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Adelaide Medical School - change your world

2017 Honours and postgraduate research opportunities

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Change your world

The Adelaide Medical School is offering exciting opportunities for researchers at the Honours, Masters and PhD levels. This booklet details honours and postgraduate research projects available in 2017. These research opportunities are open to a broad range of backgrounds, from science to medicine. If you are interested in human health, consider furthering your research career with us - there are sure to be projects that match your interests and background.

The University of Adelaide is well known for our role in training medical doctors, and has a proud record of vigorous and diverse translational medical research programs. These range from basic sciences to clinical research. This booklet showcases projects across the twelve disciplines of the School: Disciplines of Anatomy and Pathology, Pharmacology, and Physiology (medical sciences); Disciplines of Acute Care Medicine, Ophthalmology and Visual Sciences, and Psychiatry (medical specialties); Disciplines of Paediatrics, and Obstetrics and Gynaecology (paediatrics and reproductive health); Disciplines of Orthopaedics and Trauma, and Surgery (surgical specialties); the Discipline of Medicine; the Discipline of General Practice; the Discipline of Rural Health and The Centre for Traumatic Stress Studies.

We offer a stimulating research environment, excellent facilities and supervisors who are respected internationally for their work. Our researchers have widespread collaborations with major research institutes both in Australia and internationally. In addition, there are exciting new international partnerships with Universities in Nagoya (Japan), Freiberg (Germany) and Nottingham (UK). In 2017 the new Adelaide Health and Medical Sciences (AHMS) building at the city's west end will be fully operational, with some of our research groups moving to this exciting facility, opening a new chapter in medical research at the University of Adelaide.

When you join the Adelaide Medical School you're part of a vibrant research community that has a great past – and a bright future. At any one time there are over 500 students enrolled in Honours, Masters and PhD programs.

Interested?

If you'd like to explore your research future with us, use this booklet to find a research project that excites you, and contact the listed lead researcher. There are often a range of additional possible research projects available so don't hesitate to use the contacts provided to explore all possibilities.

If you're not sure where to start and would like further details of our research streams contact one of our Adelaide Medical School Honours Coordinators at health.adelaide.edu.au/medicine/current-students/honours/ or our Postgraduate Coordinators at adelaide.edu.au/graduatecentre/staff/postgraduate-coordinators/pgc-list

Location of laboratories and research groups:

UA/RAH

University of Adelaide/Royal Adelaide Hospital Frome Road precinct.

BHI/TQEH

Basil Hetzel Institute for Translational Health Research, The Queen Elizabeth Hospital, Woodville.

SAHMRI

South Australian Health and Medical Research Institute

WCH

Women's and Children's Hospital

HC

Hamstead Campus

LMH

Lyell McEwin Hospital

Our record

The Adelaide Medical School has a proud track record in research with Nobel Laureates Howard Florey and, more recently, J. Robin Warren counted among our graduates. Rather than resting on our track record, the Adelaide Medical School is continually working to maintain our position as one of Australia's medical research powerhouses. Our researchers continue to attract significant research funding and publish in the top peer reviewed medical journals. The translational research projects highlighted in this booklet are partnered with the Royal Adelaide, Queen Elizabeth, Women's and Children's, Lyell McEwin and Modbury hospitals, the Basil Hetzel Research Institute, and the South Australian Health and Medical Research Institute (SAHMRI).

Core facilities

Honours and postgraduate students have access to core facilities including the latest in next-generation DNA sequencing, proteomics and animal house facilities. Advanced imaging equipment provides state-of-the-art instrumentation from sub-cellular level and live cell imaging, through to instruments able to accommodate a range of small and large animals.

Research opportunities

Our researchers are recognised nationally and internationally for their achievements. Research covers the range from inquiry into fundamental questions, through to work having a direct clinical application. Supervisors of our research projects are drawn from both our own staff and those of the school's many affiliates in diverse health care settings. Many students will find that their host laboratory is part of a broader research grouping that provides excellent opportunities for involvement at many levels in an active research community, and enables projects that cross traditional discipline boundaries.

Basil Hetzel Institute for Translational Health Research (BHI)

The Basil Hetzel Institute is the productive research arm of The Queen Elizabeth Hospital (TQEH), is headed by Professor Guy Maddern and hosts 19 research groups. These groups undertake laboratory, clinical and population projects focussing 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 currently available in South Australia. Research areas include: cardiovascular disease, cancers, immunological diseases, chronic inflammation, population epidemiology, transplantation immunology, vascular surgery, drug response, stroke, and surgical technologies and training.

South Australian Health and Medical Research Institute (SAHMRI)

SAHMRI is an independent flagship health and medical research institute located adjacent to the new Royal Adelaide Hospital and our new Adelaide Health and Medical Sciences (AHMS) building with Professor Steve Wesselingh as Executive Director. Located within SAHMRI are researchers and affiliates of the University of Adelaide. Newly established resources within SAHMRI include the Australian Cancer Research Foundation (ACRF) Flow and Laser Scanning Cytometry facility which provides access to biomedical imaging technologies. Such technologies include: advanced flow cytometry, magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET) and single photon emission computed tomography (SPECT). In addition, the David R Gunn Genomics Suite houses the latest DNA sequencers, the largest unit capable of generating a terabase of DNA sequence data in a single run. This facility will be available to local researchers to help understand the complex genomic landscape of diseases, including cancer and brain disorders.

The Adelaide Health and Medical Sciences (AHMS) Project

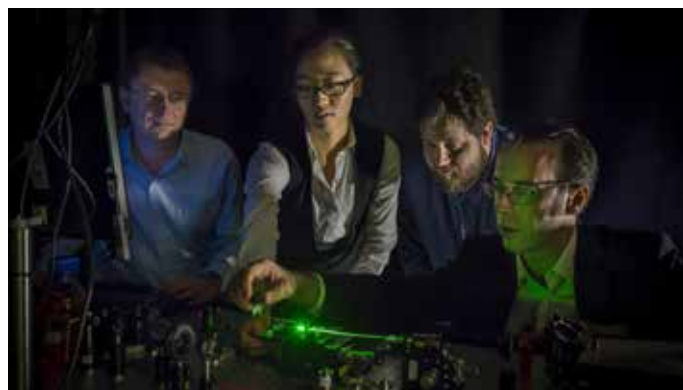
The AHMS is an exciting new building and facility (see front cover) that will support Adelaide Medical School researchers, and its integration with the new Royal Adelaide Hospital (nRAH) and South Australian Health and Medical Research Institute (SAHMRI) and will continue to build on more than 130 years of University of Adelaide partnership with the RAH. The design concept incorporates features introducing a diversity of new generation spaces including small collaborative group study areas, laboratories within technology-rich environments, in a backdrop of sweeping terracing, courtyards, cloisters, connecting stairs, unique social spaces, materials and textures, to encourage a peer to peer learning culture. A number of researchers from the current Frome Street precinct will be moving to AHMS in early 2017. This new environment will provide a more comprehensive research experience with opportunities to interact and collaborate with researchers from across the School and easier access to a wide range of cutting edge techniques and equipment.

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Trans-disciplinary research projects

Bioengineering and imaging laboratory



Bioengineering and Imaging Lab researchers, (Rodney Kirk, Jiawen Li, Bryden Quirk, Prof Robert McLaughlin far left)

ARC Centre of Excellence for Nanoscale BioPhotonics

Lead Researcher:

Prof Robert McLaughlin

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Our group brings together engineers, clinicians, physicists and computer scientists to design and build novel imaging devices to explore the body, and then translate these devices into clinical usage. We have a particular focus on developing new optical imaging technologies, and have strong research programs in optical coherence tomography and fluorescence imaging. Much of our work involves our 'imaging needle' technology, highly miniaturised optical imaging probes small enough to be encased within a needle, and we have active programs extending this work to brain cancer and lung disease. For additional information see: cnbp.org.au

Research projects

We have a range of PhD and Masters projects, extending from theoretical developments in optical modelling, through hardware and software development, and to clinical translation. Most projects will focus on one of these aspects, but may involve aspects of all of them. Specific projects include:

- > 3D printing of miniaturised optical lenses.
- > Accurate quantification of brain cancer using intra-operative fluorescence by developing a mathematical model to correct for fluorescence attenuation.
- > Development of high-speed imaging needles for intra-operative guidance.
- > Development of image processing techniques for automatic quantification of blood flow using optical coherence tomography.
- > Use of convolutional neural networks for segmentation of optical images.

Honours projects

Our Honours projects are closely integrated with the work of our post-doctoral researchers. Your project will form a part of one of the larger Research projects in the group, typically focused on optics hardware, software development, or clinical application of optical imaging. The PhD and Masters projects listed above give a good indication of the range of potential projects, but are adapted to a one-year Honours timeline. You are encouraged to come and talk to the head of the group, Prof Robert McLaughlin, to discuss the currently available topics.



An imaging needle for improved intra-operative guidance, developed by the Bioengineering and Imaging Lab (Prof Robert McLaughlin).

Clinical pharmacology laboratory



Lead researcher: A/Prof Betty Sallustio

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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.

For additional information see: basilhetzelinstitute.com.au

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 perhexiline 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.

Clinical pharmacogenomics



Lead researcher: Prof Andrew Somogyi

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The research that we conduct aims to improve the use of medicines and reduce their harmful effects by identifying patients with a genetic predisposition in the way they, absorb, distribute and eliminate medicines (pharmacokinetics) and how the medicine interacts with its receptor (pharmacodynamics). We have projects in acute and chronic pain opioids, drugs for depression, for transplantation, studies in Aboriginal Australians, and HIV/AIDS medicines in Papua New Guinea. We conduct drug metabolism studies using our liver biobank, pharmacokinetic studies using LC-MS and genome testing. The research group comprises Prof Andrew Somogyi, Dr Daniel Barratt and Dr Janet Coller.

For further details see: adelaide.edu.au/directory/andrew.somogyi

Research projects

> Ketamine pharmacogenetics in treatment-resistant depression

This is a NHMRC-funded clinical trial in over 200 patients in whom we are testing the efficacy and adverse effects to ketamine and through plasma concentration monitoring and genetic analysis, we will aim to identify the most important factors leading to treatment response. This research is being done in collaboration with Prof Bernhard Baune (Psychiatry).

> Pharmacogenetic studies in Aboriginal Australians

We are conducting unique studies to identify whether personalised medicine for our first peoples should be the same as Caucasians. Our initial studies indicate that a different personalised approach needs to be used in order that the medicines work better and don't cause harm. This is funded by the NHMRC and involves pharmacogenetic testing of the most common drug receptors, metabolizing enzymes and transporters in cohorts of Aboriginal Australians.

> Ancient DNA and pharmacogenetics

Genetic polymorphisms for drug receptors and metabolizing enzymes show enormous variability between different ethnicities leading to different drug dosages in specific populations. The evolution of these polymorphisms is not known. In collaboration with Prof Alan Cooper (Director Australian Centre for Ancient DNA) we are in a unique position to track the evolution of some of these polymorphisms as peoples migrated out of Africa. The project would be ideally suited to a student with Anthropology, Pharmacology and Genetics background.

> Pain genetics

Investigations into the genetic control of chronic persistent pain following surgery will allow us to identify those people who will require a different approach to post-surgical pain including the use of nonopioids. Studies will require knowledge of pain mechanisms, immunology and epigenetics.

Honours project

> Antidepressant studies with buprenorphine using mouse models of depressive-like behaviour

A recent study has suggested that the opioid buprenorphine might be a suitable antidepressant via its effect on kappa receptors. However, given that its metabolite norbuprenorphine also binds to kappa receptors, its contribution is not known and needs to be investigated.

Mucosal immunology group



Lead researcher: Dr Harshita Pant

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Our research team from ENT Surgery (Dr Pant), Centre for Cancer Biology (Prof Lopez, A/Prof Grimbaldston), Centre for Clinical and Experimental Transplantation (Prof Coates) and Chronic Inflammatory Lung Disease Research Laboratory (Prof Sandra Hodge, Dr Hai Tran) bring a unique set of skills aimed at improving the diagnosis and treatment of patients with recalcitrant mucosal inflammation and human papilloma virus associated oropharyngeal squamous cell carcinoma. Our internationally recognised research group is committed to providing a stimulating and supporting environment for our students.

Research projects

- > Systemic allergy is often absent in nasal polyp patients yet the mucosa contains abundant eosinophils, mast cells, IgE, IgG3, IgG4 and cytokines (GM-CSF, IL-3, IL-5 and IL-9). This PhD project aims to identify prognostic biomarkers and novel therapies by using our recently developed tools to modulate allergic inflammation *in vitro*, which will be assessed *in vivo* models of disease. Nasal polyps from patients with recalcitrant and severe inflammation have an accumulation of CD8 T cells with unique phenotype and function. In particular, their response to common fungal antigens is altered and is clinically associated with fungal accumulation and bone remodelling of the sinuses. This PhD project aims to investigate the nature and function of these CD8 T cells to common antigens and the effects of modulating their function on nasal polyp growth and healing in an animal model.
- > Patients with oropharyngeal squamous cell carcinoma with viral association (HPV) have a better prognosis and this is believed to be due to the effects of specific immune cells within the tumour. This PhD project aims to define the roles of specific T cells and host stromal cells in tumour growth and differentiation using *in-vitro* techniques.

Honours project

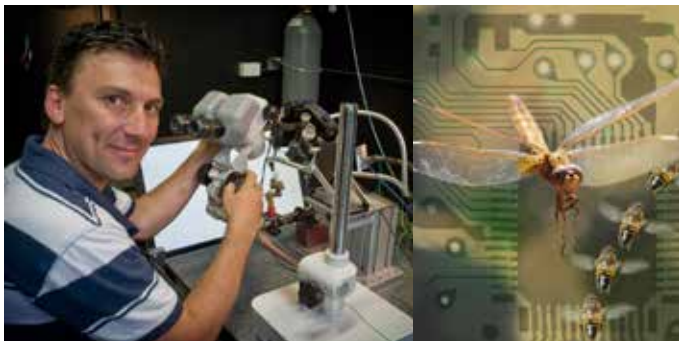
- > Tumours of the upper aerodigestive tract, eg. oropharynx, often present late and with non-specific symptoms. Early diagnosis is essential to good outcomes and improved survival. This Honours project aims to study high risk patients and compare the current standard of care for the diagnosis of oropharyngeal SCC with some novel diagnostic markers and techniques.

Visual physiology and neurobotics laboratory



Lead researcher: Dr Steven Wiederman

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Dr Steven Wiederman

Consider a human catching a ball, a dog leaping at a Frisbee or a dragonfly hunting prey amidst a swarm. Brains large and small evolved the ability to predictively, focus attention on a moving target, whilst ignoring distracters and background clutter. We use electrophysiological techniques to investigate how flying insects see the world and build autonomous robots that emulate these neuronal principles. We study this at behavioural, computational and physiological levels, with a multidisciplinary team covering fields of neuroethology, neurobiology, psychology, computer vision and engineering.

Research projects

> Target-tracking neurons in the insect visual system

Visual target detection against a cluttered, moving background is a challenging problem for any visual system, natural or artificial. We study a set of neurons from the brain of insects, which achieve this in spectacular fashion. Our most recent work suggests that the insects use sophisticated mechanisms of attention similar to those in primates, to aid in the selection of one feature even in the presence of distracters (e.g. feeding in a swarm). This project aims to explore physiological responses to single or multiple targets moving along natural trajectories, typical of pursuits in real-world environments.

We will also explore how the electrophysiological properties of these neurons (e.g. their complex receptive fields) are matched to the underlying morphology of the neurons. This project is composed of several sub-projects, suited to students with different educational and work experiences (e.g. electrophysiological recording).

> Neurobotics: active vision systems

The physiological data obtained in our laboratory feeds into our robotics projects, as we implement neuronal processing onto an autonomous platform. This project involves computational modelling or hardware development, and is therefore suited to those with mathematical or engineering backgrounds. If desired, we have collaborators in both Mechanical Engineering and Computer Vision to establish jointly supervised projects.

> Nanoscale biophotonics

We are investigating the *in vivo* application of fluorescent nanoparticles for the purpose of recording neuronal function in behaving organisms. This project combines life and physical sciences as we explore properties of the nanoparticles, the tapering of optical fibers and their interaction with nervous tissue. This project is part of the ARC Centre for Nanoscale BioPhotonics and is in collaboration with the Institute for Photonics and Advanced Sensing (IPAS).

Honours project

> Modulation of early vision by higher-order processes

The commonly accepted view is that photoreceptor and 1st order interneuron responses depend only on the intensity of the light source presented within their receptive field. That is, these early visual neurons represent changes in light in a feed-forward manner, passing this information to higher-stages of visual processing. However, in the fly's visual system there are neurons that synapse back onto the retina and lamina layers and the functionality of this neuronal architecture is yet to be completely understood. This project will explore what is currently a hot topic in neuroscience - how early sensory neurons may be modulated by higher-order processes, such as expectation and attention.

The solid cancer regulation research group



Lead researcher: Dr Paul Drew

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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 and 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.

Cancer biology and treatment

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.

> 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 and 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 and 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.

Honours project

> 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.

Colorectal cancer research group



Lead researcher: Prof Tim Price

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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.

For additional information see:

basilhetzelinstitute.com.au/research/research-theme/cancer/colorectal-cancer-research-group/

SAHMRI colorectal node

Lead researcher: A/Prof Joanne Young

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SAHMRI Colorectal Node researchers, 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.

For additional information see:

researchgate.net/profile/Joanne_Young4

Research projects

> Early onset colorectal cancer and metabolic syndrom

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.

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 DHIthSc, Yoko Tomita MBBS FRACP MSc, inset Eric Smith PhD

Research projects

> Role of aquaporins 1 and 5 in colon cancer growth, angiogenesis and metastasis

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 Prof 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. (PhD or Honours).

> **Genome-wide association studies**

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. Adaptable to both Honours and PhD projects.

> **Investigation of circulating DNA mutations in colorectal cancer (CRC)**

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. Adaptable to both PhD and Honours projects.



Western blot analysis (Hilary Dorward)

Liver metastasis research group



Lead researcher: Dr Ehud Hauben

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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.

For additional information see:

basilhetzelinstitute.com.au/profile/ehud-hauben/

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

Immunotherapy and graft-versus-leukaemia (GVL) research group



Lead researchers:

A/Prof Agnes Yong

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Dr Amy Hughes

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(L-R) Dr Amy Hughes, A/Prof Agnes Yong, Ms Jade Clarson

The Immunotherapy and GVL research group studies the mechanisms of immunogenicity of haematological cancers, and immune responses against leukaemia-associated antigens (LAAs) WT1, proteinase 3, PRAME and BMI-1, in chronic myeloid leukaemia (CML), myelodysplasia (MDS) and multiple myeloma. We aim to enhance anti-leukaemia immune responses in the setting of allogeneic stem cell transplantation with the graft-versus-leukaemia effect, or in an autologous setting targeting LAAs. We are also developing chimeric antigen receptor (CAR) T cells for myeloid leukaemia targeting leukaemia stem cells.

Research projects

> Characterisation of Interleukin-1 receptor accessory protein (IL-1RAP) monoclonal antibody in AML and CML

15-30% of CML patients fail to respond optimally despite modern therapies and 50% of AML patients relapse, with most patients dying from the disease. Persistence of leukemic stem cells (LSCs), a quiescent population within the bone marrow, is a major mechanism for disease relapse in these patients. IL-1RAP is over-expressed on the surface of candidate AML and CML LSC and is therefore a promising candidate for targeted therapy. We have developed a human IL-1RAP monoclonal antibody (mAb) and will assess the functionality of the IL-1RAP mAb to target and kill AML and CML LSCs using antibody-dependent cell-mediated cytotoxicity assays (ADCC) and colony-forming unit assays (CFUs) against AML and CML progenitor cells.

Honours projects

> Evaluation of Natural Killer Cell phenotype and immune effector function in Chronic Myeloid Leukaemia

Natural Killer (NK) Cells are effector cells in the innate immune defence against tumour and virus infected cells. As with many cancers, NK cells are decreased in Chronic Myeloid Leukaemia (CML). Low NK cell numbers and poor cytokine secretion may predict CML relapse following tyrosine kinase inhibitor (TKI) discontinuation. We will study NK cell phenotype by undertaking extensive immune-profiling of NK cell maturation/activation status and expression of cell surface receptors critical to NK cell function. In addition, NK cell cytotoxicity will be determined in newly diagnosed CML patients and following administration of TKI and/or allogeneic stem cell transplantation. We aim to investigate the prognostic significance of NK cell immune effector phenotype and function in the context of TKI discontinuation.

Leukaemia research group



Lead researchers:

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Leukaemia Research Lab, Cancer Theme, SAHMRI

The Leukaemia research group is a translational and basic research group primarily involved in research into haematological malignancy: chronic myeloid leukaemia (CML) and acute lymphoblastic leukaemia (ALL). Work in CML will provide insight into how therapy can be improved, by furthering the understanding of leukaemic cell responses to tyrosine kinase inhibitors. The ALL research is focused towards characterising the underlying biology and determining therapeutic responsiveness of a subgroup of paediatric and adult ALL patients with very high-risk disease.

For additional information see:

sahmri.com/our-research/themes/cancer/theme/theme-overview

Research projects

> Determining the prerequisites for the achievement of treatment-free remission in CML to aid the development of new therapeutic approaches

Tyrosine kinase inhibitors (TKIs) are used in the treatment of CML. Many patients will eventually achieve a stable complete molecular response (CMR) and approximately 40% of these patients can cease TKI therapy and remain in CMR, or treatment-free remission (TFR) long-term. Why the remaining 60% of patients relapse rapidly when TKI therapy is ceased remain undetermined, but likely hold the key to understanding and maximising TFR – one of the biggest challenges for CML clinicians today. The aims of this project are to determine:

1. Any difference in the quantity or quality of residual leukemic cells in patients with stable CMR who relapse when they cease TKI therapy compared to patients who achieve TFR.
2. Whether these patients have different immune responses.
3. Whether CMR and subsequent TFR are associated with specific genomic features.

> Investigating mechanisms of drug resistance, and therapeutic approaches to reverse/prevent resistance, in models of high-risk Ph-like ALL treated with targeted therapies.

Recent advances in genomic profiling have defined ALL as a heterogeneous disease with multiple subgroups. A new subtype of high-risk ALL, termed Ph-like ALL, has been identified which exhibits a gene expression profile similar to BCR-ABL1+ (Ph+)

ALL and harbors a diverse range of genetic alterations activating tyrosine kinases, but are BCR-ABL1 negative. These kinases provide therapeutic targets for which safe and active drugs are already available for clinical use. It has been demonstrated in Ph+ leukaemia that TKI therapy often results in resistance. The aims of this project are to develop in vitro and in vivo models of treatment strategies in Ph-like ALL, to understand drug efficacy, disease persistence and resistance in this subtype of ALL where current prognosis is poor.

Honours projects

> Generation of resistance to combinations of the new anti-leukaemic agent ABL001 and imatinib or dasatinib using BCR-ABL1+ cell-lines.

Phase I clinical trials for the treatment of CML are currently underway using ABL001, an allosteric inhibitor, alone and in combination with ATP-competitive tyrosine kinase inhibitors (TKIs: imatinib, nilotinib or dasatinib), to inhibit the constitutively active tyrosine kinase Bcr-Abl. Generation of resistant cell lines in the laboratory setting provides a useful tool for predicting and studying patient responses in vivo. In this project, BCR-ABL1+ cell lines will be exposed long term to gradually increasing concentrations of ABL001 in combination with dasatinib or imatinib. Mechanisms of resistance will be interrogated during resistance development and once overt resistance is observed.

