging threat of multidrug resistance, new treatments are urgently required. Our laboratory has identified a novel antimicrobial treatment that can kill multidrug resistant *P. aeruginosa* strains. We have shown that the treatment can eliminate bacteria from within mammalian cells, indicating its potential to kill invasive *P. aeruginosa* infections. This project will evaluate the potential of this new treatment to kill *P. aeruginosa* from within mammalian cells (epithelial cells and macrophages) in vitro and in vivo in an infected wound model.
Development of a new treatment for *P. aeruginosa* airway infections (Supervisors: Prof PJ Wormald, A/Prof S Vreugde, A/Prof A Psaltis)

Chronic Rhinosinusitis (CRS) is one of the most common manifestations in patients with Cystic Fibrosis (CF) accounting for significant morbidity and contributing to CF lung disease. The frequent and often long-term use of antibiotics significantly contributes to the threat of Multi Drug Resistant (MDR) pathogens. There is an urgent need for the development of new treatments that are effective at eliminating infections with MDR pathogens. Bacteriophage (phage) is a virus that targets and kills one specific bacterial species, leaving the human mucosa and commensal species unaffected. Phage therapy has been considered in the West as early as the 1940’s, and has recently regained interest for its potential to treat MDR bacterial infections. However, phage’s suitability for therapeutic application is hindered by the existence and/or rapid emergence of Bacteriophage Insensitive Mutants (BIM) in the presence of phage. We have identified specific compounds that can re-sensitize *S. aureus* BIM to phage. This project will evaluate the potential of these compounds to resensitise *P. aeruginosa* BIM to phage and study their effect on modulating inflammation.

A new treatment for cystic fibrosis upper airway infection (Supervisors: Prof PJ Wormald, A/Prof S Vreugde)

Chronic Rhinosinusitis (CRS) is one of the most common manifestations in patients with Cystic Fibrosis (CF) accounting for significant morbidity and contributing to CF lung disease. We have recently identified a new treatment that is highly effective to kill antibiotic resistant *S. aureus* infections, frequently causing chronic relapsing infections in the CF airways. This project will develop the pharmaceutical delivery and formulation of this new product to the sinuses and test its safety and efficacy in a sheep model of sinusitis.
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