Myeloma research laboratory



Lead researchers: Prof Andrew Zannettino

Contact: +61 8 8128 4390 or andrew.zannettino@adelaide.edu.au

The primary focus of the lab is multiple myeloma (MM) disease development, the second most common blood cancer that remains almost universally fatal. Key areas: the identification of genetic, transcriptional and epigenetic changes that trigger the progression from an asymptomatic condition to full MM disease; to determine why the bone marrow is a “hot-spot” for MM plasma cell metastasis. Other research: how does the skeleton control systemic glucose metabolism; identifying bone cell-derived factors that control haemopoiesis; and characterising the function a novel mesenchymal stem cell marker.

Research projects

> Characterisation of cell-surface HSC70 in Mesenchymal Stem Cells (MSC)

MSCs are characterised by their ability to differentiate into multiple cell types and to modify immune cells. Clinically, MSCs are used to repair tissues and suppress immune responses in disorders including graft vs. host disease. Immune-phenotyping has been used to identify and purify the MSC population and STRO-1 was the first antibody used to prospectively immune-select MSCs from the bone marrow (BM). STRO-1 selected BM-MSCs possess the hallmarks of pluripotent MSCs i.e. vivo quiescence, high telomerase activity and multi-lineage differentiation. We recently identified the antigen identified by STRO-1 as heat shock cognate 70, a cytoplasmic chaperone protein. The aims of this project are to determine a) how HSC70 is expressed at the cell surface, b) the role of HSC70 in BM-MSC self-renewal and differentiation, c) the cognate ligand of cell surface HSC70, and d) examine the immunomodulatory properties of HSC70.

Honours projects

> Role of MSC-secreted Chemokine-Like Factor 1 (CKLF-1) in normal haemopoiesis and B-cell development

Stromal cells of the bone marrow (BM) provide a supportive environment that is essential for normal blood cell production. Haemopoietic stem cells (HSCs) reside within specific niches in the BM and directly interact with surrounding stromal cells that provide critical survival and proliferative signals to the HSCs. Stromal cells also secrete factors that act on HSCs to direct lineage-specific differentiation. Most notably, stromal-cell secreted CXCL12 binds to its cognate receptor CXCR4 on HSCs and is essential for B-cell development. We have recently shown that Chemokine-Like Factor 1 (CKLF-1) is secreted by stromal cells and antagonises CXCL12/CXCR4 signalling. This finding suggests that CKLF-1 may play a significant role in HSC and B cell development. In this project, the role of CKLF1 in normal haemopoiesis and B-cell development will be investigated.

> RNA-editing induced truncation mutations of Sp140 in mouse myeloma cells

Multiple myeloma (MM) is a bone marrow cancer caused by the clonal outgrowth of terminally differentiated B cells called plasma cells (PCs). Patients with MM have a diverse range of mutations in different genes in their cancerous PCs, including premature termination codon (PTC) mutations of the gene encoding the nuclear antigen protein Sp140. The Zannettino laboratory recently discovered that a commonly used mouse myeloma cell line, derived from a spontaneous MM tumour in a myeloma-prone strain of mice, also has a PTC in 50% of its Sp140 mRNA transcripts. This PTC mutation is not observed at the genomic level and we now believe that it is caused by aberrant RNA-editing mediated by an Apobec cytidine deaminase enzymes. In this project, we will investigate the exact enzyme(s) and cofactor(s) responsible for this RNA editing, and will study the impact of this editing on the oncogenic properties of truncated Sp140.

> TLE1 as an oncoprotein in multiple myeloma

Multiple myeloma (MM) is a bone marrow cancer caused by the clonal outgrowth of terminally differentiated B cells called plasma cells (PCs). Many genes have dysregulated expression in myeloma PCs, and the Zannettino laboratory uses a mouse model of myeloma to model the effects of either overexpressing or knocking down/knocking out these MM candidate genes. We have observed that the expression of the transcriptional co-repressor protein Tle1 confers a dramatic growth advantage to mouse myeloma cells which is manifest both in vitro and in vivo. Global transcriptional profiling in these cells using RNASeq has identified a number of candidate gene expression changes that could be responsible for this phenotype. In this project, the exact molecular basis for the pro-oncogenic properties of TLE1 in mouse and human myeloma cells will be investigated.

Robinson research institute reproductive cancer group



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Prof Martin Oehler
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The Reproductive Cancer group seeks to understand the mechanisms involved in ovarian cancer spread, resistance to chemotherapy and the identification of novel biomarkers for detection.

For additional information see:

adelaide.edu.au/directory/carmela.ricciardelli

Research projects

> Versican as a target to inhibit cancer metastasis

Proteoglycans are major components of the extracellular and have been shown to regulate cell adhesion, cell signalling, apoptosis, migration and invasion. Increased expression of the chondroitin sulfate (CS) proteoglycan, versican in the peritumoral stromal matrix is associated with a poor outcome in many cancers, including breast and ovarian carcinoma. Although there is the accumulating in vivo evidence that versican is pivotal in promoting cancer cell metastasis in different cancer types, the means of preventing actions of versican in carcinomas have not been explored. This study we will evaluate using in vitro and in vivo cancer models whether selective versican inhibition by versican siRNA, in addition to drugs known to inhibit versican synthesis; genistein, budesonide, formoterol and montelukast, can inhibit cancer invasive behaviour and block cancer metastasis.

> Exploring ovarian cancer-peritoneal cell interactions

Ovarian cancer spreads by detaching from the surface of the ovary and attaching to and invading the mesothelium which lines the organs of the abdominal cavity including the omentum. Unlike other cancer types it rarely spreads via the bloodstream. Once the ovarian cancer cells adhere to the mesothelium, they can invade through the peritoneal cell layer and gain access to local organs, like the bowel, and form secondary tumors which eventually results in the death of the patient. A greater understanding of these processes will lead to the discovery of novel molecular targets to block this critical step of ovarian cancer metastasis. This project will identify specific alterations in the metastatic peritoneal microenvironment involved in the first steps of ovarian cancer metastasis using Maldi tissue imaging and characterise the function of key molecules using in vitro and in vivo models.

Honours projects

> The annexin A2 signalling pathway: Novel therapeutic targets for ovarian cancer

We have recently shown that annexin A2 is highly expressed in 90% of serous ovarian cancers (most common subtype) and is actively involved in the process of ovarian cancer metastasis. Several annexin A2 targeting strategies are available to either block annexin A2 function (annexin A2 peptide, annexin A2 blocking antibodies, src inhibitor to block annexin A2 phosphorylation), inhibit annexin A2 synthesis (annexin A2 siRNA, all trans retinoic acid) or block the interaction with annexin A2 interacting proteins (S100A10 blocking antibody, S100A10 siRNA and plasmin inhibitors). This project will assess the effectiveness of these inhibitors to inhibit serous ovarian cancer invasion using in vitro and in vivo models of ovarian cancer. This project will utilise a broad range of techniques including cell motility, cell invasion, western blotting, immunohistochemistry, qPCR and in vivo ovarian cancer models.

> Targeting the hyaluronan signalling pathway to overcome chemoresistance

Our recent studies have linked chemoresistance with the production of the extracellular matrix component hyaluronan (HA). We have shown that HA can increase the expression of ABC transporters in ovarian cancer cell lines expressing the HA receptor, CD44, and thereby induce resistance to the chemotherapeutic drug, carboplatin. HA-CD44 interactions have been shown to activate several signalling pathways including the P13K, MAPK and Rho K pathways. Genes of the P13K/Akt cascade have also recently been shown to induce drug resistance to cisplatin. We plan to determine whether HA treatment activates these pathways in ovarian cancer cells and if specific inhibitors of these pathways can alter ovarian cancer sensitivity to carboplatin. This project will utilise a broad range of techniques including cell proliferation, western blotting, immunohistochemistry and qPCR.

Community insights in public health research

Lead researcher: Dr Jaklin Elliott

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Our research focuses on how communities respond to and participate in healthcare, with emphasis on public health issues. We aim to ensure that the views and experiences of community members, including citizens, patients, consumers and stakeholders, are included in health research, policy, and service/treatment delivery. We use a variety of research methods, (qualitative, quantitative and deliberative methods) often through an ethical lens or with a critical stance. We collaborate widely, within the University, and more broadly with researchers, clinicians and policy makers.

For additional information see:

health.adelaide.edu.au/public-health/research/areas/cipher/

Research projects

Sarcoma has a high but predictable rate of recurrence, with most occurring within the first two years following initial treatment. Treatment typically involves surgery and/or radiation therapy. Good prognostic data is available, but there is limited data available regarding the patient experience following treatment. Current treatment follow-up screening occurs 3-monthly for two years, then 6-monthly to 5-years post-treatment, but evidence is lacking that this improves survivorship, or the impact of this on quality of life. Screening incurs costs, both for patients (anxiety levels increase at screening), and for clinicians and the healthcare system in general (use of limited clinician time and resources). This project will focus on the quality of life for patients (and families) completing treatment for sarcoma, within a private healthcare setting. This project could be tailored to meet the skills set and interests of the applicant.

Centre for Cancer Biology Cell Signalling laboratory

Lead researcher: A/Prof Yeessim Khew-Goodall

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Understanding and counteracting what drives metastasis is a major priority of this laboratory. In solid cancers, which make up 80% of human cancers, metastasis remains the main cause of patient mortality. We study metastasis in breast cancer and neuroblastoma using a range of state-of-the-art techniques, which combine molecular and cell biology, live-cell imaging, phosphoproteomics, animal models and analyses in human specimens.

For additional information see:

centreforcancerbiology.org.au/research/laboratories/cell-signalling-laboratory/

Research projects

Tyrosine phosphatase PTPN14 is mutated/under-expressed in invasive breast cancer and its loss enhances metastasis, thus implicating it as a metastasis suppressor. We have determined that PTPN14 functions as a master regulator of vesicular trafficking, a process that controls degradation versus recycling of cell surface receptors. PTPN14 regulates the phosphorylation state of protein substrates that control these processes.



PhD project

> Identification of the tyrosine kinase(s) that phosphorylate PTPN14 substrates and their role in cancer progression.

- Identify tyrosine kinases (TK) that promote cell surface presentation of receptors using a high throughput functional screen and validate identified TK candidates.
- Assay the effects of the TKs on; 1) receptor recycling and degradation, 2) ability to phosphorylate PTPN14 substrates.
- Generate TK knockout cells using a CRISPR/Cas9 targeting approach and assess effects on metastasis in breast cancers using xenograft mouse models.

Honours projects

> Investigation of candidate tyrosine kinases that regulate EGFR trafficking in breast cancer

Preliminary data in the lab has identified two kinases Brk and Fer as candidates for regulating EGFR trafficking in breast cancer cells.

1. Investigate how knock-down or over-expression of each kinase affects cell surface and total EGFR levels
2. Assay the effect of kinases on signalling down-stream of EGFR and cell growth
3. Identify which PTPN14 substrates are regulated by these candidate kinases.

> Investigate the role of the PTPN14 substrate RIN1 in endosomal trafficking

Investigate the effect of RIN1 and phospho-Y36-RIN1 (the PTPN14 regulated phospho-site) on

1. Receptor recycling and degradation,
 2. Trafficking of EGFR within endosomal compartments using immunofluorescence staining and live-cell imaging
 3. Signalling down-stream of EGFR and cell growth
- Investigate how RIN1 and specifically phospho-Y36-RIN1 affect cell surface receptors and endosomal profiles in breast cancer via immunofluorescence staining of patient specimens.

Neuroblastoma is the second most common solid tumour in children. Neuroblastomas arise from impaired differentiation of cells destined to form sympathetic neurons. The gene encoding the microRNAs miR-200a, miR-200b and miR-429 is frequently deleted in neuroblastomas. Using the targets of these microRNAs to guide us in understanding what drives metastasis in neuroblastoma, we uncovered proteins that drive cell invasiveness.

PhD project

> Identify targets of miR-200 that inhibit neuroblastoma cell invasion

A number of miR-200 targets form part of the Rho signalling pathway that regulate dynamic changes to the actin cytoskeleton, which is central to cell invasion.

- Identify Rho-GEFs targeted by miR-200b to inhibit cell migration and invasion.
- Identify downstream effectors of Rho signalling as targets for inhibiting cell invasion
- Determine whether miR-200 targets that act on different arms of the signalling network can synergise to regulate cell invasion.

Honours project

> Identify the mechanism by which miR-200a induces differentiation of neuroblastoma cells

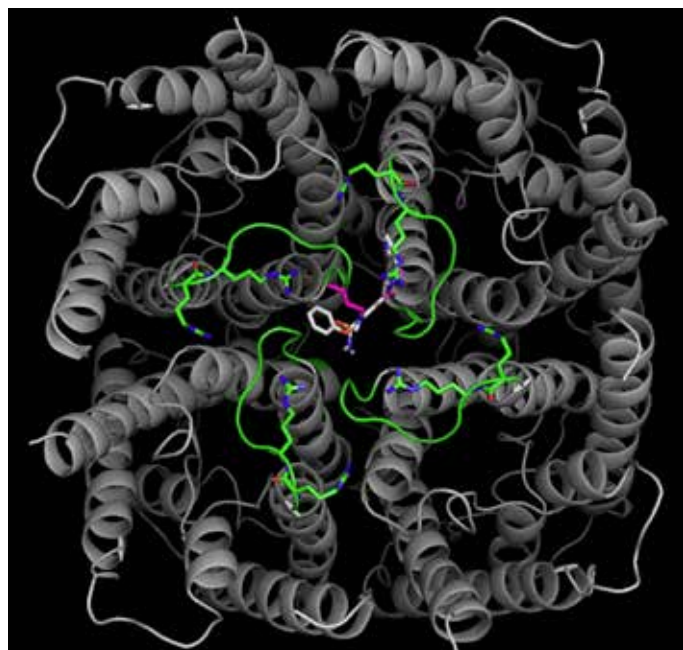
Neuroblastomas arise as a result of impaired differentiation of cells destined to form neurons of the sympathetic nervous system. As the more differentiated tumours have better prognosis, differentiation therapy is a strategy for treating neuroblastoma. We have shown that Akt phosphorylation downstream of miR-200a activates Akt and this activation is crucial to differentiation of neuroblastoma cells.

- Identify inhibitors of Akt activation that are targets of miR-200a.
- Determine whether reduced Erk activity synergises with Akt activation to promote neuroblastoma differentiation
- Determine whether activating Akt or inactivating Erk, or a combination of both, suppresses neuroblastoma metastasis in vivo.

Aquaporin physiology and drug discovery research program

Lead researcher: Prof Andrea Yool

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Docking of a novel small-molecule blocker (AqB011) at the intracellular face of the Aquaporin-1 channel, via intracellular loop domains (green) that control channel gating. (Kourghi et al., 2016. *Molecular Pharmacology* 89:133-140)

Targeting pharmacological agents to aquaporin (AQP) water channels offers new hope for treatment of cancers and brain oedema. The Yool lab focuses on the structure and function of mammalian AQPs, their role in cancer cell migration, and the discovery of novel aquaporin drugs. AQP1 channels localised at the leading edges of aggressive glioblastoma, colon and other cancer cells are essential for metastasis. AQP roles are analysed with cell culture, confocal, molecular, electrophysiology and immunocytochemistry techniques. New AQP drugs that restrain metastasis hold promise for cancer therapy.

For additional information see:

adelaide.edu.au/directory/andrea.yool

Research projects

HDR projects are customised to fit with areas of interest for students. Targeting mammalian aquaporins offers new methods for treating various cancers, as well as potential applications for intervention in brain injury, stroke, gastrointestinal, kidney and other diseases. AQP1 is localised in the leading edges of aggressive cancer cells, and its level is diagnostic of the grade of severity.

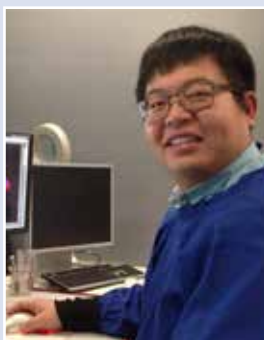
Aims to be selected based on the project of interest include analyses of:

1. molecular structures of permeation pathways,
2. sites for drug docking,
3. patterns of aquaporin AQP expression,
4. mechanisms of regulation of AQP water and ion channel activity,
5. migration assays in cancer cell lines measuring the effects of AQP modulators; and
6. (aquaporin new drug discovery and characterisation.

Ongoing collaborations with other groups nationally and internationally provide expertise in chemistry and translational work in vivo for designing and testing the new pharmacological agents.

Research projects

Honours projects focus primarily on new drug discovery using in vitro migration assays comparing AQP expressing and non-expressing cancer cell lines to measure the effects of candidate AQP modulators. Drug discovery strategies offer students opportunities to explore natural medicinal plants used in traditional Chinese and Indian alternative medicines, which are proving to be a source of novel pharmacological agents that modulate aquaporins.



“During my PhD years in the Aquaporin Physiology and drug discovery laboratory, I have really enjoyed the opportunity to learn about a wide range of research. I have experienced a very supportive and encouraging environment with the help and advice provided by my supervisors and other staff members in the school. With the benefit of multidisciplinary collaborations, I have been able to gain insight into cutting-edge areas such as confocal microscopy, live cell imaging, laser photonics and micro-structure optical fibre technology. All these invaluable experiences will allow me to find and fit into my future career successfully and quickly.”

Jinxin Victor Pei, PhD student in Physiology



Dame Roma Mitchell cancer research laboratories staff and students

Lead researcher:: Prof Wayne Tilley

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The DRMCRL is an inspiring place for young researchers wishing to delve into medical research, with strong mentoring support and access to the tools, facilities, networks and guidance necessary to embark upon a successful biomedical career. Researchers at the DRMCRL actively collaborate with local, national and international research groups and clinicians, which ensures our research is competitive on the world stage. In 2017 the DRMCRL will move into the new Adelaide Health and Medical Science building (AHMS) with state of the art research facilities.

Prostate cancer research group

Lead researchers:

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The Prostate cancer research group

The DRMCRL Prostate cancer research group actively collaborates with local, national and international research groups and clinicians, which ensures our research is competitive on the world stage. Our research program is well funded by grants from the National Health and Medical Research Council, Prostate Cancer Foundation of Australia and the US Department of Defence. The student environment within DRMCRL is exciting and fulfilling, and is an excellent base for a career in biomedical research. In 2017 the DRMCRL will move into the new Adelaide Health and Medical Science building (AHMS).

For additional information see:

health.adelaide.edu.au/medicine/drmcrl

Research projects

Our research is focused on two broad programs:

- i) Defining the molecular mechanisms of androgen receptor (AR) action in prostate cancer development and progression,
- ii) Investigating the role of microRNAs in prostate cancer metastasis and their use as potential biomarkers of disease. We utilise clinically relevant models of prostate cancer (xenografts, tissue explants, patient-derived xenografts) and cutting-edge genomic/transcriptomic/proteomic techniques in addition to classical molecular biology and biochemical approaches.

Projects:

- > Defining the role of androgen receptor splice variants and gain-of-function mutants in lethal prostate cancer
- > Defining interplay between androgen receptor and other prostate cancer-associated transcription factors.
- > Proteomic identification and characterisation of new androgen receptor co-regulators
- > MicroRNAs as mediators and markers of prostate cancer metastasis
- > Inhibiting prostate cancer metastasis using microRNA-modulating drugs



“Undertaking a PhD with the Cancer treatment toxicities group has been incredible. It has taken me all over the world to collaborate with other researchers and present at conferences. The group, and in particular my wonderful mentors, foster excellence in research in an exceedingly supportive, encouraging and friendly environment. I have been fortunate enough to conduct state-of-the-art experiments with the group, which has given me invaluable experience in the research setting, and has been crucial to my success in receiving various scholarships and funding. I could not be more grateful for the experience of conducting a PhD under the supervision of the Cancer treatment toxicities group.”

Ysabella Van Sebille, PhD candidate

Breast cancer research group



Lead researchers:

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Dr Theresa Hickey

Dr Gerard Tarulli
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Our team has a reputation for world-class research into hormonal regulation of normal breast tissue and breast cancer, with collaborations across Europe, Asia and the Americas. The DRMCRL is an inspiring place for young researchers wishing to delve into medical research, with strong mentoring support and access to the tools, facilities, networks and guidance necessary to embark upon a successful biomedical career. In 2017 the DRMCRL will move into the new Adelaide Health and Medical Science building (AHMS) with state of the art research facilities.

For additional information see:

health.adelaide.edu.au/medicine/drmcrl

Research projects

Our group investigates the genetic control of hormone action in the breast, with the aim of developing personalised breast cancer therapies. We apply clinically relevant models of breast cancer including primary human tissue, xenografts and transgenic mice. We marry these with cutting edge molecular techniques including proteomic RIME, transcriptome profiling via microarray and RNA-sequencing, ChIP-seq to map genome-wide transcription, real time PCR, Western blotting, cloning, transactivation assays, gene manipulation and expression systems. With these tools we test novel therapies that harness the powerful actions of hormones as targeted breast cancer treatments.

Projects:

- > **The dynamics of steroid receptor crosstalk between the androgen, estrogen, and progesterone receptors in breast cancer**
- > **The evidence-based application of androgen receptor antagonists and agonists to treat women with breast cancer.**
- > **Harnessing hormone action as breast cancer prevention**

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## Cancer treatment toxicities group

Lead researcher: Dr Joanne Bowen

Contact: +61 8 8313 1374 or joanne.bowen@adelaide.edu.au



Members of the Cancer treatment toxicities group

The Cancer treatment toxicities group is a partnership between four highly active research laboratories; Gastrointestinal Pathophysiology (Leader Dr Bowen); Gut Microbiome (Leader Prof Gibson), Clinical Pharmacogenetics (Leader Dr Collier) and Mucositis (Leader Prof Keefe). This collaboration brings together expertise in a wide range of techniques to conduct multidisciplinary research spanning discovery to clinical translation projects in the rapidly rising field of cancer supportive care and survivorship.

### Research projects

> Chemotherapy drugs used to treat cancer commonly cause damage to the normal gastrointestinal lining, leading to adverse symptoms such as intestinal inflammation and ulceration. There are currently no effective preventative strategies and a lack of understanding surrounding the mechanisms initiating damage. Recently, the innate immunity receptor, Toll-like Receptor 4 (TLR4), has been proposed to play a role in chemotherapy-induced gastrointestinal damage. As such, this project will investigate the effects of TLR4 gene deletion on the development of gastrointestinal inflammation in response to the chemotherapy drug, irinotecan.

*Project aims:* This project will use TLR4 knockout mice treated with irinotecan to measure effects on intestinal damage. Research techniques include; histological analysis, immunofluorescence, real time PCR and small animal handling. Results of this study will provide direct evidence of TLR4 signalling in mediating this important side effect of therapy.

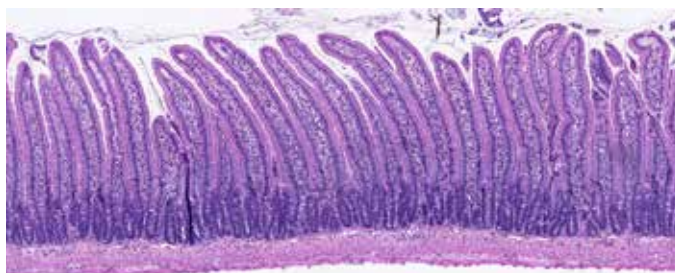
> Treatment of cancer with drugs that inhibit the epidermal growth factor receptor (EGFR) is associated with numerous unwanted side effects. One of the most common and costly side effects is diarrhoea. However, the mechanisms underpinning its development are poorly understood. Recent research has implicated EGFR signalling in the control of barrier function and healing in the gastrointestinal tract. Therefore these drugs may induce diarrhoea through dysregulation of EGFR pathways. In collaboration with Pfizer, we will uncover how their drug, dacomitinib, causes diarrhoea and explore potential therapies to prevent its occurrence.

*Project aims:* This project will investigate the mechanisms of EGFR inhibitor induced diarrhoea by using in vitro and in vivo models. Techniques will include cell culture, Ussing chambers, rat models, histopathology and immunohistochemistry. Results of this study will enhance our understanding of this important clinical toxicity and management in the future.

> Radiation treatment for cancers in the abdominal and pelvic cavity is associated with many severe side effects. We have developed a novel rat model of fractionated abdominal radiation that causes gastrointestinal injury reflecting what is seen clinically in colorectal cancer patients. It is known that acute radiation-induced injury correlates with severity of late-onset and chronic intestinal symptoms. What is poorly understood are the mechanisms that set up these later changes, or at what point is best to intervene.

*Project aims:* This project will characterise the early and late changes that occur throughout the gastrointestinal tract in response to radiation. Techniques will include immunohistochemistry, inflammatory and fibrotic assays, as well as investigating changes in intestinal microvasculature. Results of the study will inform new targets for prevention of radiotherapy-induced gastrointestinal complications.

All projects are available as both higher degree and honours. Each can be tailored to the student.



Photomicrograph of rat intestine



“Completing my PhD in the Cancer treatment toxicities group with Dr Joanne Bowen, Professor Rachel Gibson and Dr Janet Collier has been an incredibly positive experience. The support I received throughout my PhD has allowed me to become an independent and driven researcher, passionate about improving the supportive care that cancer patients receive. During my PhD I have been given many opportunities to attend large international conferences to present my research findings and collaborate with some of the leading experts within my field. The skills I have gained being a part of this research group have allowed me to pursue a postdoctoral fellowship programme in The Netherlands.”

Dr Hannah Wardill

# Cardiovascular health

## Clinical physiology of vascular function research group

**Lead researcher:** Prof John Beltrame

**Contact:** +61 8 8222 6740 or john.beltrame@adelaide.edu.au



Staff and 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.

## HIPER: Healthcare innovation, policy and evaluation research

**Lead researcher:** Prof John Beltrame

**Contact:** +61 8 8222 6740 or john.beltrame@adelaide.edu.au



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 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 policymaking to reduce unanticipated hospitalisations.

## Stroke research programme (SRP)



### Lead researchers:

Prof Simon Koblar

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A/Prof Anne Hamilton-Bruce

+61 8 8222 6411 or [anne.hamilton-bruce@sa.gov.au](mailto:anne.hamilton-bruce@sa.gov.au)



Students and staff from the Stroke research programme.

The 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).

For additional information see: [adelaide.edu.au/srp](http://adelaide.edu.au/srp)

### Research projects

#### > Dental Pulp Stem Cell (DPSC) therapy for stroke

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.

Contact: Prof Simon Koblar: [simon.koblar@adelaide.edu.au](mailto:simon.koblar@adelaide.edu.au)

#### > Npas4 and Stroke

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.

Contact: Dr Fong Chan Choy: [fongchan.choy@adelaide.edu.au](mailto:fongchan.choy@adelaide.edu.au)

#### > Proteomics of Stroke and Transient Ischaemic Attack (TIA)

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.

Contact: Prof Simon Koblar: [simon.koblar@adelaide.edu.au](mailto:simon.koblar@adelaide.edu.au)

#### > Animal Assisted Therapy (AAT) for Stroke Victims

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.

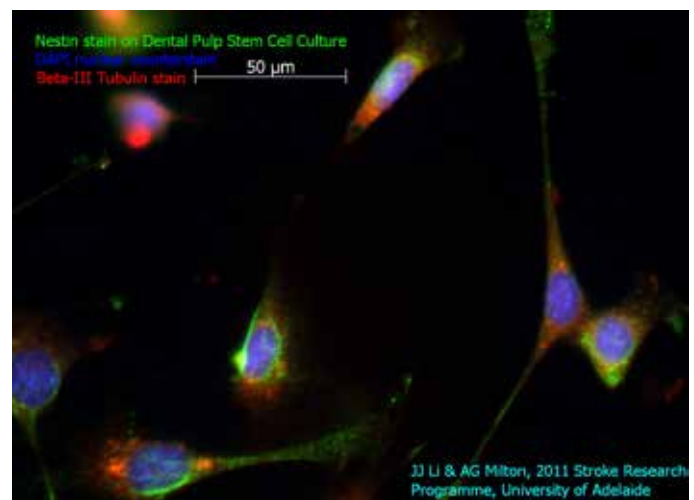
Contact: A/Prof Anne Hamilton-Bruce:

[anne.hamilton-bruce@sa.gov.au](mailto:anne.hamilton-bruce@sa.gov.au)

#### > Clinical Translation of Stroke Treatment

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

Contact: Prof Simon Koblar: [simon.koblar@adelaide.edu.au](mailto:simon.koblar@adelaide.edu.au)



Human Dental Pulp Stem Cells (DPSC)



## Northern cardiovascular research group

Lead researcher: A/Prof Margaret Arstall

Contact: +61 8 8182 9439 or [margaret.arstall@health.sa.gov.au](mailto:margaret.arstall@health.sa.gov.au)



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.

For additional information see:

[health.adelaide.edu.au/discipline-medicine/research](http://health.adelaide.edu.au/discipline-medicine/research)

### Research projects

#### Honours projects

##### > 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.

LMH

## Cardiovascular obstetric research of Northern Adelaide (CORONA)

### Lead researchers:

Prof Claire Roberts

+61 8 8313 3118 or [claire.roberts@adelaide.edu.au](mailto:claire.roberts@adelaide.edu.au)

A/Prof Margaret Arstall

+61 8 8182 9439 or [margaret.arstall@sa.gov.au](mailto:margaret.arstall@sa.gov.au)

LMH



Cardiovascular obstetric research of Northern Adelaide (CORONA) at the Lyell McEwin Hospital

CORONA is an exciting new collaboration between the cardiology and obstetrics departments at the Lyell McEwin Hospital. We are a vibrant interdisciplinary team of clinicians and basic scientists. We are passionate about reducing the risk of pregnancy complications and eliminating the burden of future premature cardiovascular disease in women and offspring through pioneering world-class clinical research. We also undertake basic cellular and molecular experiments to elucidate mechanisms that govern normal and abnormal placental development (see Placental development laboratory).

For additional information see:

[health.adelaide.edu.au/discipline-medicine/research](http://health.adelaide.edu.au/discipline-medicine/research)

### Research projects

Risk for cardiovascular disease (CVD) after pregnancy complications and the effect of lifestyle interventions. CVD accounts for 57% of global female mortality. This emphasises the need for medical and lifestyle interventions. Early detection of high risk individuals provides an opportunity to maximise the benefit of targeted interventions. It is well established that women who develop preeclampsia, gestational diabetes, deliver small for gestational age infants, deliver preterm or experience recurrent miscarriage are at increased risk of subsequent CVD. Current clinical practice does not provide a service for screening and follow up of women who experience adverse pregnancy outcomes and research to date has not investigated the benefit of early CV and metabolic risk reduction interventions following pregnancy complications. We aim to identify CV risk 1 year post-partum, provide medical and life style interventions when required and to assess the outcome of early interventions.

### Honours projects:

#### > Maternal haemodynamics in pregnancy

Supervisors: Prof Claire Roberts, Prof Gus Dekker, Dr Petra Verburg

In pregnancy, maternal organ systems undergo complex adaptations. The cardiovascular system shows an increase in blood volume and cardiac output, while mean arterial pressure and systemic vascular resistance decline. These adaptations ensure adequate placental perfusion as well as nutrient and gaseous transport to sustain fetal development. Inadequate maternal haemodynamic adaptations in early pregnancy are related to adverse pregnancy outcome. Measurements of maternal

haemodynamics may be used as part of a predictive algorithm for adverse pregnancy outcomes, including pre-eclampsia, gestational diabetes mellitus, preterm birth and small for gestational age. A prospective cohort study underway at the Lyell McEwin hospital, will assess the maternal haemodynamic profile throughout pregnancy in relation to the development of adverse pregnancy complications.

#### > **Cardiac-Obstetric Registry of South Australia (COROSA)**

Supervisors: A/Prof Margaret Arstall, Prof Claire Roberts, Prof Gus Dekker, Dr Petra Verburg

COROSA is a new collaborative between cardiology and obstetrics at the Lyell McEwin Hospital. We know that women with heart disease are more likely to have pregnancy complications but we have limited understanding about preventative and treatment options for these patients. By collecting medical and demographic information from pregnant women who have heart disease to compile an ongoing registry, important advancements may be made towards improvement in care and prevention of deterioration. Projects can be tailored to suit interests of students.

#### > **The Cardiovascular assessment after Obstetric complications**

Supervisors: A/Prof Margaret Arstall, Prof Claire Roberts, Prof Gus Dekker, Dr Petra Verburg

Follow-up For Education and Evaluation (COFFEE) study is another exciting new collaborative between cardiology and obstetrics at the Lyell McEwin Hospital. Women who experience complications of pregnancy have a much higher risk of developing cardiovascular disease. The COFFEE study aims to initiate a clinical-based postnatal programme for women who have had pregnancy complications. We have a variety of projects available with a strong emphasis on research that can be translated to clinical practice.

#### > **Maternal and child cardiovascular health after pregnancy complications**

Supervisors: Prof Claire Roberts, Prof Gus Dekker, A/Prof Margaret Arstall, Dr Prabha Andraweera

The association between adverse pregnancy outcomes and later life metabolic and vascular diseases is now well established. Women who develop preeclampsia, gestational diabetes, deliver small for gestational age (SGA) infants or deliver preterm are at increased risk of later life vascular diseases compared to women who have uncomplicated pregnancies. Emerging evidence suggests that children born of a complicated pregnancy may also be at increased risk. Few studies have shown that children born to preeclamptic women have higher blood pressure during childhood. However, the relationship between pregnancy complications and subsequent cardio-metabolic health in the mother-child pairs has not been investigated. This project aims at following up women and kids of the SCOPE pregnancy cohort to identify cardiovascular risk factors 10 years after delivery of the first child.

#### > **Renal and cardiovascular function subsequent to gestational proteinuria**

Supervisors: Prof Claire Roberts, Dr Shilpanjali Jesudason, Prof Gus Dekker, Dr Prabha Andraweera

Gestational proteinuria is defined as proteinuria of > 0.3g/d after 20 weeks gestation and disappearing 12 weeks postpartum. According to current guidelines, women with proteinuria alone are not diagnosed as having preeclampsia until they also exhibit hypertension. Pregnancy outcomes for women with gestational proteinuria alone do not differ largely from women after uncomplicated pregnancies. However, there is limited knowledge on the long term outcomes for these women. This project will compare haemodynamic parameters (peripheral and central blood pressure, cardiac output, microvascular function), renal function and renal biomarkers between women with gestational proteinuria and women who had uncomplicated pregnancies, 10 years post-partum. **The student for this project is supported by the Central and Northern Adelaide Renal and Transplantation Service (CNARTS) Honours Scholarship (\$5000).**

## PhD project

### > **Risk for cardiovascular disease after pregnancy complications and the effect of lifestyle interventions**

Supervisors: Prof Claire Roberts, Prof Gus Dekker, A/Prof Margaret Arstall, Prof Ben Mol, Dr Prabha Andraweera  
CVD accounts for 57% of global female mortality. This emphasises the need for medical and lifestyle interventions. Early detection of high risk individuals provides an opportunity to maximise the benefit of targeted interventions. It is well established that women who develop preeclampsia, gestational diabetes, deliver small for gestational age infants, deliver preterm or experience recurrent miscarriage are at increased risk of subsequent CVD. Current clinical practice does not provide a service for screening and follow up of women who experience adverse pregnancy outcomes and research to date has not investigated the benefit of early CV and metabolic risk reduction interventions following pregnancy complications. We aim to identify CV risk 1 year post-partum, provide medical and life style interventions when required and to assess the outcome of early interventions.

## Cardiovascular pathophysiology and therapeutics



**Lead researcher:** Prof John D Horowitz

**Contact:** +61 8 8222 7539 or john.horowitz@adelaide.edu.au

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.

## Honours projects

### > **Impact of BNP on stabilization and function of the myocardium**

Supervisors: 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**

Supervisors: 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**

Supervisors: 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**

Supervisors: 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.

## Vascular Research Centre

Lead researcher: Prof Stephen Nicholls

Contact: +61 8 8128 4501 or [louise.pittman@sahmri.com](mailto:louise.pittman@sahmri.com)



The Vascular Research Centre group at SAHMRI.

Our mission is to understand the factors that influence the natural history of atherosclerosis, the leading cause of death in our community. Using a range of experimental approaches, we undertake translational studies that aim to elucidate the molecular pathways that influence vascular risk, develop novel biomarkers for the assessment of cardiovascular risk and evaluate the impact of potentially protective therapies. Our studies span the spectrum from early laboratory discovery through to clinical trials and ultimately studies to determine how novel treatments are applied in clinical practice.

For further details see: [sahmri.com](http://sahmri.com)

### Research projects

#### > Revisiting the origins of macrophages in atherosclerosis, through a new paradigm of adventitial macrophage progenitor cells.

Our group has identified for the first time the existence of macrophage progenitor cells in the adventitia or outer lining of adult arteries. Current and future projects are focused on acquiring a better understanding of these adventitial macrophage progenitor cells (AMPCs), including

1. where they come from in embryonic development and how they arrive in blood vessels,
2. (how they are regulated and
3. what roles they play in normal and diseased blood vessels.

#### > Investigating the link between PCSK9 and Vascular Disease

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is an enzyme involved in the metabolism of the low density lipoprotein receptor (LDLr). PCSK9 is involved in the degradation of the LDLr in hepatocytes. High activity of PCSK9 results in elevated plasma LDL concentrations as LDL is not as cleared from the plasma as effectively. Genetic variation of PCSK9 activity have been shown to be associated with plasma LDL cholesterol concentration in humans and mice. Clinical studies have also shown that gain-of-function missense mutations of the PCSK9 gene is linked to familial hypercholesterolemia and coronary artery disease (CAD) while loss-of-function is associated with decreased CAD risk. PCSK9 is now recognised as a therapeutic target for cardiovascular disease and there are multiple ongoing clinical trials. However, there is still wide gaps in knowledge regarding the role of PCSK9 in other lipid systems.

#### > Investigation into the role of the novel lipogenesis protein TTC39B in endothelial cells and its regulation by high-density lipoproteins

The tetratricopeptide repeat domain protein (T39) has recently been shown to be a novel regulator of lipogenesis and cholesterol efflux, both key functions in the pathogenesis of atherosclerosis. Mice with deletions in T39 were found to have increased plasma high-density lipoprotein (HDL) cholesterol (the good cholesterol) and increased liver X receptor (LXR) protein (regulator of cholesterol efflux). Whether or not T39 can be regulated by HDL is however, unknown, and its role in endothelial cells is currently unexplored. This study will first determine if HDL can regulate TTC39B expression in human coronary artery endothelial cells. Then, using siRNA knockdown of TTC39B, we will determine the role of TTC39B in mechanisms of endothelial inflammation including monocyte adhesion, adhesion molecule expression and chemokine expression.

### Honours projects

#### > By what mechanisms does dietary modification improve atherosclerosis?

Dietary and lifestyle changes are the first line of treatment for conditions such as type II diabetes, obesity and a range of diseases. These changes are economically viable and unlike drug interventions, have minimal side effects. Dietary modifications also improve the burden of atherosclerosis however, the mechanisms by which this is achieved is still unknown. Whether this is due to improved lipoprotein profiles, increase functionality of the "good cholesterol" or a combination of several mechanisms remains to be determined. This study will investigate the mechanisms involved with atherosclerotic regression and improved cardiovascular risk.

#### > Investigating the role of inflammation and calcification in peripheral artery disease

Peripheral artery disease (PAD) is a blocking or narrowing of the arteries and is one of the major macrovascular complications of type 2 diabetes. Inflammation and atherosclerosis is recognized as the most direct and important cause of PAD, but acute or chronic limb ischemia may be the result of various risk factors. The role of calcification in PAD is unclear but is related to the site and location of calcification within the arterial layers. Patients with diabetes are at increased risk of macrovascular complications, particularly PAD. This project will identify the role of calcification in the progression of PAD.



## Centre for Heart Rhythm Disorders



**Lead researcher:** Prof Prashanthan Sanders

**Contact:** +61 8 8222 2723 or prashanthan.sanders@adelaide.edu.au



Prof Prashanthan Sanders, Director -  
Centre for Heart Rhythm Disorders

The Centre for Heart Rhythm Disorders (CHRD) consists of a highly experienced team of cardiologists, research scientists and allied health professionals working closely with collaborators nationally and internationally. The Centre's research program covers a broad spectrum of themes including:

- > Risk factor management for patients with cardiac arrhythmias.
- > Animal studies of arrhythmia risk factors and novel treatment pathways.
- > Integrated care management of AF.
- > Exercise interventions for patients with cardiac arrhythmias and devices.

For additional information see: [adelaide.edu.au/chrd](http://adelaide.edu.au/chrd)

### Research projects

- > **Integrated care in atrial fibrillation management**  
Supervisors: Dr Jeroen Hendriks, Dr Dennis Lau, Prof Prash Sanders
- > **Risk factor management and weight loss for patients with cardiac arrhythmias**  
Supervisors: Dr Dennis Lau, Dr Rajiv Mahajan, Dr Jeroen Hendriks, Dr Adrian Elliott, Prof Prash Sanders
- > **Exercise-based interventions for patients with cardiac devices**  
Supervisors: Dr Adrian Elliott, Dr Rajiv Mahajan, Prof Prash Sanders
- > **Mechanistic pathways associated with atrial fibrillation development and management**  
Supervisors: Dr Dennis Lau, Dr Rajiv Mahajan, Dr Adrian Elliott, Prof Prash Sanders

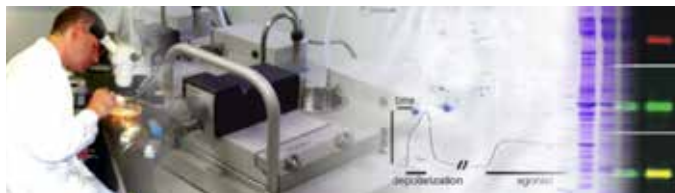
Please contact the Centre for Heart Rhythm Disorders for a full list of available projects.

### Honours projects

#### > Atrial remodelling in the athlete's heart

Supervisors: Dr Adrian Elliott, Dr Rajiv Mahajan, Prof Prash Sanders

Please contact the Centre for Heart Rhythm Disorders for a full list of available projects.



A montage of approaches used in Dr Wilson's Research Group: vascular function through molecular mechanism.

## Clinical and molecular physiology of vascular function research group



### Lead researchers:

Dr David P Wilson

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Dr Benjamin Reddi (Senior ICU consultant)  
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[robert.fitridge@adelaide.edu.au](mailto:robert.fitridge@adelaide.edu.au)

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[Joe.dawson@gmail.com](mailto:Joe.dawson@gmail.com)

Mr Stefan Court-Kowalski  
[stefan.court-kowalski@student.adelaide.edu.au](mailto:stefan.court-kowalski@student.adelaide.edu.au)



Dr David P Wilson

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, acute vasospasm and hypertension. A new project explores the value of a novel matrix metalloproteinase inhibitor in managing the progression of abdominal aortic aneurysm. The research team is involved in both preclinical, basic research, and translational research using a three-pronged approach, which includes:

- > Clinical characterisation of vasomotor disorders
- > Discovery of underlying molecular mechanisms
- > Exploring novel therapies in basic and clinical studies.

For additional information see:

[adelaide.edu.au/directory/david.p.wilson](http://adelaide.edu.au/directory/david.p.wilson)

### Research projects

- > **Molecular mechanisms regulating vasodilatation in septic shock**
- > **Novel strategies to improve vascular tone in the hypotensive critically ill patient**
- > **The molecular basis for heterogeneous vasomotor responses in human and animal models**
- > **Acute vasospasm: novel strategies to limit vascular calcium entry and calcium sensitisation in the vasculature**
- > **Reactive oxygen species: the molecular basis for altered calcium sensitivity in skeletal and cardiac muscle**
- > **NEW Project- Exploring the role of a novel matrix metalloprotease inhibitor in a preclinical model of Abdominal Aortic Aneurysm- contingent on funding**

## Honours projects

- > **Molecular mechanisms regulating vasodilatation in septic shock**
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## Pulmonary vascular gene and cell therapy unit

UA/RAH

### Lead researchers:

Prof Paul Reynolds  
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Dr Rebecca Harper  
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The Vascular Research Centre group at SAHMRI.

Our work is aimed at developing gene and cell therapies to combat pulmonary vascular disease such as pulmonary arterial hypertension (PAH). We use endothelial progenitor cells (EPCs) as a vehicle to deliver a gene of interest to the pulmonary endothelium to cure PAH in a pre-clinical model. We are now moving on to develop this therapy for direct clinical application using silicon nanowire technology, as well as investigate the molecular pathways that are altered as a result of our treatment. Additionally, we are investigating exosomes as the mechanism of the therapeutic effect seen.

For additional information see:

[www.rahresearchfund.com.au/rah-research-institute/researchers](http://www.rahresearchfund.com.au/rah-research-institute/researchers)

## Research projects

- > **Exosome characterisation from EPCs and investigation of potential therapeutic effects in a pre-clinical PAH model**  
Isolate, characterise and use exosomes derived from EPCs as a therapy in pre-clinical PAH models. Examine their cargo and potential for acting as a vehicle to deliver a gene of interest.

## Honours projects

- > **EPC manipulation via Silicon Nanowire technology**  
Utilising the nanowire technology at the Cell Manufacturing CRC, we are developing a clinically safe method for inserting a gene of interest into the EPCs. Optimisation of the nanowires will involve assessing the length, shape and diameter that will give the best transfer of the gene into the cells without affecting their viability, and allowing them to be lifted off the wires and injected safely into humans.
- > **Culture of EPCs from peripheral blood samples of patients with PAH**  
Developing a strategy to successfully culture EPCs from patients with PAH, with the focus on assessing their function against EPCs

from healthy controls, before and after the up-regulation of a gene of interest. The ultimate goal of this project is to develop a strategy for autologous cell therapy in humans.

- > **Bio-distribution and dosage studies of intravenously injected EPCs and exosomes derived from EPCs in a pre-clinical model**  
Developing a stable EPC line which expresses luciferase (a reporter gene) and use these to intravenously inject into animals to conduct a bio-distribution study, time-course of gene expression and dosage response using a live animal imager.
- > **Exosome characterisation from EPCs and investigation of potential therapeutic effects in a pre-clinical PAH model**  
Isolate, characterise and use exosomes derived from EPCs as a therapy in pre-clinical PAH models. Examine their cargo and potential for acting as a vehicle to deliver a gene of interest.
- > **Assess the molecular mechanisms that are involved in the reversal of PAH to better understand the pathophysiology of disease**  
Using proteomic and gene analysis tools to investigate the relevant molecular pathways involved in PAH pathogenesis.

## Extracellular matrix laboratory

UA/RAH

**Lead researcher:** Dr Mark Gibson

**Contact:** +61 8 8313 5337 or mark.gibson@adelaide.edu.au



Research students in the ECM lab

This lab has focused on the molecular assembly of elastic fibres and on the role they play in growth factor regulation. This process becomes aberrant in incurable fibrotic diseases involving major organs such as heart, lung, kidney and liver and genetic diseases such as Marfan syndrome. Currently Dr Gibson's lab is investigating the role of elastic fibre-associated Latent TGF-beta Binding Proteins (LTBPs) in cellular and tissue models of fibrosis and fibrotic diseases.

For additional information see:

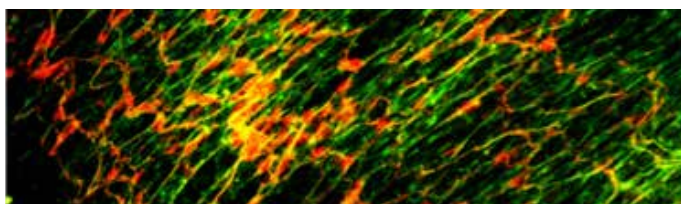
[researchers.adelaide.edu.au/index.php/profile/mark.gibson](http://researchers.adelaide.edu.au/index.php/profile/mark.gibson)

## Research projects

Fibrosis causes incurable, fatal disease in heart and other organs and contributes to 45% of all deaths. Fibrosis is complex with activation of growth factor TGF- $\beta$  central to the process. Inactive TGF- $\beta$  is stored in matrix on elastic fibres and is activated by tissue damage. A current focus is the function of elastic fibre component LTBP-2, which is highly expressed in fibrotic tissues and upregulates TGF- $\beta$ . Research includes a) expression patterns and localisation of LTBP-2 with key molecules in cellular fibrosis models; b) how LTBP-2 upregulates TGF- $\beta$  in cells via cell receptors and signalling pathways; c) the significance of LTBP-2 inactivation of growth factor FGF-2, a potent regulator of TGF- $\beta$  and fibrosis. We can tailor a project to suit a student's background, skills and aspirations. Techniques: confocal microscopy; cell culture; protein, DNA and RNA analysis, quantitation and purification; molecular binding assays and knock-downs; QPCR; r-protein production and mutagenesis etc.

## Honours projects

Fibrosis causes incurable, fatal disease in heart and other organs and contributes to 45% of all deaths. Fibrosis is complex with activation of growth factor TGF- $\beta$  central to the process. Inactive TGF- $\beta$  is stored in matrix on elastic fibres and is activated by tissue damage. A current focus is the function of elastic fibre component LTBP-2, which is highly expressed in fibrotic tissues and upregulates TGF- $\beta$ . Research includes a) expression patterns and localisation of LTBP-2 with key molecules in cellular fibrosis models; b) how LTBP-2 upregulates TGF- $\beta$  in cells via cell receptors and signalling pathways; c) the significance of LTBP-2 inactivation of growth factor FGF-2, a potent regulator of TGF- $\beta$  and fibrosis. We can tailor a project to suit a student's background, skills and aspirations. Techniques: confocal microscopy; cell culture; protein, DNA and RNA analysis, quantitation and purification; molecular binding assays and knock-downs; QPCR; r-protein production and mutagenesis etc.



Confocal localisation of matrix components in fibrotic tissue

## Complex medication research group



**Lead researcher:** Prof Sepehr Shakib

**Contact:** +61 411 100 278 or sepehr.shakib@adelaide.edu.au

This research group explores real life research questions faced by health care practitioners involved in multidisciplinary research and management of patients. The scope of this group is quite large ranging from frail hospital inpatients, and multi-morbid outpatients to complex electronic decision support tools. The research is all clinical, involved the disciplines of medicine, pharmacy, nursing, and allied health, as well as epidemiology, statistics and health economics.

### Research projects

#### > The impact of system design in improving medication safety with electronic prescribing

This research project will involve the assessment of decisions made with SA Health's EPAS Electronic health record program, and will evaluate the impact of these decisions in improving medication safety.

Electronic prescribing is being rolled out to many public hospitals, and the design decisions regarding the choice of drop down menus, defaults, alert etc will have a dramatic impact on the prescribing patterns of users. The aim of this research will be to concentrate on a number of high risk or high visibility projects and to evaluate the impact of design changes on outcomes.

#### > The impact of a multidisciplinary service on the outcomes of patients with multiple chronic diseases

Multi morbidity is becoming increasingly common, with patients increasingly having not one but multiple chronic diseases. This research project will evaluate outcomes associated with a novel multidisciplinary holistic service for the management of patients with multiple chronic disease at the Royal Adelaide Hospital.

The research will include data analysis, patient interviews and surveys, as well as assessment of health outcomes e.g. hospitalisation, mortality.

## Vascular research group



**Lead researcher:** Prof Robert Fitridge

**Contact:** +61 8 8222 7711 or robert.fitridge@adelaide.edu.au



Research students in the ECM lab

The Vascular 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).

## Vaccinology and immunology research trials unit



**Lead researcher:** Helen Marshall

**Contact:** +61 8 8161 8115 or helen.marshall@adelaide.edu.au



Associate Prof Helen Marshall.  
Director, Vaccinology and immunology research trials unit

The Vaccinology and immunology research trials unit is a team of doctors, nurses, scientists and research staff who all specialise in immunisation and infectious disease research and clinical trials. Located in the Department of Paediatrics at the Women's and Children's Hospital (WCH), VIRTU undertakes Research projects aimed at improving prevention of infectious diseases and optimising vaccine programs and policy. VIRTU is affiliated with The Robinson Research Institute, School of Medicine, University of Adelaide, SAHMRI, and is part of a national vaccine research network within Australia.

For additional information see:

[adelaide.edu.au/directory/helen.marshall](http://adelaide.edu.au/directory/helen.marshall)

### Research projects

#### > PARIS

Currently, very little is known about the burden of respiratory illnesses during pregnancy for Australia women. This study will investigate the causes and frequency of acute respiratory infections during pregnancy using participant diary cards and self-collected nasal swabs. The study will also examine the impact of these illnesses on infant health.



### > Systematic reviews

Many topics are available for systematic reviews to evaluate the current knowledge and level of evidence available to support vaccine programs and policy decisions. We are currently undertaking a systematic review of the safety of vaccination during pregnancy.

### > OptiMum

This study aims to investigating the impact of obesity on immune responses. Several projects are planned to evaluate immune responses following influenza vaccination in various populations such as pregnant women and adolescents.

### > PAEDS

This study involves active surveillance for vaccine preventable diseases, including a NHMRC partnership grant to explore why children are still hospitalised with vaccine preventable diseases.

### > FluMum

FluMum is a national NHMRC funded study which aims to assess the effectiveness of flu vaccination during pregnancy for preventing infant influenza illness.

### > Prevalence and predictors of influenza vaccination uptake in women with high risk medical conditions

Influenza vaccine is recommended and nationally funded for all people aged six months with high risk medical conditions. Uptake of the vaccine in pregnant women with high risk medical conditions is not systematically monitored in Australia. The aim of this project is to determine vaccine coverage in this group and develop and implement strategies to improve protection against influenza infection for pregnant women with high risk medical conditions. This study will use quantitative data collected as part of national study to explore the prevalence along with the motivators and predictors of influenza vaccination in women with high risk medical conditions who are recommended to receive the annual influenza vaccine.

## Honours projects (clinical):

### > Validity of hospital discharge coding to identify children with high risk medical conditions

The evidence generated by administrative hospital data can be used to determine health outcomes and changes in practice and policy and more increasingly through data linkage, to evaluate impacts on broader aspects of children's lives such as education and development. This study aims to assess the accuracy of hospital discharge coding to identify children with high risk medical conditions.

### > Health-related quality of life in children with high risk medical conditions

For a child, a high risk medical condition, or a diagnosis of one, often leads to a significant change in lifestyle for the affected child or teenager and their family. High risk medical conditions can affect many aspects of the lives of children with consequences that continue into adulthood and it is not surprising; therefore, that children with a high risk medical condition would have a reduced health-related quality of life. This study will use quantitative data to explore quality of life in children with high risk medical conditions from parental perspective. There is scope within this project to focus on particular disease groups such as diabetes.

### > Motivations and experiences of participating in paediatric clinical research

Clinical trials are research investigations that use human subjects to contribute to knowledge that can be applied to benefit society. Little is known about the factors that influence willingness to participate in vaccine trials, particularly for children. Designing strategies that enhance vaccine trial recruitment and retention are critical and developing informed consent processes and standards of care have ethical implications. This study will use qualitative and quantitative research methodologies to explore the motivators, social-demographic profile and experiences of participating in clinical trials in the VIRTU, located in a major paediatric hospital.

# Fertility and conception

## Reproductive immunology laboratory

**Lead researcher:** Prof Sarah Robertson

**Contact:** +61 8 8313 4094 or [sarah.robertson@adelaide.edu.au](mailto:sarah.robertson@adelaide.edu.au)



Reproductive immunology laboratory, Robinson Research Institute

The female immune system supports survival and growth of the fetus, with immune system dysregulation leading to pregnancy disorders such as recurrent miscarriage and preterm birth. Seminal fluid, delivered to

the female reproductive tract at coitus, provides signalling molecules which allow the female immune system to set up in preparation for pregnancy. We investigate how these signalling molecules influence cytokine expression and immune cell phenotypes in the uterus to understand how incorrect immune activation causes poor embryo growth, placental development and reproductive outcomes.

For additional information see:

[adelaide.edu.au/robinson-research-institute/researchers/group-leaders/robertson](http://adelaide.edu.au/robinson-research-institute/researchers/group-leaders/robertson)

## Honours projects

### > Novel toll-like receptor mechanisms of sperm signalling in the female reproductive tract

*Supervisors: Prof Sarah Robertson, Dr John Schjenken, Dr David Sharkey*

Seminal fluid delivered to the female reproductive tract at coitus interacts with epithelial cells on the cervix and uterus to induce cytokines and chemokines which are required for the female immune system to adapt for pregnancy. Sperm play an important role in signalling to the female tissues to elicit this response, however the specific mechanism remains undefined, although TLR4 is implicated. This project will employ TLR4 knockout mice

to identify the role that TLR4 signalling pathways play in sperm signalling. Techniques utilised will include quantitative PCR, luminex bead array, immunohistochemistry and in vitro based models using cultured human cervical cell lines. Findings will help us understand the induction of the maternal immune response that allows successful pregnancy and why some men have reduced fertility.

> **T regulatory cell stability and plasticity in immune tolerance during early pregnancy**

*Supervisors: Prof Sarah Robertson, Dr Lachlan Moldenhauer*  
Treg cells are heavily involved in the establishment of maternal immune tolerance towards paternally derived antigens expressed by the embryo, this tolerance is required for pregnancy success. The aim of this project is to investigate, in mice, how signalling molecules in seminal fluid act on the female Treg cell population after mating. In particular the importance of seminal plasma TGFβ and the role of male MHC antigens in semen will be investigated. The project will employ cytokine knockout mice, flow cytometry and quantitative RT-PCR. The findings will help us understand the induction phase of the maternal immune response permitting successful pregnancy, and have broader relevance to the transmission of STDs and immune-mediated pathologies linked with infertility.

> **Macrophage regulation of preterm birth**

*Supervisors: Prof Sarah Robertson, Dr Loretta Chin, Dr Lachlan Moldenhauer*  
The gestational tissues contain many macrophages throughout pregnancy and are implicated in controlling the timing of birth, including preterm birth, which affects ~10% of pregnancies. Our recent studies suggest that anti-inflammatory M2 macrophages exert potent immune suppressive functions up until pregnancy reaches term, in order to prevent the pro-inflammatory immune response that drives labour. Using transgenic mice to specifically delete macrophages, this project aims to investigate the roles of macrophages during late gestation, including their role in the timing of labour and preterm labour. This includes how macrophages control other immune cell populations including Treg cells, NK cells and Th17 cells that are involved in the timing of labour. Techniques will include quantitative RT-PCR, immunohistochemistry and flow cytometry.

> **MHC disparity and placental vascular supply**

*Supervisors: Prof Sarah Robertson, Prof Claire Roberts*  
MHC disparity between paternal and maternal genomes in pregnancy is beneficial to fetal growth and pregnancy success. This is linked with activation and expansion of maternal Treg cell populations that support pregnancy. As well as inhibiting cytotoxic immunity towards the conceptus tissue, these T cells may help to promote placental development and robust access to the maternal blood supply. To investigate the role of T cells in placental development and transformation of maternal decidual vessels, this project will utilise wildtype and T cell-deficient female mice mated with males of varying genetic backgrounds. The effects of T cell deficiency in different genetic mating combinations will be determined by comparing pregnancy outcomes such as litter size and placental development. Techniques in the project will include immunohistochemistry and quantitative RT-PCR.

> **The effect of maternal anti-viral immune responses on reproductive success**

*Supervisors: Dr Kerrilyn Diener, Prof John Hayball, Prof Sarah Robertson*  
Viruses such as cytomegalovirus and Zika virus are known to affect fetal development. Dr Kerrilyn Diener, in collaboration with Prof Sarah Robertson and Prof John Hayball, are interested in

understanding how the maternal immune response to such viral infections during pregnancy can impact on reproductive outcomes. Of particular interest is dissecting out how the maternal innate immune response can change immune and neurodevelopment in the fetus such that offspring exhibit altered immune responses and behavioural abnormalities upon further immune challenges after birth. For further information see: [www.adelaide.edu.au/directory/kerrilyn.diener](http://www.adelaide.edu.au/directory/kerrilyn.diener).

> **The role of HMGB1, a damage-associated molecular pattern (DAMP), in neonatal sepsis**

*Supervisors: Dr Kerrilyn Diener, Prof John Hayball, A/Prof Michael Stark, Dr Nicki Hodyl*  
Sepsis, an overwhelming infection, remains a leading cause of death in both adult and neonatal intensive care units, with preterm babies being particularly vulnerable to hospital-acquired infections. Dr Kerrilyn Diener, in collaboration with Prof John Hayball, A/Prof Michael Stark and Dr Nicki Hodyl are investigating how high-mobility box group 1 (HMGB1) potentiates disease. Building on previous studies performed with adult human samples and adult mouse models of disease, we aim to continue development of a passive antibody treatment for septic neonates that will increase survival and reduce the long term morbidity often observed in survivors of neonatal sepsis. For further information see: [adelaide.edu.au/directory/kerrilyn.diener](http://adelaide.edu.au/directory/kerrilyn.diener)

> **The role of mir-155 during the periconception period of pregnancy**

*Supervisors: Prof Sarah Robertson, Dr John Schjenken, Dr David Sharkey*  
Immune adaptation occurs in the female reproductive tract after coitus to generate T regulatory (Treg) cells which mediate tolerance towards paternally-derived antigens and allow embryo implantation. Various molecules regulate this immune response, including small non-coding microRNAs (miRNA), which downregulate target expression. Recently we identified an important Treg cell miRNA, miR-155, is induced following coitus and may play a role in the generation of Treg cells in early pregnancy. Using miR-155 knockout mice this project aims to determine the role of miR-155 during pregnancy. Techniques utilised include quantitative miRNA assays, quantitative PCR, luminex bead array and immunohistochemistry. This study will help us understand the role of miRNAs in immune regulation during pregnancy.

## Reproductive biotechnology group



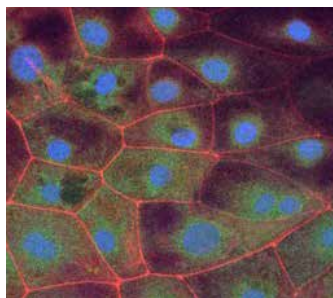
**Lead researcher:** A/Prof Mark Nottle

**Contact:** +61 8 8313 4087 or [mark.nottle@adelaide.edu.au](mailto:mark.nottle@adelaide.edu.au)

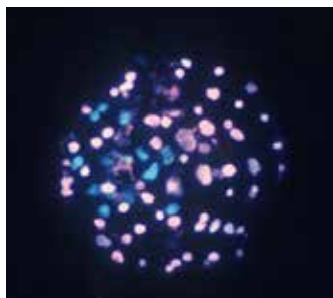
The Reproductive Biotechnology group has an international reputation in the general areas of reproductive biology and the development of associated technologies for biomedical and agricultural applications. Current work is increasingly focused on embryonic stem cells and their therapeutic applications. We also undertake research on improving human assisted reproduction outcomes and the development of reproductive technologies for the animal industries. Honours and PhD and Masters projects are available in these general areas many of which also provide industry experience.

For further information see:

[adelaide.edu.au/directory/mark.nottle](http://adelaide.edu.au/directory/mark.nottle)



**Pig blastocyst.** By adding factors to maturation media we may be able to double the number of inner cell mass (blue) cells which give rise to the fetus which may allow us to collect immature eggs and mature these in vitro without the need for hormonal stimulation in patients.



**Porcine retinal epithelial cells produced by directed differentiation of porcine ESCs.** Similar cells derived from human ESCs are in early trials.

## Research projects

### > Development of a new embryonic stem cell type for human cell therapies

Human embryonic stem cells (ESCs) offer considerable promise for curing a range of intractable diseases such as Type 1 diabetes and injuries such as those to the spinal cord, which constitute a significant health burden estimated to cost billions of dollars globally. We have isolated a new embryonic stem cell type from an earlier stage in embryo development than that currently used. These cells have been extensively characterised and may have advantages in terms of the development of cell based therapies. Several projects are offered in this general area. These range from isolating our cell type in other species to the development of differentiation protocols for producing cell types for various treatments. Students will receive experience in a variety of areas from cell and molecular biology to embryology.

### > Improving human IVF outcomes

We have pioneered the ability to mature pig oocyte or eggs in vitro to generate embryos for research applications. In collaboration with other researchers from the Robinson Institute current research is focused on extending this to other livestock species as well as to humans to overcome the need for patients to monitor their cycle and undergo hormonal stimulation during IVF. Projects will examine the effects of various hormones, growth factors and cytokines present in the prevulatory follicle can have on in vitro oocyte maturation and embryo development following their addition to maturation media. Students will receive experience in a variety of areas from cell and molecular biology to embryology.

### > Using single nucleotide polymorphisms to reduce early embryonic loss.

The Australian sow ovulates around 22 oocytes but only has a litter size of 11. In collaboration with Stefan Hiendler from the School of Animal and Veterinary Sciences and support from Industry we are examining whether single nucleotide polymorphisms (SNPs) in imprinted genes involved in reproduction can be used as selection markers to reduce this loss by examining differences between European and Chinese breeds. Early results have proven extremely promising and we are looking to extend this work to other species as well as humans in an attempt to overcome early miscarriage. Students will receive hands on experience in range of molecular techniques as they identify prospective SNPs.

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## Molecular immunology

WCH

**Lead researcher:** A/Prof Simon C Barry

**Contact:** +61 423 771 246 or [simon.barry@adelaide.edu.au](mailto:simon.barry@adelaide.edu.au)

We are a molecular biology lab interested in the maintenance of balance in the immune system. We are using genome wide approaches to understand the gene regulation networks required to maintain immune tolerance, and what changes arise in these networks when autoimmune disease occurs. A key player in immune tolerance is the regulatory T cell, and it is dependent on the transcription factor FOXP3 for formation and function. We are examining how FOXP3 controls other genes to establish function, and the role of enhancers in enforcing the regulatory phenotype.



A/Prof Barry

## Research projects

### > The molecular basis of regulatory T cell function in health and disease

The objective of this PhD project is to apply state-of-the-art genomics to fine map the chromatin landscape in children who develop type 1 diabetes. We aim to reveal for the first time how genetic risk and epigenetic landscape combine to trigger progression in some but not all children at risk of type 1 diabetes. In particular we will interrogate a set of key immune cells using three complementary genomic techniques to fully map the gene regulation networks in type 1 diabetes impacted by genetic risk. We will define the regions of the genome that are actively driving gene expression by combining:

1. a new high resolution chromatin accessibility analysis named ATAC seq.



- > Immunotherapy using engineered T cells

To do this we will use these molecular tools:

- With these tools we will test the engineering of:

- In vivo T cell selection occurs in the thymus and this selection process requires exposure of T cells to antigens presented on MHC class 2, and the affinity and avidity of the engagement with the MHC complex determines whether that T cell is selected to survive or not. The microenvironment of the thymus contains all of the signals, cytokines and cell to cell interactions to shape the normal immune repertoire, but this has not yet been modelled in 3D *ex vivo*.

Heatmap showing the expression of 100 genes across 10 cell lines. The genes are grouped into 10 clusters (A-J) based on hierarchical clustering. The color scale ranges from -2 (blue) to 2 (red).

Gene list (from top to bottom):

- CCNA4
- CCNA9
- CCNA10
- CCNA11
- CCNA12
- CCNA13
- CCNA14
- CCNA15
- CCNA16
- CCNA17
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- CCNA98
- CCNA99
- CCNA100

High resolution image of a human T cell

Differential gene expression analysis from human regulatory T cell

## Diabetes research group



**Lead researcher:** Prof Jenny Couper

**Contact:** +61 8 8161 6424 or [jennifer.couper@adelaide.edu.au](mailto:jennifer.couper@adelaide.edu.au)



**Members of the ENDIA study team based at the Women's and Children's Hospital**

The incidence of type 1 diabetes (T1D) has increased worldwide, particularly in younger children and those with lower genetic susceptibility. These observations indicate that the modern environment may play a role in initiating and accelerating of the autoimmune process that leads to the destruction of insulin-producing beta cells. The Environmental Determinants of Islet Autoimmunity (ENDIA) Study is investigating candidate environmental exposures and gene-environment interactions that may contribute to the development of islet autoimmunity and T1D.

For further details see: [endia.org.au](http://endia.org.au)

## Honours project

Early infant feeding practices and the composition of the infant diet may have relevance to T1D risk. The ENDIA Infant Feeding Diary has been custom designed to capture dietary information from birth until 12 months of age. It is intended to be completed by the infant's primary caregiver weekly using a smartphone app. The aim of this honours project is to evaluate the validity of the ENDIA Infant Feeding diary by comparison with weighed food records at 6, 9 and 12 months of age. The candidate will design the study, recruit participants, administer the investigation, and analyse the results. This will require the use of the software Foodworks for calculating food composition data. The project will be undertaken within the NHMRC/JDRF Centre of Research Excellence for the Protection of Pancreatic Beta Cells led by Prof Jenny Couper.

# Frailty mobility and bone health

## Mesenchymal stem cell laboratory

Lead researcher: Prof Stan Gronthos

Contact: +61 8 8128 4395 or stan.gronthos@adelaide.edu.au



Mesenchymal stem cell laboratory

Postnatal mesenchymal stem cells (MSC) derived from connective tissues are capable of developing into multiple cell lineages (myelosupportive stroma, adipocytes, smooth muscle cells, myoblasts, ligament cells, chondrocytes and osteoblasts). Our Lab examines the transcriptional, epigenetic and signalling factors that regulate MSC self-renewal, proliferation, multi-differentiation and immune cell modulation. These molecular processes are being investigated as underlying mechanisms mediating tissue repair, inflammation, tumour cell development and aged related diseases.

For additional information see:

[adelaide.edu.au/directory/stan.gronthos](http://adelaide.edu.au/directory/stan.gronthos)

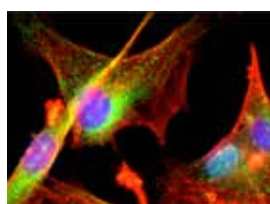
[sahmri.com/our-research/themes/cancer/groups/mesenchymal-stem-cell-research-group](http://sahmri.com/our-research/themes/cancer/groups/mesenchymal-stem-cell-research-group)

### Research projects

- > Twist-1 inhibits mesenchymal stem cell osteogenic differentiation through suppression of the tyrosine kinase receptor, c-ros-oncogene 1 (c-ros-1 kinase)
- > The role of ephrinB1 in osteoblast maturation function and communication with osteoclast
- > Hydroxymethylation of DNA regulates mesenchymal stem cell self-renewal, proliferation and cell fate determination

### Honours projects

- > Identification of Twist-1 regulated microRNAs, which control cranial bone development in children
- > Investigating the role of ephrinB1 during tooth formation
- > Investigation of the importance of ephrinB1 in bone and cartilage development
- > Epigenetic regulation of mesenchymal stem cell bone and cartilage cell differentiation via H3K9 methylation



Mesenchymal stem cells

## The clinical autoimmunity and inflammation research group

Lead researchers:

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A/Prof Vidya Limaye

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Dr Pravin Hissaria

+61 8 8222 3471 or pravin.hissaria@sa.gov.au



Dr Pravin Hissaria, A/Prof Susanna Proudman and A/Prof Vidya Limaye (left to right)

The Clinical autoimmunity and inflammation research group undertakes research into the aetiology and outcomes of autoimmune diseases through the study of well-characterised patient cohorts. Studies of biological samples paired with clinical data, aim to discover and validate novel biomarkers of disease. A/Prof Proudman's research focuses on recent onset rheumatoid arthritis and systemic sclerosis, with Dr Hissaria. A/Prof Limaye's research focus is inflammatory muscle disease with an emphasis on autoantibodies.

### Research projects

#### > Recent onset rheumatoid arthritis

- Examination of the clinical and biochemical effects of fish oil in patients with rheumatoid arthritis.
- Models for predicting outcomes of treat-to target therapy including pharmacogenetics.
- Association with periodontal disease

#### > Systemic sclerosis

- Studies of complications such as calcinosis and gastrointestinal disease.
- Collaborative studies looking at the cellular mechanisms of fibrosis and vasculopathy, which are the principal pathophysiologic mechanisms responsible for disease manifestations such as pulmonary arterial hypertension.

#### > Inflammatory muscle disease

- Studies of the epidemiology, clinical, serological, and genetic features of inflammatory muscle disease, as well as the role of the innate immune system in myositis

## Bone and joint



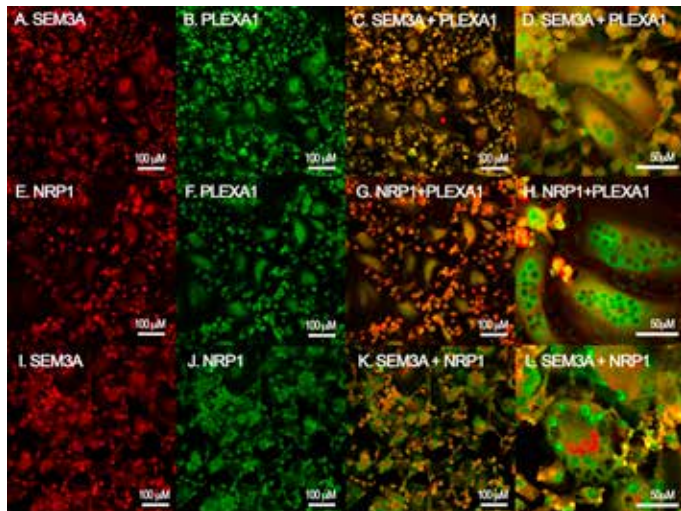
### Lead researchers:

Prof David Haynes

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Dr Melissa Cantley

+61 8 8313 3180 or melissa.cantley@adelaide.edu.au



Immunofluorescence labelling in human osteoclasts by honours student Sylvia Saad, published in S Sadd et al *Acta biomaterialia* 30, 311-318, 2016.

Our group investigates ways of manipulating bone metabolism to treat bone pathologies based on our understanding of the mechanisms of bone loss in rheumatoid arthritis, periodontal disease and orthopaedic implant related bone loss. We have developed animal models to all these diseases and in vitro assays to investigate the mechanisms in detail. Human mesenchymal stem cells, osteoblasts, osteocytes and osteoclasts are routinely used. We also have access to an array of unique drugs (e.g. epigenetic regulators of cells) and novel biomaterials. Projects in areas relating to these may be possible.

For additional information see:

[health.adelaide.edu.au/anatomy-pathology/research/](http://health.adelaide.edu.au/anatomy-pathology/research/)

### Research projects

- > Periodontal disease (PD) is the most common bone loss pathology. There are very few treatments available and PD is associated with many other significant diseases, such as, cardiovascular disease. Stem cells (SC) have been recognized as a potential therapy to many diseases where damaged tissue needs repair. Our approach in this proposal is different whereby epigenetic manipulation of stem cells at the sites of tissue damage is used to maintain and develop endogenous SC to promote repair. Histone deacetylation (HDAC) is a very important way we modify gene expression that does not involve changes in nucleotide sequences. Modulation of these enzymes using HDAC inhibitors is emerging as an effective treatment for a wide variety of diseases. This project aims to extend the current work on catabolic bone pathology in PD to investigate the regulation of HDAC in bone healing by SC. Aim: To determine if inhibition of HDACs can enhance stem cell numbers in vitro and/or in an animal model.  
Successful osteointegration of orthopaedic implants after surgery is a significant issue particularly in our aging population. Hence it is important to develop materials that can provide the ideal natural environment for bone cells to develop. Hydroxyapatite (HA), as a coating on metallic implants, has been used with some success.

Recent studies have suggested that a negative surface charge benefited implant fixation [1]. Surface charge may also promote formation of more bone [2]. This work will determine the effects of high negative surface charge on human mesenchymal stem cells (MSC) properties. We hypothesised that surfaces with increased negative charge enhance MSC growth and development into bone forming cells.

- > Osteoarthritis (OA) is a painful degenerative joint disease that robs sufferers of good quality of life, and is hugely costly in terms of loss of productivity/independence and health dollars. Its aetiology has so far been elusive, blocking the development of disease modifying treatments. Exciting recent research in mice has found that TGFbeta over-expression in the subchondral bone (beneath the cartilage) has a critical causal role in OA pathogenesis. The OA bone changes seen in mice closely resemble what we find in human OA bone in zones that display the most severe changes, which correspond to bone marrow lesions identified by MRI. This HDR project will explore the link between TGFbeta expression with structural, cellular and molecular changes in human subchondral bone marrow lesions. This project will investigate TGFbeta as a candidate driver of human OA, which is an essential precursor to testing pharmacologic alteration of TGFbeta activity as a therapeutic strategy.

### Honours projects

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# Centre for Orthopaedic and Trauma Research (COTR)

## Lead researchers:

### *Clinical:*

Prof Donald Howie  
+61 8 8222 5661 or [donald.howie@adelaide.edu.au](mailto:donald.howie@adelaide.edu.au)

Prof Brian Freeman  
+61 8 8222 4466 or [brian.freeman@sa.gov.au](mailto:brian.freeman@sa.gov.au)

### *Scientific:*

Prof David Findlay  
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Prof Gerald Atkins  
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The COTR Directors (L-R Prof Howie, Prof Findlay, Prof Atkins and Prof Freeman)

The Centre for Orthopaedic and Trauma Research (COTR) was formed in 2012 and its members include orthopaedic surgeons, clinical researchers and biomedical scientists. This diverse combination of researcher expertise enables the scientific study of highly clinically-relevant topics pertaining to the human musculoskeletal system. The research aims to better understand bone and joint diseases and conditions, including arthritis and joint replacement, pathological bone loss, infection, spinal conditions and fracture.

For additional information see: [adelaide.edu.au/ortho-trauma](http://adelaide.edu.au/ortho-trauma)

## Joint replacement and reconstruction research unit



### Lead researchers:

Prof Bogdan Solomon  
+61 8 8222 2665 or [bogdan.solomon@sa.gov.au](mailto:bogdan.solomon@sa.gov.au)

Mr Stuart Callary  
+61 8 8222 4788 or [stuart.callary@sa.gov.au](mailto:stuart.callary@sa.gov.au)

The Joint replacement and reconstruction research unit conducts research into a broad range of areas related to primary and complex revision hip and knee replacement as well as joint reconstruction for congenital joint disorders. The research opportunities include epidemiology using a joint replacement registry, clinical studies, basic bone biology and pathology, diagnostics, anatomy and surgical techniques, gait analysis and biomechanical testing.

For additional information see:  
[adelaide.edu.au/directory/lucian.solomon](http://adelaide.edu.au/directory/lucian.solomon)

### Research projects

- > Risk factors for complications after joint replacement surgery using a 30 year hip and knee replacement outcomes registry
- > Biomechanical, histological and diagnostic investigations of the mechanisms of failure of hip and knee replacement implants
- > Optimising surgical techniques for joint replacement and reconstruction

### Honours projects

- > Studies of early prosthesis stability that predict later loosening

## Orthopaedic trauma group



### Lead researchers:

Prof Bogdan Solomon  
+61 8 8222 5661 or [bogdan.solomon@sa.gov.au](mailto:bogdan.solomon@sa.gov.au)

A/Prof Mellick Chehade  
+61 8 8222 5661 or [mellick.chehade@sa.gov.au](mailto:mellick.chehade@sa.gov.au)

Through orthopaedic trauma research, we aim for optimal management of musculoskeletal injury. We have a multifaceted research program, supported by a long-term prospective clinical database, covering bone biology, advanced imaging, biomechanics, anatomy, pathology, clinical trials and epidemiology.

For additional information see:  
[adelaide.edu.au/directory/lucian.solomon](http://adelaide.edu.au/directory/lucian.solomon)

### Research projects

- > The anatomy and epidemiology of fracture and outcomes of fracture management
- > Optimising the care process, the management and outcomes of hip fractures in the elderly patient using a comprehensive hip fracture registry

### Honours projects

- > Redefining weight-bearing regimes after pelvic and lower limb fractures to reduce complications and improve acute care

## Bone cell biology group (BCBG)



In 2017, the BCBG will move into the new Adelaide Health and Medical Science building (AHMS) on North Terrace.

**Lead researcher:** Prof Gerald Atkins

**Contact:** +61 8 8222 3107 or [gerald.atkins@adelaide.edu.au](mailto:gerald.atkins@adelaide.edu.au)



Research assistant in the bone biology laboratory

The BCBG is a highly productive, research-intensive group that has published seminal studies on the biology of human bone remodelling, the physiological process that underlies many diseases of the skeleton. We are internationally recognised and run an integrated program of research into the cell biology of the major bone cell types, osteoclasts, osteoblasts and osteocytes. We have active research collaborations with lead researchers in Europe and the USA. Importantly, we are uniquely associated with the orthopaedic and trauma surgery unit, which allows us to perform human disease-relevant translational research into the pathobiology of fracture, osteoarthritis, orthopaedic implant loosening and bone infection (osteomyelitis and periprosthetic joint infection), as well as other conditions. We combine the use of novel transgenic mouse models, human and mouse tissue culture-based models, culture of freshly isolated cells from human bone, cutting-edge molecular analyses (e.g. micro-array, micro-RNA analysis, RNA Sequencing), gene expression in human bone samples and histology. Our work is funded by competitive grants from the NHMRC. The group consists of four post-docs, two research assistants and five current HDR students.

For additional information see:

[adelaide.edu.au/directory/gerald.atkins](http://adelaide.edu.au/directory/gerald.atkins)

[scholar.google.com.au/citations?user=AlwB\\_DkAAAAJ&hl=en](https://scholar.google.com.au/citations?user=AlwB_DkAAAAJ&hl=en)

### Projects are available at honours, masters and PhD levels:

- > Elucidating novel molecular and cellular pathways of bone biology in health and disease
- > The central role of osteocytes in bone pathophysiology
- > The pathobiology of implant-derived wear particles
- > The relationship between patient activity and cell biology at sites of skeletal pathology
- > The biology of human fracture repair
- > The role and immunology of bone cells in bacterial infection of bone
- > Bone and beyond - the influence of bone cells on other organs

## Adelaide spinal research group



### Lead researcher:

Prof Brian Freeman

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Dr Claire Jones

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Dr Julia Kuliwaba

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The Instron testing machine allows spinal implants to be tested in six degrees of freedom.

The Adelaide Centre for Spinal Research (ACSR) is one of the most vibrant spinal research groups in Australia. It brings together clinicians, engineers and scientists in a multidisciplinary program spanning clinical and pre-clinical research, biomechanics, and bone and intervertebral disc structure and biology, all relating to the healthy, disordered, and injured spine and spinal cord. Our research facilities include a well-equipped biomechanics laboratory with 6-axis simulator, Instron testing machine, Optotrak motion capture system, high speed cameras, and cadaver preparation facilities.

For additional information see:

[adelaide.edu.au/directory/claire.jones](http://adelaide.edu.au/directory/claire.jones)

### Research projects

- > Characterising the bone microstructure and biomechanical properties of spinal tissues, and the effects of age, gender, trauma and disease
- > Clinical and biomechanical investigation of injury mechanisms of acute spinal and spinal cord injury and chronic spinal conditions
- > Biomechanical evaluation of spinal surgery techniques and implants
- > TGF- $\beta$  as a critical factor in human osteoarthritis:

The aetiology of the painful degenerative joint disease osteoarthritis (OA) has so far been elusive, blocking the development of disease modifying treatments. Exciting recent research in mice has found that TGF- $\beta$  over-expression in the subchondral bone (beneath the cartilage) has a critical causal role in OA pathogenesis. The OA bone changes seen in mice closely resemble what we find in human OA bone in zones that display the most severe changes, which correspond to "bone marrow lesions" identified by MRI. This HDR project will explore the link between TGF- $\beta$  expression with structural, cellular and molecular changes in human subchondral bone marrow lesions. This project will investigate TGF- $\beta$  as a candidate driver of human OA, which is an essential precursor to testing pharmacologic alteration of TGF- $\beta$  activity as a therapeutic strategy.

## South Australian spinal cord injury service



**Lead researcher:** Dr Jillian Clark

**Contact:** +61 8 8222 1651 or [jillian.clark@sa.gov.au](mailto:jillian.clark@sa.gov.au)

The South Australian Spinal Cord Injury Research Centre brings together clinician-researchers from the disciplines of Epidemiology, Traumatology, Orthopaedics, Endocrinology and Medical Rehabilitation. Collaborations formed between our group and our basic science colleagues have been instrumental in advancing our investigations of deficiencies in understanding of the pathophysiology of spinal cord injury and the pathogenesis of its detrimental consequences. The long term goal is to develop an understanding that will underpin medical diagnostics and guide clinical practice.

For additional information see:

[adelaide.edu.au/ortho-trauma/research](http://adelaide.edu.au/ortho-trauma/research)

### Research projects

Our Research projects investigate fundamental principles of the physiological and biological responses to spinal cord injury. We endeavour to characterise the clinical phenotype in order to shed light on the interplay between body systems and increase our understanding of the cell types and signalling pathways involved. We employ laboratory, advanced imaging, physiological, behavioural and data-linkage techniques to answer biological questions that have important clinical implications for mitigating secondary injury, augmenting tissue repair, restoring function and promoting health.

Our projects are highly translational, affording opportunities for bench-bedside and bedside-bench research involving diagnostics, therapeutics, and clinical practice guidelines. We welcome expressions of interest from honours, masters, and PhD candidates.

## Upper limb musculoskeletal biomechanics research program



**Lead researchers:**

Dr Claire Jones

+61 8 8222 3056 or [claire.jones@adelaide.edu.au](mailto:claire.jones@adelaide.edu.au)

Prof Greg Bain

+61 8 8222 3056 or [greg.bain@adelaide.edu.au](mailto:greg.bain@adelaide.edu.au)

There are a range of projects available in the area of upper limb musculoskeletal biomechanics, surgery and medical device development and evaluation. The Centre's biomechanics laboratory houses an Instron 8874 biaxial materials testing machine, and custom testing apparatus, and accesses a variety of other equipment via the Adelaide Centre for Spinal Research.

For additional information see:

[adelaide.edu.au/directory/claire.jones](http://adelaide.edu.au/directory/claire.jones)

### Research projects

- > Microstructure and function of upper limb tendons, suture-tendon interaction
- > Biomechanical evaluation of novel rotator cuff repair techniques and anchors



# Men's health

## The Freemasons Foundation Centre for Men's Health



### Lead researcher:

Prof Gary Wittert

+61 8 8313 0514 or [menshealth@adelaide.edu.au](mailto:menshealth@adelaide.edu.au)

The Freemasons Foundation Centre for Men's Health supports a trans-disciplinary research program in clinical, basic and behavioural sciences, public health, sociology and epidemiology, to advance our knowledge of disease risk and consequences, better treat prostate cancer and the leading chronic diseases in men (diabetes, heart disease and depression), innovate in how we deliver preventative health to men for healthier ageing and optimise the delivery of health services for men to encourage timely uptake. A selection of the many projects available are described here. Scholarships available.

For further details see: [adelaide.edu.au/menshealth](http://adelaide.edu.au/menshealth)

### Research projects

#### > Leveraging masculinity to improve the health of men

*Supervisors: Prof Gary Wittert, Dr Megan Warin, Prof Christine Beasley, Prof Sarah Robertson, Dr Sean Martin. Site: SAHMRI, North Tce campus.*

For this project you will draw expertise from the Fay Gale Centre for Research on Gender, the Freemasons Foundation Centre for Men's Health and the Robinson Research Institute in order to develop a framework that aims to integrate biological and social aspects of men's health. Specifically, the framework will be built around the construct of masculinity and men's health behaviours and how this may be best utilised to rethink how we conduct gender related research, reform the delivery of health care, public health interventions and social marketing strategies. The program proposes that rather than portraying masculinity as an inevitable obstacle to health, by understanding masculinity in a contemporary social context, it can be leverage to improve the health of men.

#### > Personalised website and mobile app based intervention for lower urinary tract symptoms in men

*Supervisors: Dr Camille Short, Dr Sean Martin, Dr Niranjana Bidargaddi, Prof Gary Wittert, Dr Andrew Vincent, Dr Billy Kaambwa. Site: SAHMRI*

Lower urinary tract symptoms (LUTS) are highly prevalent in men and associated with risk of chronic disease. E-health (websites and apps) has been shown to improve overall health and erectile function in men. This program will involve 1. The development of a tailored e-health intervention with a data-driven decision support tool to support behaviour change from an existing expert system, guided by focus group research. 2. Its evaluation by RCT; outcomes being LUTS symptoms, health service utilisation, quality of life, lifestyle modification and BMI at 3 and 6 months, and participant usage as an effect modifier. This research will inform the utility of an e-health intervention in improving health outcomes among men with LUTS.

#### > The relationship between mental health and use of health care services in middle-aged to elderly men.

*Supervisors: Dr Sean Martin, Dr Phillip Tully, Prof Gary Wittert.*

*Site: SAHMRI*

We have shown that despite middle-older aged men's use of health care being comparable to age-matched women, depression and anxiety remain under-diagnosed. Using a longitudinal cohort of community-based men with an extensive bio-psychosocial dataset, this project will determine how men with incident depression and anxiety differ in their use of health services and what other demographic, lifestyle, and behavioural factors may act as mediating influences in this usage. A mixed methods program of research will also investigate how General Practitioners treat theoretical patients and compare these approaches to standard guidelines; the goal being to optimise use and delivery of services to reduce mental illness in men.

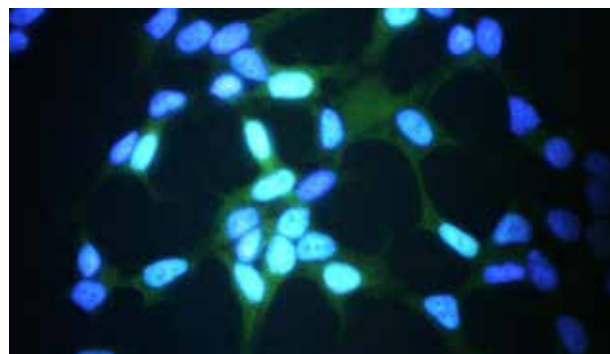
#### > Defining the molecular mechanisms of androgen receptor action in prostate cancer development and progression.

*Supervisors: Dr Luke Selth, Prof Wayne Tilley. Site: Dame Roma Mitchell Cancer Research Laboratories, SAHMRI.*

Building on a program involving international collaborators, three projects are available to further our understanding of the androgen receptor (AR) and its role in prostate cancer, in order to develop more effective therapies.

1. The role of AR splice variants and gain-of-function mutants in lethal prostate cancer.
2. The interplay between AR and other cancer-associated transcription factors.
3. Proteomic identification and characterisation of new AR co-regulators.

Clinically relevant models of prostate cancer and cutting-edge genomic/transcriptomic/proteomic techniques in addition to classical molecular biology and biochemical approaches immunohistochemistry, ChIP, transcriptional reporter assays, qRT-PCR and Western blotting will be used.



Fluorescent stained androgen receptor positive nuclei of human prostate cancer cells

- > **Investigating the role of microRNAs in prostate cancer metastasis and their use as potential biomarkers of disease.**  
Supervisors: Dr Luke Selth, Prof Wayne Tilley. Site: Dame Roma Mitchell Cancer research laboratories, SAHMRI.

The need to develop improved biomarkers of disease, disease aggressiveness and treatment response is a priority area of prostate cancer research. Two projects are available that build on our current biomarker program aiming for clinical translation.

1. MicroRNAs as mediators and markers of prostate cancer metastasis.
2. Inhibiting prostate cancer metastasis using microRNA-modulating drugs.

Clinically relevant models of prostate cancer and cutting-edge genomic/transcriptomic/proteomic techniques in addition to classical molecular biology and biochemical approaches immunohistochemistry, ChIP, transcriptional reporter assays, qRT-PCR and Western blotting will be used.

- > **CHAMPS: Cardiovascular Health in Anxiety or Mood Problems Study**

Supervisor: Dr Phil Tully

Cardiovascular disease (CVD) and mental illness are leading causes of disability and death worldwide. Cumulative evidence and recent systematic reviews indicate that mental healthcare in CVDs is constrained by a narrow focus on depression thereby neglecting common anxiety disorders. The CHAMPS project aims to treat anxiety disorders alongside depression disorders to determine their unique and conjoint effects on CVD outcomes, quality of life, cardiovascular health behaviours and mental health. Using data from CHAMPS (intervention vs. usual care and a non-distressed control group), this project involves; identifying mental illness prevalence, treatment preferences, cardiovascular health behaviours, and whether anxiety intervention influences outcomes.

- > **Poo Time! Pooing on Occupational Over Time**

Supervisor: Dr Phil Tully

Work hours and shift work are linked with risk of gastrointestinal disorders including cancer, gastroesophageal reflux disease, colitis, and change in defecation routines. It remains largely unknown whether disturbances in gastrointestinal functioning are related to changes in dietary pattern, sleep and stress or occupational factors such as workload. The project aims are twofold and students may participate in one or both aspects; 1) to analyse shift work, occupational stress, sleep and diet in relation to gastroesophageal reflux disease using a well-defined dataset, and 2) perform a systematic review of work hours and shift work in relation to gastrointestinal outcomes.

- > **i-Share: Internet-based Students Health Research Enterprise**

Supervisor: Dr Phil Tully

Improving student health and welfare is an important pursuit for universities and the future workforce worldwide. Unfortunately, university students face increasing demands to balance their studies with work, sport and social lives, leading to compromised sleep, mental health and unhealthy coping strategies. This project aims to explore university student health and wellbeing using an ongoing survey of French university students (i-Share online at <http://www.i-share.fr/>). Potential projects include evaluating university students' internet use, sleep, alcohol and tobacco use, academic stress, and factors relating to wellbeing and mental health.

## Honours projects

- > **Adverse childhood events and health and well-being in men**  
Supervisors Dr Sean Martin, Dr Phil Tully, Prof Gary Wittert.  
Site: SAHMRI.

There is a known link between adverse childhood events (ACEs) and subsequent anxiety and depression, but less is known about whether ACEs increase the risk of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) in later life. It also remains unclear whether at-risk behaviours are directly related to ACEs or other psychosocial factors or whether ACEs independently raise the risk of CVD and T2DM. Using a longitudinal cohort of community-based men with an extensive bio-psychosocial dataset, this project will examine the association between self-reported ACEs and health outcomes in adulthood. The student will examine i) the prevalence of CVD and T2DM; ii) the proportion of men with high-risk behaviours, and iii) psychosocial mediating factors that prevent the development of CVD, T2DM, or adoption of at-risk behaviours in adulthood.

- > **Effect of weight loss in obese men on sperm structure and function.**

Supervisors: Dr Nicole McPherson, Prof Michelle Lane, Prof Gary Wittert, Dr Andrew Vincent. Site: SAHMRI, RAH.

We have shown in our mouse model of paternal obesity that diet and exercise interventions restore obesity induced sperm dysfunction, and embryo and offspring metabolic ill-health. This project will assess the impacts of weight-loss by bariatric surgery on males by comparing against a control group of men who choose not to receive lifestyle advice. Blood and semen samples will be collected before intervention, after the initial strict caloric restriction phase and at other time intervals after surgery. Clinical metabolic and cardiovascular measures will be related to laboratory markers of sperm function, epigenetic and oxidative damage. The aim of this project is to develop an evidence base of interventions that can be offered to men in a family planning context. (Honours and PhD)

- > **An on-line platform to support maintenance of behaviour change in a face-to-face peer-led men's health program.**

Supervisors: Dr Camille Short, Prof Gary Wittert. Site: SAHMRI

The Centre has validated and successfully rolled out a face-to-face peer-led 12 week community-based lifestyle modification program for men to address the growing problem of overweight and obesity and chronic disease among Australia's men through promotion of healthy eating, physical activity, good sleep habits, stress management and health literacy. Participant evaluation has identified the need for post-program peer-support to help maintain lifestyle change. This, and focus group data, will be used to develop and trial an on-line platform using active program participants.

- > **The relationship between depression and lower urinary tract symptoms in men.**

Supervisors: Dr Sean Martin, Dr Phillip Tully, Prof Gary Wittert.  
Site: SAHMRI

Depression is under-diagnosed in men. We have shown that men with lower urinary tract symptoms (LUTS) are more likely to report depressive-type symptoms, however the nature and mechanisms of this relationship remain unclear. Using a longitudinal cohort of community-based men with an extensive biopsychosocial dataset, this project aims to further examine the association between

depression and LUTS by exploring the mediators of the depression and LUTS association, what type of LUTS cluster with particular depressive symptoms and whether LUTS treatment leads to decreases in depressive symptoms. Given LUTS is frequently raised and treated in primary care but men appear reluctant to initiate discussions around mental health, the results may have important clinical implications for men with undiagnosed depression.

**> Behaviour change strategies to increase men's uptake of screening for colorectal cancer.**

*Supervisors: Prof Deborah Turnbull, Dr Ian Zajac, Prof Carlene Wilson. Site: North Tce campus, CSIRO*

Participation in the Australian government's National Bowel Cancer Screening Program is markedly lower amongst men compared to women, yet men are at increased risk of being diagnosed with, and dying from, colorectal cancer compared to women. We have applied our understanding of differences between sexes in attitudes and perceived barriers to cancer screening to improve screening participation rates by men, but further work is required. Projects are available as an honours or HDR that address the suboptimal participation rates from multiple angles; using on-line decision-enhancing tools to address attitudes and behaviours, tailoring invitation letter used by the FOBT program and through better screening education in primary care.



As a PhD student member of the Freemasons Foundation Centre for Men's Health, I have been fortunate in receiving financial support by way of a top-up scholarship and multiple travel awards, as well as professional and personal support over the 3 years of my PhD candidature. Being part of a multidisciplinary network spanning basic sciences, preventative health, clinical and public health, I have extended the breadth of my learning and interactions, and the opportunities that arose from these have greatly assisted in developing the skills I require for my future career in health research. My PhD studies focused on examining the molecular chaperone Hsp90 protein which is responsible for regulating the activity of hundreds of proteins involved in prostate cancer progression. I have since taken up a postdoctoral research position with The Centre of Excellence for Gastrointestinal Inflammation and Immunity Research at the University of Alberta in Canada. Without the support of the centre, I would not have been able to achieve such success, and for this I am forever grateful.

Heather Armstrong, PhD candidate



# Metabolic and nutritional health

## Centre for Nutrition and Gastrointestinal Disease



### Lead researcher:

Prof Gary Wittert  
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### Nutrition and Metabolism logo

The Centre for Nutrition and Gastrointestinal Diseases, which is located at the new purpose built South Australian Health and Medical Research Institute (SAHMRI), is led by Prof Gary Wittert, Head of the Discipline of Medicine at the University of Adelaide.

The overarching goals of the centre are to improve treatment of digestive diseases by identifying and understanding the interactions between the nervous system and the gastrointestinal tract, promoting translational research from single cells through to the patient and preventing metabolic disease by modulating nutritional delivery.

### Research projects

Specific projects on offer in 2015 from team leaders: A/Prof Stuart Brierley, Dr Andrea Harrington, A/Prof Leonie Heilbronn, Dr Patrick Hughes, A/Prof Amanda Page, A/Prof Grigori Rychkov, and Dr Richard Young are listed below.

## Visceral pain group

### Lead researcher:

A/Prof Stuart Brierley  
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Our research focuses on chronic pain with particular emphasis on Irritable Bowel Syndrome (IBS). We determine the mechanisms responsible for detecting painful events and how they change during acute and chronic pain. It is clear that certain mechanisms are reprogrammed during chronic pain, which fail to 'reset' back to normal. Overall, understanding how these mechanisms are changed is the first step in finding new therapeutic treatments for chronic pain. Our research is published in Nature, Nature Communications, Nature Reviews Gastroenterology and Hepatology, Gastroenterology and Gut.

For further details see: [adelaide.edu.au/directory/stuart.brierley](http://adelaide.edu.au/directory/stuart.brierley)

### Research projects

#### > Ion channels: Critical targets for the treatment of chronic abdominal pain.

This project will follow up on our recent Nature paper to investigate novel ion channels in sensory neurons, and how their function changes across acute and chronic pain models. We will also determine how ion channel expression is altered in tissue from human patients with chronic visceral, thereby linking altered ion channel function with patient symptoms. Project funded by NHMRC Australia.

#### > G-protein coupled receptors: The cause of and solution to chronic abdominal pain?

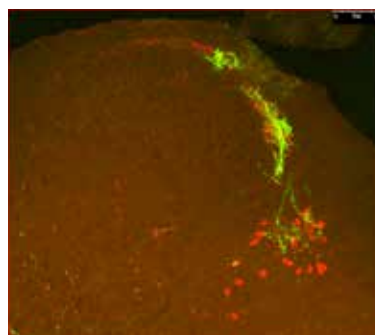
This project will follow up on our recent Nature Communications paper to investigate how novel G-protein coupled receptors are activated in chronic pain. We will also determine how receptor expression is altered in tissue from human patients with chronic visceral pain, thereby linking altered ion channel function with symptoms. Project funded by NHMRC Australia.

## Spinal pathways of visceral pain research group

### Lead researchers:

Dr Andrea Harrington  
+61 8 8128 4831 or [andrea.harrington@adelaide.edu.au](mailto:andrea.harrington@adelaide.edu.au)

A/Prof Stuart Brierley  
+61 8 8128 4831 or [stuart.brierley@adelaide.edu.au](mailto:stuart.brierley@adelaide.edu.au)



Calcium imaging in spinal cord slices to characterise the neurons receiving input from sensory nerves innervating the viscera (red and green) and how they are changed in chronic pain states.

Our research is aimed at characterising the spinal cord circuits that relay pain from visceral organs into the brain. We use a range of integrative physiological approaches from whole animal to in vitro preparations to identifying the neuroanatomy, molecular expression and pharmacology of these important neuronal pathways. We identify how these properties change in conditions of chronic pain,

in particular Irritable Bowel Disease, overactive bladder and acid reflux. For additional information see:

[adelaide.edu.au/directory/andrea.harrington](http://adelaide.edu.au/directory/andrea.harrington)

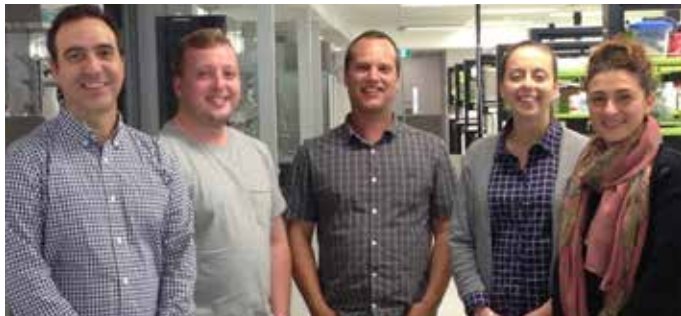
### Honours projects

- > Identify the role of TRPV1 expressing pain signalling nerve fibres in colorectal pain. Using pre-clinical models of visceral pain and calcium imaging you will identify the role TRPV1 expressing colorectal afferent nerves have in signalling pain into the spinal cord.
- > Identify changes in spinal cord neuron sensitivity as a consequence of colonic inflammation. Using calcium imaging techniques in spinal cord slices you will identify the level of sensitivity of spinal cord neurons in health and after colonic inflammation to colorectal afferent input and excitatory peptide signalling.
- > Characterise the molecular expression profile of spinal cord neurons processing visceral pain. You will use quantitative PCR to identify the genes expressed by spinal cord neurons that are activated by colonic and bladder pain. These neurons will be isolated using laser capture micro dissection from the general population of spinal cord neurons. Changes in gene expression in models of chronic visceral pain will be identified.
- > Identify regions of the brain activated by visceral pain. Using various techniques you will identify the neurons in the brain activated by colorectal pain and how this changes in models of chronic visceral pain.

## Gastrointestinal neuroimmune interactions

### Lead researcher:

Dr Patrick Hughes  
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Gastrointestinal neuroimmune interactions laboratory

The gastrointestinal tract is constantly bombarded with foreign antigen, from the food we eat to viruses and bacteria. These threats are usually contained by an extensive nervous system and a powerful immune system, but abnormal responses by either the immune or nervous systems underlie several severe diseases including Inflammatory Bowel Diseases (IBD) and functional gastrointestinal diseases such as Irritable Bowel Syndrome (IBS) and Functional Dyspepsia (FD). The major theme of this group is dissecting how the immune and nervous systems communicate in the gut, and how this is altered in gastrointestinal diseases.

For further details see:

[www.sahmri.com/our-research/themes/nutrition-metabolism/groups](http://www.sahmri.com/our-research/themes/nutrition-metabolism/groups)

### Research projects

We use human tissue and animal models to investigate the role of the immune and nervous systems in diseases of the lower GI tract including Inflammatory Bowel Disease (IBD) and Irritable Bowel Syndrome (IBS).

- > **Is naive and relapsing inflammation of the colon the same? Investigate immune and nervous system in acute and relapsing models of chronic inflammation.**
- > **How do microbial products maintain immune and physiological homeostasis in the colon? Investigate the effects of microbial products on colonic immune and nervous systems.**
- > **How does activation of the immune system contribute toward symptoms in Irritable Bowel Syndrome?**
- > **Novel techniques for imaging colonic inflammation**

These projects are funded by the NHMRC and the University of Adelaide.

### Honours projects

Parts of the above projects are applicable for shorter honours projects.

## Vagal afferent research group

### Lead researcher:

Prof Amanda Page  
+61 8 8128 4840 or [amanda.page@adelaide.edu.au](mailto:amanda.page@adelaide.edu.au)



Prof Amanda Page

Our productive group located at SAHMRI is a leading authority on vagal innervation of the gut and how it relates to major disease states including obesity, gastro-oesophageal reflux disease and functional dyspepsia. This has involved pioneering studies on the phenotypic specialisation and regulation of vagal sensory endings. With a strong clinical focus we use a combination of behavioural, electrophysiological and molecular techniques to understand the role

of these afferents in mediating the development of obesity and/or resistance to weight loss and to identify modifiable targets.

For additional information see:

[sahmri.com/our-research/themes/nutrition-metabolism/theme-theme-overview](http://sahmri.com/our-research/themes/nutrition-metabolism/theme-theme-overview)

### Research projects

It is increasingly appreciated that the stomach plays an important role in appetite regulation. It is targeted in bariatric surgery and gastric vagal electrical stimulation to treat obesity. A greater understanding of vagal afferent sensitivity to gastric stimuli (nutrient or distension) is one of the most promising areas for novel pharmacological approaches to the management of obesity. We have shown that the effects of the satiety hormone leptin on vagal afferent endings switch from excitatory (anorexigenic) in lean mice to inhibitory (orexigenic) in obese mice. This project will expand upon these findings and determine the mechanisms behind this switch.

### Honours projects

Gastric vagal afferents are important in the control of food intake and demonstrate a high degree of plasticity in order to finely control the amount of food consumed. We have demonstrated that feeding a high fat diet (HFD) reduces the ability of gastric vagal afferents to signal mechanical stretch compared to feeding a standard laboratory diet (SLD). An understanding of the regulatory mechanisms involved in gastric vagal afferent mechanosensitivity and the changes that occur in HFD-induced obesity to reduce satiety signalling are essential for the development of novel approaches to the pharmacotherapy of obesity. We propose dampened gastric vagal afferent satiety signals are a result of disruption in the cross talk between cannabinoid receptors (CB1) and the capsaicin receptor (TRPV1). This project involves characterisation of the expression of TRPV1 and CB1 in gastric vagal afferent neurons under different nutritional states including HFD-induced obesity.

## Liver metabolism/molecular physiology of ion channels

### Lead researcher:

A/Prof Grigori Rychkov  
+61 8 8128 4854 or grigori.rychkov@adelaide.edu.au

### Research focuses on:

#### > Role of TRPM2 channels in oxidative damage and drug toxicity in liver.

Oxidative damage and enhanced hepatocellular death are the hallmarks of many liver disorders, including liver damage by paracetamol overdose and ischemia-reperfusion injury. Often in these conditions hepatocellular death is preceded by an increase in intracellular Ca<sup>2+</sup> concentration. In this project we will investigate the role of a particular type of Ca<sup>2+</sup> channels on the surface of hepatocytes in mediating Ca<sup>2+</sup> influx and liver damage produced by paracetamol and ischemia-reperfusion.

### Honours projects

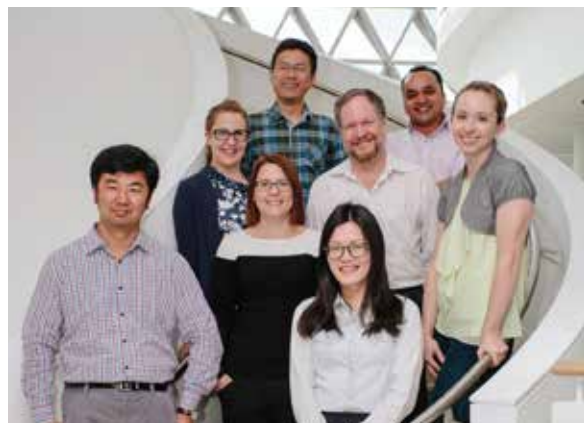
#### > Molecular mechanisms of store-operated Ca<sup>2+</sup> entry

Store-operated Ca<sup>2+</sup> channels play a central role in the functions of all animal cells. They participate in generating the cellular responses to hormones, antigens, growth factors and other physiological stimuli. The aims of this project are to elucidate cellular mechanisms that regulate interaction between the molecular components of store-operated Ca<sup>2+</sup> channel, Orai1 and STIM1.

## Obesity and metabolism laboratory

### Lead researcher:

A/Prof Leonie Heilbronn  
+61 8 8128 4838 or leonie.heilbronn@adelaide.edu.au



Members of the obesity and metabolism laboratory: Leonie Heilbronn, Gary Wittert, Amy Hutchison, Briohny Johnston, Bo Liu, Victor Chen, Prabin Gyawali

Our research is at the interface between basic and clinical science, and the research goal of the lab is to reduce chronic disease risk and insulin resistance through a greater understanding of nutrition and metabolism, and mechanisms underpinning these relationships particularly in muscle and adipose tissue.

For additional information see:

[www.sahmri.com/our-research/themes/nutrition-metabolism/groups](http://www.sahmri.com/our-research/themes/nutrition-metabolism/groups)

### Research projects:

We have a range of projects that will suit either Honours or PhD students interested in clinical or laboratory based research into nutrition, obesity and type 2 diabetes risk.

### Available projects:

- > Studying the role of intermittent fasting periods on reducing the risk of diabetes and cardiovascular risk in overweight humans, and in mice.
- > Studying the role of time restricted feeding in reversing glucose intolerance in individuals at risk of developing type 2 diabetes.
- > Determining whether we can reverse glycaemia in shift workers simply by limiting food intake at night, in humans and mice.
- > Understanding how over-nutrition contributes to metabolic dysfunction in human obesity, with a particular focus on inflammation and adipose tissue remodeling.
- > Determining how obesity and over-nutrition contribute to altered lipid metabolism and disease risk in skeletal muscle in humans."

### Honours projects

Whilst the above projects can be modified to suit the time schedule for an honours degree we have additional projects examining:

- > Whether daily or intermittent energy restriction impacts mood, food preferences and quality of life?
- > Impact of hyperbaric oxygen therapy on insulin sensitivity.

## Intestinal nutrient sensing group

### Lead researcher:

Dr Richard L Young  
+61 8 8128 4845 or richard.young@adelaide.edu.au



Intestinal nutrient sensing group, SAHMRI. Left to right: Nada Cvijanovic (PhD Candidate), Nicole Isaacs (Senior RA), Richard Young (Lab Head), Nektaria Pezos (Senior RA). Absent: Gudrun Schober (Postdoctoral Scientist), Jason Yam (Honours Student)



Intestinal nutrient sensing group, SAHMRI

Our group studies the mechanisms of nutrient detection and uptake within the upper gut. These are essential processes to maintain control of blood glucose and effective nutrition. Defects in these pathways can worsen control of blood glucose leading to under-nutrition, and impact on patients with diabetes, obesity and critical illness. Better understanding of these defects will provide new and novel therapies. Our translational research group has a strong clinical focus, wide access to patients and disease models, and expertise in anatomical, molecular and functional techniques.

For additional information see:

[adelaide.edu.au/directory/richard.young](http://adelaide.edu.au/directory/richard.young)



## Research projects

Our group offers HDR projects that are tailored to the individual, and expand on project areas outlined in listed Honours projects. These projects are backed by research support from government (NHMRC, ARC) and industry.

HDR projects range from clinical research and trials with patients and in the community, through to basic research including genetic and disease models in animals. This provides you an opportunity for either a focused or bench-to-bedside HDR project.

The research of our group is at the forefront of knowledge on how nutrients are detected in the gastrointestinal tract. This work holds the potential to control entry of nutrients to the body, benefiting patients with metabolic diseases and critical illness.

Your HDR will be undertaken in the state-of-the-art South Australia Health and Medical Research Institute, and within a Centre of Research Excellence in Translating Nutritional Science to Good Health - one of the strongest groups in Nutritional Physiology internationally.

literacy and other biomedical markers with the presence of risk factors for musculoskeletal disease.

## Honours projects

### > Why do sweetened drinks link to type 2 diabetes?

Consumption of artificial sweeteners is high and increasing in the community, and in heavy regular consumers may increase the speed that sugars, such as glucose, enter the blood from the gut. This may increase the risk of developing type 2 diabetes in the community. We have shown that patients with type 2 diabetes already have defective control of gut sensors for glucose (sweet taste receptors) and an increased rate of glucose uptake. We have an Honours project on offer that will investigate basic mechanisms linking sweetener consumption to altered glucose uptake in mice that lack sweet taste receptors. This project will involve experiments with mice, as well as anatomical and molecular approaches.

### > Molecular mechanisms of carbohydrate malabsorption in critical illness

Critically ill patients are frequently malnourished due to a defect in their ability to detect and transport sugars, such as glucose, from their gut into their body. This can compromise their clinical outcomes and functional recovery. We have shown that defects in controlling the gut sweet taste receptor and a glucose transporter in critically ill patients is the likely basis of this malabsorption, and is identical in a mouse model of critical illness.

We have an Honours project on offer that will assess new approaches to restore lost absorptive function. This project will involve experiments with mice, as well as anatomical and molecular approaches.

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Lysosomal diseases research unit

Nutrition and Metabolism theme, SAHMRI

Lead researcher:

Prof Christopher Proud

+61 8 8128 4810 or Christopher.Proud@sahmri.com



Staff and students of the Lysosomal diseases research unit

The Lysosomal diseases research unit is a world research leader in the biochemistry, cell biology and genetics of the lysosome. The Unit's research has delivered state-of-the-art diagnostics and commercialised first-ever treatments for two lysosomal storage disorders. The lysosomal network is increasingly being implicated in disorders such as stroke, heart disease and neurodegenerative disorders such as Alzheimer's. The Unit brings its core strength in lysosomal research to investigate the contribution of the lysosomal network in these disorders, with a particular focus on neurodegeneration.

For additional information see:

sahmri.com/our-research/research-groups/lysosomal-diseases-research-unit

Honours projects

> Characterisation of endocytic machinery of lysosomal storage disorder cells

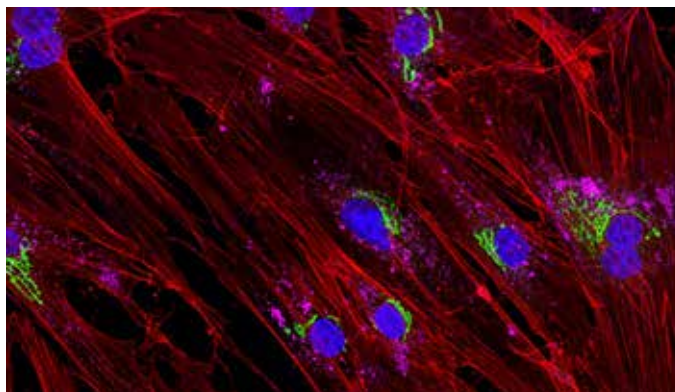
Endocytosis is a process by which cells import materials from their surroundings. Impaired endocytosis has been implicated in the lysosomal storage disorder Sanfilippo type A, a progressive childhood neurological disorder caused by a defect/absence of the lysosomal enzyme, sulphamidase, and accumulation of its substrate, heparan sulphate. This leads to progressively severe clinical problems and premature death in the majority of cases. This project examines and characterises intracellular trafficking mechanisms to identify the pathways that interfere with endocytic vesicular trafficking, and evaluate whether they can be manipulated or normalised to alleviate clinical pathology. The student will utilise fluorescence immunohistochemistry, confocal microscopy, enzyme assays and Western blot analysis.

More information: Drs Makoto Kamei: makoto.kamei@sahmri.com or Adeline Lau: adeline.lau@sahmri.com

> Evaluation of a novel drug as a potential therapy for the treatment of an early-onset form of dementia.

This project examines the therapeutic efficacy of a novel drug for the treatment of Sanfilippo syndrome, a group of five progressive neurological childhood disorders that result from a defect or absence of specific lysosomal enzymes, which leads to the cellular accumulation of its substrate, heparan sulphate. In turn, this leads to progressively severe clinical problems and premature death in the majority of

cases. This project utilises *Drosophila* models of Sanfilippo disorders to examine a novel drug for its ability to reduce heparan sulphate storage and improve clinical disease pathology. The student can expect to utilise techniques such as behavioural/neurological testing, mass spectrometry and immunostaining/microscopy. More information: Dr Adeline Lau: adeline.lau@sahmri.com



Human skin fibroblast cells stained for golgi (green), actin (red), lysosomes (magenta) and nuclei (blue). Image taken using the Leica TCS SP8X confocal microscope located at the Lysosomal Diseases Research Unit. Scale bar = 10 μ m.

Perioperative Model of Care

Lead researcher: Prof Guy Ludbrook

Contact: +61 8 8222 5422 or guy.ludbrook@adelaide.edu.au

For elective surgery, there are the dual challenges of older and sicker patients requiring surgery and resource limitations. To continue to deliver high quality care to these patients requires significant changes to health care delivery, based around robust processes of patient triage and streaming to the care pathways best matched to patients' individual needs. These include (i) call centre-based computer-assisted self-assessment, (ii) centralized collection and (iii) assimilation of patient data, and referral to centres with capacity (staff, services and infrastructure) best meeting a patient's needs. The group will continue to collect data through studies involving hospitals and clinical trials.

Research projects

> **A perioperative model of care and preoperative predictors of postoperative adverse effects:** novel approaches to preoperative assessment and management before elective surgery are warranted to ensure that a sustainable high quality service is provided to patients. This requires significant changes to health care delivery. It is proposed that a new Model of Care is needed, based around robust processes of patient triage and streaming to the care pathways best matched to patients' individual needs.

An electronic information system underpins this Model, providing the tools for communication, and data collection, analysis and storage, necessary to provide a high quality yet efficient service. Each step in the Model is formally studied, providing data on quality and cost to allow an evaluation of the overall value. Computer algorithms are starting to generate evidence- and consensus-based decision support tools to guide clinical decision making. Further studies are indicated to assess the quality of information gathered and its utility as part of a model of preoperative care.

For further details see: health.adelaide.edu.au/acm/

Centre of Research Excellence in Translating Nutritional Science to Good Health

Director and contact:

Prof Michael Horowitz
+61 8 8222 2960 or michael.horowitz@adelaide.edu.au



CRE Members Back (L-R): Christine Feinle-Bisset; Ian Chapman; Peter Clifton; Michael Horowitz; Chris Rayner; Amanda Page; Karen Jones

The CRE was established in 2007 and seeks to encourage and promote clinical research in the area of nutritional physiology. The Chief Investigators, with backgrounds in endocrinology, gastroenterology, nutritional science, nuclear medicine, psychology, epidemiology and nursing, bring unique technical skills, unparalleled in this country, and a sustained record of productivity in clinical nutritional research, attested to by a high international profile, substantial impact on clinical practice, and the capacity to communicate a healthy nutrition philosophy to the public.

For further details see: adelaide.edu.au/cre-nutrition

Research projects

> Postprandial Hypotension

Lead researcher: Prof Karen Jones karen.jones@adelaide.edu.au

Postprandial hypotension, defined as a fall in systolic blood pressure greater than 20mmHg, occurring within two hours of a meal, is now recognised to be an important clinical problem by predisposing to syncope and falls.

We have established that the hypotensive response to meals is dependent on the rate of small intestinal nutrient delivery i.e. the magnitude of the fall in blood pressure is dependent on the rate of gastric emptying. Conversely, gastric distension attenuates the fall in blood pressure. Hence, treatment of postprandial hypotension could be directed at facilitating gastric distension and/or slowing the rate of gastric emptying and small intestinal absorption. Given its high prevalence and significant sequelae, particularly in an ageing population, postprandial hypotension has received inappropriately little attention.

> Nutrition in the elderly

Lead researchers:

Prof Ian Chapman ian.chapman@adelaide.edu.au
Dr Stijn Soenen stijn.soenen@adelaide.edu.au

Among older people, obesity and undernutrition have become more common over recent decades. Both conditions are associated with increased morbidity and mortality.

- Ageing and state of nutrition

We have shown that oral, gastric and small intestinal mechanisms are pivotal to the regulation of appetite and energy intake, and that many of these mechanisms are modified substantially by ageing. The suppression of energy intake by oral, or intraduodenally infused, protein is significantly less in healthy older than younger adults.

- Effects of oral health on state of nutrition

The project will determine the effect of ageing on the relation between oral health and appetite and state of nutrition.

- Effects of ageing on the outcomes of bariatric surgery

The project will determine the effect of ageing on outcomes of bariatric surgery

> Intensive Care Research

Lead researchers:

Prof Marianne Chapman marianne.chapman@sa.gov.au

Dr Yasmine Ali Abdelhamid

Lee-anne Costello lee-anne.costello@adelaide.edu.au

We are a dynamic and competitive group of ICU consultants, dietitians, nurses, scientists and PhD candidates based in Intensive Care at the Royal Adelaide Hospital. Led by Prof Chapman, ICU Research is a world-leader in nutrition, GI function and glucose metabolism in critical illness. Our research investigates altered GI motility, nutrient absorption and interplay between GI hormones and glucose metabolism to improve patient care. Our emphasis is on clinically-focused, technically-challenging studies ranging from physiological studies to large NHMRC-funded RCTs to pharmaceutical-sponsored research.

Our programme is particularly well-suited to students with an interest in acute care medicine, anaesthetics, endocrinology or gastroenterology.

> Gastrointestinal Function and Appetite Regulation

Lead researcher:

Prof Christine Feinle-Bisset christine.feinle@adelaide.edu.au

Our research focuses on the role of gastrointestinal (GI) factors, including GI hormones and GI motility, and effects of specific dietary nutrients, in the regulation of appetite and energy intake, and blood glucose control, using a range of state-of-the-art techniques. We perform studies in healthy humans, and patients with obesity and/or type 2 diabetes. The ultimate aim of our research is to identify nutrients that have the ability to modulate GI function in a way that helps to control appetite and energy intake. Research projects include;

- Effects of specific amino acids on gut functions, energy intake and blood glucose
- Effects of ingestion of combinations of nutrients on subsequent energy intake and blood glucose
- Effects of interactions between oral, intragastric and small intestinal stimuli on gut functions and appetite

> Gastrointestinal function in diabetes mellitus

Lead researcher:

Prof Chris Rayner chris.rayner@adelaide.edu.au

Our group has established an international reputation in the area of gastrointestinal function in diabetes and have a history of supervising higher degree students from a broad variety of clinical and scientific backgrounds. We have the capacity to measure gastric emptying with scintigraphy, ultrasound or breath tests, gastroduodenal pressure events with manometry, release of small intestinal hormones (eg. GLP-1, GIP, CCK) by assays on plasma samples, gut sensations by validated visual analogue scores, and appetite and food intake by ad libitum buffet meals. Research projects include evaluation of dietary or drug interventions to control postprandial hyperglycaemia, or physiological studies seeking to understand the basis of disordered gastric or small intestinal function in diabetes.

> Gastrointestinal Function and Appetite Regulation

Lead researchers:

Prof Christine Feinle-Bisset christine.feinle@adelaide.edu.au

Dr Tanya Little tanya.little@adelaide.edu.au

Our research focuses on the evaluation of gastrointestinal (GI) factors, such as GI hormones and GI motility, interactions between nutrients and receptors in the gut wall, in the regulation of appetite and energy intake, and blood glucose control, in humans, using a range of state-of-the-art techniques. We have a particular interest in the role of the macronutrients, fat and protein. While overconsumption of fat leads to weight gain, fat, when administered directly into the small intestine, has effects on GI functions that may contribute to suppression of appetite and energy intake.

- Effects of specific amino acids on gut functions and energy intake in humans: High-protein diets lead to sustained weight loss, due to the superior satiating capacity of protein, and improve blood glucose control. Since specific amino acids may mediate the effects of whole protein, this project will determine the impact of isolated amino acids (aromatic, branched chain, etc.) on gut hormone release, gut motor activity, appetite, energy intake and blood glucose control in healthy humans. We use a wide range of state-of-the-art clinical techniques in our work.
- Effects of obesity on oral and gastrointestinal mechanisms involved in the sensing of dietary fat and implications for the regulation of food intake and postprandial triglyceride metabolism.



“A PhD within the Centre of Research Excellence (CRE) in Translating Nutritional Science to Good Health, located in the School of Medicine, has enabled me to build strong foundations for both my personal and professional development as a clinician scientist. The CRE's world-class facilities and strong links with the Royal Adelaide Hospital provides outstanding research and training opportunities as well as a structured and supportive learning environment.”

Lee-Anne Costello, PhD candidate

Professorial oesophago-gastric surgical unit

Lead Researcher:

A/Prof Sarah Thompson
SD 1538 through RAH switch or
sarah.thompson@adelaide.edu.au

Research Projects

Our surgical unit consists of four upper gastrointestinal surgeons, with a focus on academic surgery. Projects are clinical in nature and will usually involve patient contact. Mature students with an interest in general surgery are preferred.

Honours projects

- > A clinical project using our very mature Fundoplication Database to examine the efficacy of fundoplication as a long-term treatment option for reflux.
- > A clinical project using ultrasound to detect fatty liver in the preoperative setting prior to laparoscopic bariatric surgery.

Translational unit

SA Pathology at Women's and Children's Hospital

Lead researchers:

A/Prof Maria Fuller
+61 8 8161 6741 or maria.fuller@adelaide.edu.au
Dr Nicholas Smith



Staff of the Translational unit

Our laboratory is embedded in Genetics and Molecular Pathology in the state-wide pathology service, SA Pathology, providing diagnostic provisions for patients with inherited metabolic disease. Genetic disorders, in which there is impairment in normal metabolism, arise from a deficiency of an enzyme, protein or cofactor and manifest as progressive and debilitating disease. Our primary research focus is to improve the diagnostic efficiency of these disorders through the identification of biomarkers and to develop targets for therapeutic intervention via interrogation of metabolic pathways.

UA/RAH

Research Projects

Inherited neurodegenerative disorders present throughout life, although disease burden is greatest in childhood. The diseases result in progressive loss of neurocognitive function and in the most aggressive forms inevitable declination to a dependent vegetative state and premature death. Current diagnostic pathways remain inadequate, with many patients not receiving a correct diagnosis and for others diagnosis is often delayed - stressful for both child and family. There are no cures and therapeutic intervention is limited to a small subset of cases. Using patient samples, cell and/or mouse models, metabolism in the brain will be interrogated; identifying biomarkers for diagnosis and informing new therapeutics for disease treatment. This will also establish potential for extension of therapeutic and disease prophylactics to the wider spectrum of neurocognitive illnesses (including the primary dementias) for which study models that faithfully recapitulate human disease are not clear.

Honours projects

- > Neurological disease in many untreatable inherited metabolic diseases manifests progressive neurological decline in infancy leading to premature death. The primary biochemical insult "the accumulation of a metabolite" compromises the normal metabolic state. How the cell responds to this metabolic defect involves a multitude of cellular processes and it is this complex interplay of largely unknown events that underlies disease pathophysiology. It has been known for 30 years that amongst these metabolic aberrations transpires an abnormal accumulation of lipids within the brain. Lipids are crucial for brain function and temporal regulation highly important for neuronal development, therefore brain lipid homeostasis is tightly regulated. This project seeks first to define the extent of lipid dyshomeostasis within the brain of a mouse model and/or neuronal cultures (student choice) and second, manipulate lipid metabolism via pharmaceutical intervention as a therapeutic proof-of-principle.
- > The childhood leukodystrophies are a variable spectrum of hereditary neurological diseases characterised by abnormalities in the formation and maintenance of white matter within the brain and spinal cord. Disease burden is high, with a progressive loss of neurocognitive function and premature death in the majority of cases. Therapeutic intervention is limited to a small subset of cases, however contemporary strategies are evolving; success is predicated on accurate and timely diagnosis necessitating improved diagnostic strategies. A definitive diagnosis is reached in only 50% of children and often following a protracted course of investigation. While definitive mechanisms of disease remain poorly understood, disordered lipid and fatty acid metabolism are strongly implicated, reflecting the high lipid composition of the brain. Therefore this project will employ lipidomic profiling and biomarker discovery with a view to defining diagnostic disease patterns for these childhood illnesses.

WCH

Origins of health

The Health Observatory



Lead researcher:

Prof Robert Adams
+61 8 8222 6740 or robert.adams@adelaide.edu.au

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.

For further details see: adelaide.edu.au/directory/robert.adams

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/P45WgRlc2sl>

> Musculo-skeletal medicine

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

Circadian physiology research group



Lead researchers:

Prof David Kennaway
+61 8 8313 4090 or david.kennaway@adelaide.edu.au

Dr Tamara Varcoe
+61 8 8313 8127 or tamara.varcoe@adelaide.edu.au



Prof David Kennaway

Circadian rhythms are endogenous changes in physiology, behaviour and metabolism that oscillate with a period of approximately 24 hours. Circadian rhythms are established through a negative feedback loop involving a series of clock genes expressed within every cell of the body. The objective of our research is to determine how circadian rhythms regulate and interact with diverse physiological processes including metabolism, reproduction and behaviour, and the consequences of circadian disruption to health and well-being.

For additional information see:

adelaide.edu.au/robinson-research-institute/researchers/group-leaders/kennaway

Research projects

> Does shift work exposure during gestation affect pregnancy outcomes and the long term metabolic health of the progeny?

This project, based within an NHMRC Project (APP1106674; Kennaway, Gatford and Varcoe 2016-2018), will use a large animal model to investigate the impact of simulated shift work exposure during gestation on pregnancy outcomes (fetal growth, gestational age and neonatal health and size) and the metabolic health of the progeny through until adulthood. Simulated shift work will involve controlling light exposure and food access of pregnant ewes at different stages of gestation. Lambs will be assessed at 3 and 12 months for body composition, glucose tolerance and insulin sensitivity. The student will experience a range of sampling and analytical techniques including: large animal surgery, radioimmunoassay, quantitative PCR and immunohistochemistry. The project will be jointly supervised by Dr Kathy Gatford, Dr Tamara Varcoe and Prof David Kennaway.

Honours project

> How does shift work exposure during pregnancy affect the mother and developing fetus?

This project, based within an NHMRC Project (APP1106674; Kennaway, Gatford and Varcoe 2016-2018), will use a large animal model to investigate the impact of simulated shift work exposure during gestation on maternal adaptations to pregnancy. Pregnant ewes will be exposed to a simulated shift work protocol whereby the timing of light exposure and food access is manipulated. The impact of this protocol on maternal circadian rhythms (melatonin, cortisol and peripheral clock gene expression) and maternal metabolism (glucose tolerance, insulin secretion and sensitivity) in early and late pregnancy will be assessed. Fetal ultrasounds throughout gestation will assess fetal growth and activity. This project will be jointly supervised by Dr Tamara Varcoe and Dr Kathy Gatford.

Early life programming of health and disease

Lead researchers:

Dr Kathy Gatford and Prof Julie Owens
+61 8 8313 4158 or kathy.gatford@adelaide.edu.au

Our research group are international leaders in the investigation of the intergenerational and perinatal origins of metabolic and cardiovascular health in postnatal life. We focus on how our health can be profoundly influenced by events in early life and possibly in previous generations, including diabetes, obesity and cardiovascular increasing risk of disease.

Our aims are to:

- > Understand underlying mechanisms for effects of these exposures on our later health
- > Identify interventions to either prevent or to overcome adverse programming of health in early life

For further details see:

adelaide.edu.au/robinson-research-institute/researchers/group-leaders/owens

Research projects

> Growth hormone and pregnancy: a novel approach to increase fetal growth

Supervisors: Dr K Gatford, Dr B Muhlhausler, Prof C Roberts

Fetal growth is restricted in ~10% of pregnancies and there is currently no effective treatment to prevent this. We know that injecting pregnant animals with growth hormone can increase placental function and fetal growth. We are investigating a novel approach to increase placental function and hence fetal growth, by increasing maternal ghrelin.

HDR students will jointly develop projects using three main approaches:

1. Pre-clinical models of normal and growth-restricted pregnancies in the mouse to measure the responses to treatments,
2. Use of knockout mouse models to interrogate mechanisms, and
3. Studies in a human cohort to investigate associations between maternal ghrelin and pregnancy outcomes.

Our long-term aim is to develop a safe dietary supplement that reduces the risk of IUGR in women who are identified as being at risk.

For additional projects please also see co-supervised projects under "Circadian Physiology" group

Honours project

> How does maternal ghrelin promote fetal growth?

Supervisors: Dr K Gatford, Dr B Muhlhausler, Prof C Roberts

Fetal growth is restricted (IUGR) in ~10% of pregnancies and there is currently no effective treatment to prevent this developing. Maternal ghrelin promotes fetal growth in normal murine pregnancy, and can be increased by manipulating the diet, so may provide a safe approach to prevent IUGR.

In this project, an Honours student will discover some of the underlying mechanisms by testing the effects of maternal ghrelin in normal and growth-restricted murine pregnancy. The student will gain an understanding of in utero growth, placental development and function, and growth hormone biology, and will gain skills in small animal in vivo studies (Aim 1), in vivo analysis of placental function using tracer uptake (Aim 2), and analysis of placental structure (Aim 3), data analysis, and written and oral presentation skills. For additional projects please also see co-supervised projects under "Circadian Physiology" group.

Intellectual disability research



Neurogenetics research program

Lead researchers:

A/Prof Cheryl Shoubridge

+61 8 8313 2355 or cheryl.shoubridge@adelaide.edu.au

Dr Kristie Rogers

+61 8 8313 2452 or kristie.rogers@adelaide.edu.au

Dr Matilda Jackson

matilda.jackson@adelaide.edu.au



The Intellectual disability research group in the Braggs building laboratories.

Identification of genes and understanding of molecular mechanisms leading to intellectual disabilities, autisms and some epilepsies represents a challenge of significant medical importance. Our research seeks to further our understanding of human brain function through the identification of genes and characterisation of their naturally occurring mutations implicated in various disorders of the brain. The Intellectual Disability laboratory focuses on identifying the molecular mechanisms and functional impact of mutations in genes causing X-linked intellectual disability (XLID).

For additional information see:

adelaide.edu.au/directory/cheryl.shoubridge

Research projects

> Characterise molecular and cellular changes driving improvements to disease outcomes after postnatal 17B-estradiol treatment in mice modelling intellectual disability and seizures.

We have mouse models to investigate functional impact of the two most frequent expanded polyalanine tract mutations in the ARX gene. Our ongoing work aims to establish the molecular mechanisms of disease associated with a range of expanded polyalanine tract mutations in ARX to begin to understand how these mutations underpin the intellectual disability with and without a broad spectrum of associated clinical symptoms in affected patients, including epilepsy. Our current grant seeks to characterise the drivers underpinning phenotypic improvements following postnatal treatment strategy. The key approaches will use animal models including seizure monitoring and behavioural analysis, RNASeq approaches to examine transcriptome wide changes and associated changes to interneuron populations in the developing brain.

> Investigating the pathogenic mechanisms of mutations in IQSEC2 in intellectual disability and seizures.

IQSEC2 is a guanine nucleotide exchange factor activating ARF proteins at membrane surfaces. Patients with mutations in IQSEC2 present with intellectual disability, seizures and deficits in language, with limited understanding of the pathogenic mechanisms impacting on IQSEC2 function. This project will

establish the impact of these mutations on the function of the protein, including the enzymatic capacity to activate ARFs. We have generated a knock-out mouse and will interrogate the cellular and molecular pathology of the developing brain, including behavioural and cognitive outcomes in these animals. This project will include the use of primary hippocampal cultures and iPS cell culture to establish the role of IQSEC2 in synaptic plasticity.

Honours projects

> Investigate the mechanisms by which different expanded polyalanine tract mutations disrupt the function of the ARX protein and contribute to the clinical severity.

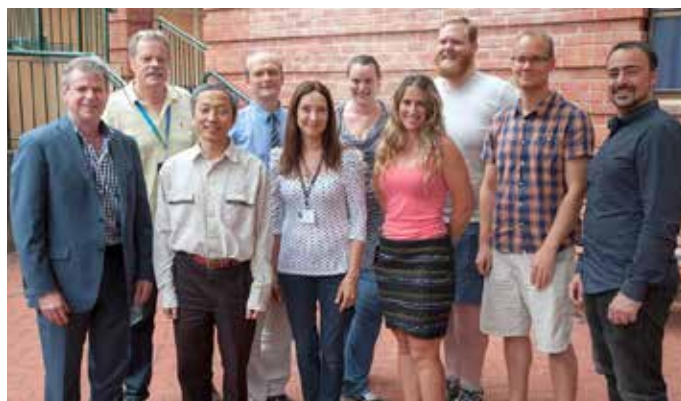
Our work aims to establish the molecular mechanisms of disease associated with a range of expanded polyalanine tract mutations to understand how these mutations underpin the intellectual disability with and without a broad spectrum of associated clinical symptoms in affected patients, including epilepsy. We are interested in more fundamental aspects of ARX biology and are currently investigating how this homeodomain transcription factor regulates target genes and how these polyalanine tracts impact on this process contributing to disease. This project utilises a range of molecular cloning techniques, cell culture and cell based assays, protein studies as well as transcriptome wide expression analysis. Honours students are encouraged to remain with our research team to undertake a Ph.D.

Chronic inflammatory lung disease research laboratory



Lead researcher:

Prof Sandra Hodge
+61 8 8222 3443 or sandra.hodge@health.sa.gov.au



The lung research team

We are a multidisciplinary, internationally recognised research team. Clinically-based investigations in chronic lung diseases (CLD) include:

- > Airway macrophage-targeted therapies: eg, novel non-microbial antibiotics to overcome the problem of microbial resistance
- > Understanding and overcoming steroid resistance
- > E-cigarettes: effects on airway inflammation, function and emphysema development.
- > Lung Biometals: eg, Zinc in diseased blood vessels and its relationship with airway autophagy
- > Potentially pathogenic bacteria that commonly colonise the airway in CLD: effects on airway macrophage dysfunction and inflammation
- > Bacterial bronchitis and bronchiectasis in Indigenous children

For further details see: adelaide.edu.au/directory/sandra.hodge

Research projects

> The effect of non-typeable *H. influenza* (NTHi) on sphingosine-1 phosphate (S1P) and IL-1 signalling systems, and its therapeutic targeting in COPD

COPD/emphysema is an incurable, cigarette-smoke related, chronic inflammatory airways disease (3rd leading cause of death in the world by 2020). No available treatments prevent disease progression. There is a defect in the capacity of airway macrophages to clear the bacteria, NTHi (potentially contributing to bacterial persistence and biofilm formation). The effects of NTHi on S1P and P2X7/IL-1 pathways (LL-37, eATP, inflammasome, NLRP3, AIM2 and IL-1) are unknown.

We will investigate phagocytosis, S1P and P2X7/IL-1 pathways in airway and lung macrophages from COPD patients and THP-1 macrophages exposed to NTHi ± cigarette smoke. The capacity of candidate therapies to restore macrophage function (eg, azithromycin, FTY720, P2X7R antagonists and new macrolides which are lacking antibiotic properties but retain their anti-inflammatory properties).

> Sphingosine signalling in childhood Protracted Bacterial Bronchitis (PBB) and bronchiectasis, and its therapeutic targeting.

Inadequate diagnosis and treatment of recurrent PBB, especially in Indigenous children, may lead to reduced lung function and lower life-expectancy. Defective airway macrophage phagocytic function in these children may contribute to a progression of PBB to bronchiectasis. We showed that macrophage dysfunction in adults with CLD was associated with changed sphingosine signalling, and this system was a therapeutic target for FTY720 (Fingolimod, a modulator of S1P signalling, approved for use in MS) and macrolide antibiotics. With Darwin collaborators, we will investigate whether airway macrophages from children with PBB or bronchiectasis:

- Have altered expression of the sphingosine signalling system that correlates with a defective ability to phagocytose bacteria
- Respond to sphingosine-targeted therapies including FTY720, and novel macrolide antibiotics that lack antimicrobial properties

> Zinc (Zn) offers new options for controlling cigarette-smoke induced pulmonary endothelial dysfunction

Patients with chronic obstructive pulmonary disease (COPD)/emphysema are at increased risk of developing cardiovascular disease. The causes are poorly understood. We have shown that Zn is critical for endothelial integrity/function, and that there is changed localization of Zn and its transporters in the airway epithelium in murine allergic asthma. We further showed reduced airway Zn in smokers with COPD. This project will characterize Zn and its transporters in the endothelium of normal/diseased blood vessels and the association of long-term smoking on vascular function. The resultant decline in endothelial Zinc levels leads to an increased susceptibility of the endothelium to cell death, dysfunction and disease. The study will advise the development of treatment strategies for major human vascular and alveolar lung diseases.

> Steroid resistant cytotoxic/pro-inflammatory lymphocytes in the lung

Glucocorticosteroids are commonly used in management of chronic lung disease; however, steroid resistance is a major challenge and the reason for the steroid resistance is both poorly understood and a major limiting factor in treatment. We have identified changes in several mediators (glucocorticoid receptor, nuclear enzyme HDAC2 and cell membrane transport proteins including Pgp) in blood and airway lymphocytes in COPD patients and severe asthmatics, and have targeted these mediators with low doses of currently available pharmaceutical drugs (used to treat other diseases) to render these lymphocytes sensitive to glucocorticosteroids. We don't know whether these steroid resistant lymphocytes invade the lung. We will collect lung tissue

from COPD patients, extract lymphocytes and use flow cytometry and cell-stimulation to identify steroid resistant lymphocytes in the lung parenchyma.

> Understanding and therapeutically targeting the migration of inflammatory/cytotoxic CD8+CD28null T-cells to the epithelium in chronic obstructive pulmonary disease (COPD)

Corticosteroids are widely applied in COPD management but they do not improve survival or alter its progression. In COPD there is an increase in prematurely senescent CD28null T-cells (derived from CD28+ precursors that have undergone repeated antigenic stimulation during chronic inflammation). These cells are significant contributors to chronic inflammation in COPD and are resistant to corticosteroids.

Intra-epithelial T-cells in COPD are predominantly CD8+ and most of these are CD28null. Sphingosine 1 phosphate (S1P), a signalling lipid, is a major regulator of lymphocyte trafficking via its interaction with S1PR1. We will investigate

- a. S1P involvement in the preferential migration of CD28null cells to the epithelium
- b. whether blocking S1PR1 or adding Fingolimod (a S1P1R regulator) has therapeutic potential

> Sphingosine kinases miss the train because of smoking a cigarette

We have pioneered the concept of defective clearance of apoptotic cells by alveolar macrophages (efferocytosis) as a leading mechanism of chronic airways inflammation in COPD. We showed that Sphingosine kinases (SPHK) are essential regulators of efferocytosis, and FTY720 (Fingolimod, a modulator of S1P signalling, now approved for management of multiple sclerosis) negated the effects of cigarette smoke on both efferocytosis and SPHK1/2 clumping.

Aims: To investigate the potential involvement of the Golgi in the subcellular localization of SPHK and regulation of efferocytosis in macrophages. We will

- a. test potential effects of Golgi blockage on subcellular localizations of SPHK in THP-1 macrophages (b) test potential effects of Golgi blockage on efferocytosis
- b. test whether FTY720/Fingolimod can alter the effects of Golgi blockage.

> Shingosine kinases (SPHK): novel therapeutic targets in COPD and lung cancer

COPD is a leading cause of death world-wide, and there are currently no effective therapies. We showed defective clearance of apoptotic cells by airway macrophages (efferocytosis) as a contributor to chronic inflammation in COPD and identified SPHK as essential regulators of efferocytosis. Effects of cigarette smoke on SPHK and efferocytosis in macrophages were negated by Fingolimod, a clinically approved modulator of S1PRs. We will collect lung tissue obtained during lung lobectomy operations from COPD and lung cancer patients and assess whether SPHK are dislocated from their normal subcellular localization, and have decreased enzyme activity as found in our cigarette smoke-exposed cell culture models. We hope to identify potential therapy targets for this disease.

> E-cigarettes: effects on airway inflammation, function and emphysema development

Despite definitive literature on the dangers of cigarette smoking, the long-term health risks of E-cigarettes are unknown. Our preliminary data showed that even non-nicotine containing E-liquids are damaging airway cells in a similar fashion to cigarette smoke. We will apply established techniques developed over the last decade, to investigate the effects of E-cigarettes using clinically-relevant airway samples from human smokers and controls, and smoke-exposed mice with emphysema.

> Exploiting increased autophagy as a new therapeutic approach for COPD

Autophagy is an important cellular responses to cell stress. Our preliminary studies show that increased autophagy is associated with COPD and smoking. This project will investigate the specific molecular mechanisms underlying the increased autophagy in response to cigarette smoke, including the causative role of autophagy in the cell death process, and evaluate the effects of therapies on autophagy and autophagy-associated apoptosis at the cellular, tissue and whole animal level and ex vivo in human COPD subjects. These studies will (a) advance our understanding of autophagy in COPD and (b) indicate novel therapeutic approaches with translational potential.

Matrix biology unit

Lead researchers:

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The mucopolysaccharidosis (MPS) group of inborn metabolic disorders arise from an inability to degrade complex sugars within the body. The build-up of complex sugars affects many tissues and organs leading to a wide range of symptoms in MPS children. The focus of our laboratory is to understand how complex sugars affect basic cell differentiation and function in order to develop treatments that resolve pathology in hard-to-treat tissues such as bone, cartilage and brain.

Research projects

> How do undegraded complex sugars affect cell differentiation?

The aim of this study is to generate pluripotent stem cells from skin fibroblasts of the following types of MPS disease, MPS I, MPS II, MPS IIIA, MPS IVA and MPS VI. The ability of these pluripotent cells harbouring an MPS mutation to become brain, bone, cartilage and fat cells will be investigated in cell culture and assessed by biochemical, histological and enzymatic methods. Specific pluripotent cells that fail to become brain, bone, cartilage or fat cells will be further analysed to determine which molecular pathways are affected. The main objective of this project is to generate in vitro cell culture models of the MPS disorders, as the mechanisms leading to the primary brain and bone disease, and the effect of MPS environment on tissue development, are poorly understood.

> Understanding the basis of growth retardation in MPS.

Children with MPS are extremely short failing below the 3rd percentile for height and this particular symptom has proven very difficult to address with current treatment modalities. The aim of this project is to understand how bone growth is dysregulated in MPS at (i) the basic molecular level and (ii) at the endocrine level. By identifying key dysregulated pathways the goal is to develop adjunct therapies that can promote normal bone growth in MPS children.

Honours projects

> How do undergraded complex sugars affect cell differentiation?

The aim of this study is to generate pluripotent stem cells from skin fibroblasts of the following types of MPS disease, MPS I, MPS II, MPS IIIA, MPS IVA and MPS VI. The ability of these pluripotent cells harbouring an MPS mutation to become brain, bone, cartilage and fat cells will be investigated in cell culture and assessed by biochemical, histological and enzymatic methods. Specific pluripotent cells that fail to become brain, bone, cartilage or fat cells will be further analysed to determine which molecular pathways are affected. The main objective of this project is to generate in vitro cell culture models of the MPS disorders, as the mechanisms leading to the primary brain and bone disease, and the effect of MPS environment on tissue development, are poorly understood.

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The Australian collaborative cerebral palsy research group

Lead researchers:

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The cerebral palsies are a diverse group of permanent movement disorders that affect one in 400 births world-wide. Cerebral palsy (CP) is an umbrella term given to these children, who often display sensory and intellectual impairments or epilepsy. Few cases are solely due to severe hypoxia or ischaemia at birth, but rather causation may occur well before labour and possibly back to conception. Risk factors include preterm delivery, fetal growth restriction, a tight nuchal umbilical cord, intrauterine infections and genetic causes, among others. We aim to understand the genetic causes of CP.

For additional information see:

adelaide.edu.au/robinson-research-institute/research/groups/cp

Research projects

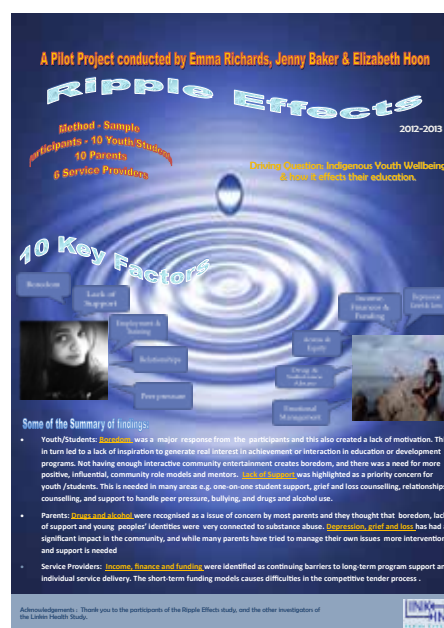
We have a potential Honours and PhD project for the right candidates to help further study the genetic causes of cerebral palsy. We are investigating how mutations arising spontaneously in the genomes of children and mutations inherited from parents might lead to CP using DNA derived from biological samples (blood and buccal swabs) in our Biobank. The CP Biobank is a large collection (repository) of DNA samples from CP cases, their parents and unaffected members of the public that can be linked with clinical health information.

The methodologies we use in our research include array-based genomic studies, DNA sequencing techniques such as whole exome (WES) and whole genome (WGS) sequencing, and animal knock-down gene models like the zebrafish to look at gene function and causative pathways to CP.

Adelaide rural clinical school

Lead researcher:

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The lung research team

- > Rural Clinical Academics across a range of disciplines
- > Stroke epidemiology and secondary analysis of rural and urban stroke data

Honours projects

- > Aboriginal health, culturally appropriate research, may be possible, but requires negotiation with the Aboriginal community
- > Stroke epidemiology and secondary analysis of rural and urban stroke data.

Neurogenetics research program

Lead researchers:

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Dr Lachlan Jolly

Dr Raman Sharma

Dr Duyen Pham



Neuro Olympics 2014

The Neurogenetics research program, which was established in year 2000, aims to understand the biology of human brain function by studying major neurological disorders which are genetically determined. By identifying and characterising the mutations implicated in intellectual disability, epilepsy and cerebral palsy, a greater understanding of the role of specific genes and proteins in normal brain function can be discovered.

The team has discovered or co-discovered in excess of 100 disease genes and actively works on about half a dozen of these using cell (including stem cell) and molecular tools.

For additional information see:

adelaide.edu.au/robinson-research-institute/researchers/group-leaders/gecz

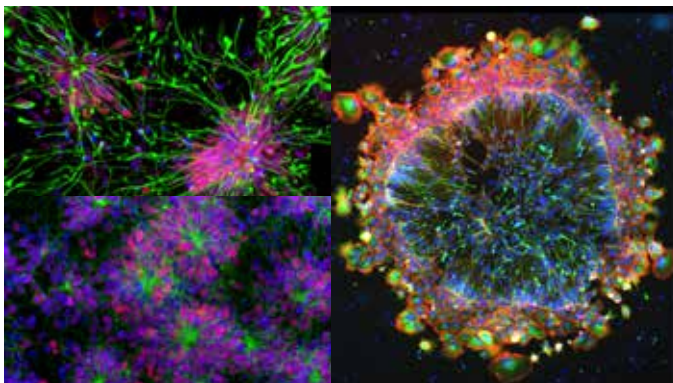
Research projects

We have 2-3 Research projects available in the field of genetics and molecular mechanisms of epilepsy and intellectual disability.

1. We are interested in the role of mRNA export pathway and in particular the THOC/TREX mRNA export complex in normal (neuronal) development.
2. We are investigating various types of genetic epilepsies using

whole genome and whole exome sequencing for novel mutation and novel gene identification together with cell and molecular validation of the relevant findings.

3. We are interested to investigate the underlying mechanism of so called 'female protective' effect." females (46, XX) have been found to tolerate genetic mutation better than males (46, XY).



Stem cells imaged by Claire Homan

Pregnancy and birth

Placental development laboratory

Lead researchers:

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Prof Gus Dekker

gustaaf.dekker@adelaide.edu.au



Placental development laboratory researchers

Our group takes a "bench to bedside" approach to discovery and solving clinical problems in pregnancy that have their origins in placental development and maternal adaptation to pregnancy. We undertake basic cellular and molecular experiments to elucidate mechanisms that govern normal and abnormal placental development. Our clinical research focuses on identifying genetic, nutritional and lifestyle factors that associate with pregnancy outcome. We also undertake clinical based projects (see Cardiovascular Obstetric Research of Northern Adelaide).

For additional information see:

adelaide.edu.au/directory/claire.roberts

Research projects

Honours projects

> Maternal diet and offspring telomere length

Supervisors: Prof Claire Roberts, Dr Tina Bianco-Miotto, Dr Jessica Grieger, Dr Tanja Jankovic-Karasoulos, Dr Prabha Andraweera

Telomeres are located at the ends of chromosomes and shorten with each cell division. In situations of high oxidative stress, inflammation or chronic disease, telomeres shorten further. There is increasing evidence that nutritional factors are associated with telomere length, thus poor quality and low micronutrient diets could potentially result in erosion of telomeres and contribute to chronic disease. There is little information about telomere length in pregnancy and infancy. Offspring exposed to adverse intrauterine exposures may have shorter telomeres at birth and during childhood, thus placing them at greater risk for chronic disease in later life. This project will investigate whether maternal diet quality is associated with telomere length in mum and baby. The student will gain experience in dietary questionnaires and quantitative real time PCR.

> Molecular regulation of placental development

Supervisors: Prof Claire Roberts, Dr Tina Bianco-Miotto, Dr Tanja Jankovic-Karasoulos, Dr Dale McAninch, Dr Amanda Highet

We have identified genes that are switched on in the placenta during distinct stages of pregnancy. Disruptions to the expression of these genes could lead to common pregnancy complications such as preeclampsia. We have a biobank of human placenta tissues from first trimester, second trimester and term pregnancies and from pregnancies complicated with common pregnancy complications. The Honours student will utilise our placenta biobank to investigate the role of a small number of genes and identify what placental cell types they are

expressed within. Students will gain experience in quantitative PCR, immunohistochemistry, and primary cell culture. This project would suit a student interested in learning molecular techniques. The outcomes of this research is to understand how the placenta changes at the molecular level throughout normal and complicated pregnancies.

> Micronutrients in pregnancy

Supervisors: Prof Claire Roberts, Dr Tina Bianco-Miotto, Dr Tanja Jankovic-Karasoulos, Dr Amanda Highet

Maternal micronutrient deficiencies including folate and vitamin D prior to and during pregnancy have been implicated in adverse pregnancy outcomes. This project investigates the role of the placenta in this association. First trimester and term placental explants will be cultured to investigate how folate alters placental explant growth, apoptosis, development, gene expression and DNA methylation status. Investigating the effect of micronutrients on placental function is a relatively new area of research with the potential to determine factors that go awry in the placenta during early pregnancy leading to placental insufficiency. This project will suit a student interested in learning more about pregnancy, maternal nutrition and placenta and will involve skills such as placenta explants and cell cultures, nucleic acid extractions, quantitative real time PCR and immunohistochemistry.

> Epigenetic regulation in placental development

Supervisors: Dr Tina Bianco-Miotto, Prof Claire Roberts, Dr Jimmy Breen

The placenta mediates fetal-maternal exchange and plays a major role in directing maternal adaptation to pregnancy. Although the placenta is a shared organ between mother and fetus, it is an extraembryonic tissue and is primarily regulated by the fetal genome. The placenta separates from mother and fetus after birth, making it a truly transient organ. For this reason, epigenetic mechanisms involved in placenta development may not be under the same constraints as other tissues. Epigenetic mechanisms regulate gene expression without altering the DNA sequence and are critical during development. By determining how epigenetic profiles change in the placenta throughout pregnancy and in response to adverse outcomes we can identify epigenetic biomarkers indicative of future risk of pregnancy complications. This project will suit a student who is interested in placental epigenetics, bioinformatics or molecular techniques.

Any of our groups' projects can be tailored for PhD students.

Evidenced based women's health care pregnancy and birth

Lead researcher:

Prof Ben Mol
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Much medical practice around the world is conducted without evidence that interventions are beneficial to the patient and will not cause harm. This group aims to develop evidence on the effectiveness of all medical interventions in this area, preferably through large collaborations in RCTs, to provide insight on the available evidence tailored to the individual patient. To achieve this, international collaboration of research agendas and the establishment of guidelines is essential. The group aims to involve young people, create large datasets and initiate international collaboration.

For additional information see:

adelaide.edu.au/robinson-research-institute/researchers/group-leaders/mol

Honours projects

> Usefulness of clinical research in Obstetrics and Gynaecology

Blue-sky research cannot be easily judged on the basis of practical impact, but clinical research is different and should be useful. It should make a difference for health and disease outcomes or should be undertaken with that as a realistic prospect. Many studies, even in major general medical journals, do not satisfy these features, and very few studies satisfy all of them (PLoS Med 13(6) 2016). Most clinical research therefore fails to be useful not due to its findings but because of its design. In this project, we will assess the usefulness of clinical research in Women's health. We will study the problem base, context placement, information gain, pragmatism, patient centeredness, value for money, feasibility, and transparency of papers published in high ranked journals. This information will fuel an altered approach and easily produce more clinical research that is useful, at the same or even at a massively reduced cost.

> Individual patient data meta-analysis (IPD-MA) of studies on induction of labour

Labour induction now exceeds 20% of all births. Many different methods have been used, but in SA prostaglandins remain a preferred method for cervical ripening and labour induction. Until now, published meta-analyses have focused on pair-wise "head to head" comparisons. IPD-MA can overcome these shortcomings. We aim to compare, through IPD-MA, in women scheduled for induction of labour, vaginal misoprostol, oral misoprostol, Prostaglandin E2 and Foley catheter. We then will assess whether individual profiles of pregnant women can be used as treatment selection markers to identify the most effective preventive strategy for subgroups of women with a particular characteristic (parity, gestational age, BMI, reason for induction). The honours student will contact individual researchers around the world, collect data, clean data, perform analysis and report in a publication and at international conferences.

Psychological and neurological health

NALHN mental health research

Lead researchers:

Prof Cherrie Galletly

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Dr Dennis Liu

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This group undertakes research with people with severe mental illness - depression, bipolar disorder, schizophrenia.

Honours project

This project looks at the transfer of patients from the Mental Health service to GPs. We are interested in who can be successfully followed up by GPs, and how to transition patients between services.

Neuromotor plasticity and development

Lead researcher:

Prof Michael C Ridding

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The Neuromotor plasticity and developmental group research interests encompass neuromotor development and neuroplasticity across the human lifespan, from prenatal and early postnatal factors influencing motor development, through to therapeutic uses of induced neuroplasticity in ageing and neuropathological disorders such as stroke and dystonia. The aim of the group's research is to inform and develop therapeutic interventions to develop, maintain and rehabilitate human motor function. For additional information see: adelaide.edu.au/directory/michael.ridding



Prof Michael C Ridding

Research projects

Neuroplasticity is the capacity of the nervous system to reorganise its connectivity in response to experience. Such plasticity is critical for learning, cognitive function and recovery from brain injury. There is some evidence linking decreases in neuroplasticity with poor cognitive function and a higher risk of dementia, however, to date little focus has been placed on the use of interventions to maintain the capacity for neuroplasticity and prevent cognitive decline in healthy ageing populations. This project will use cutting-edge non-invasive brain stimulation techniques to gain a mechanistic understanding of improvements in cognitive performance associated with a complex lifestyle intervention in the healthy ageing population.

Honours projects

> Neural correlates of cognitive ageing (Lead researcher: Dr Mitchell Goldsworthy).

Ageing is associated with a decline in cognitive performance, the profile of which can vary considerably between individuals. Marked deficits, particularly in memory and executive function, can be an early sign of neurodegeneration and future dementia. The aim of this project is to use advanced neurophysiological techniques (e.g., EEG, TMS) to characterise the neural factors associated with later life cognitive deficit.

> Cortical connectivity predicts neuroplasticity response (Lead researcher: Dr Brenton Hordacre).

Neuroplasticity is an important physiological characteristic of the brain and underpins learning, memory and recovery from injury. Neuroplasticity can be experimentally induced using non-invasive brain stimulation (NIBS). NIBS has been one of the few recent therapeutic advancements in neurological rehabilitation capable of improving functional recovery. However, neuroplasticity responses following NIBS have proven to be highly variable. This study will investigate whether cortical connectivity predicts neuroplasticity responses to various NIBS techniques. Establishing evidence for this relationship is crucial to advance the therapeutic potential of NIBS and assist neurorehabilitation.

Critical and ethical mental health research group

Lead researchers:

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Dr Melissa Raven

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The Critical and Ethical Mental Health research group (CEMH) is based within the Robinson Research Institute. Its mission is to improve the understanding of and responses to mental health issues and mental disorders, by undertaking and promoting critical and ethical appraisal and synthesis of research evidence and other discourse. Both quantitative and qualitative research methodologies are used. CEMH has strong national and international links, and it publishes internationally with like-minded researchers and practitioners, attracting significant academic and media attention.

For additional information see: ua.edu.au/cemh

Research projects

> RIAT reanalyses of drug trials (Restoring invisible and abandoned trials)

The RIAT (Restoring invisible and abandoned trials) initiative was established in 2013 to address selective/misleading reporting of outcomes of randomised controlled trials. In 2015, an international team including CEMH members published a high-profile RIAT re-analysis, 'Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence' (www.bmj.com/content/351/bmj.h4320), which found that paroxetine was ineffective and unsafe, contrary to the conclusions of the original published trial report. It demonstrated the necessity of access to primary trial data and protocols to improve the rigour of the evidence base. Other published/unpublished RCTs have been identified as warranting RIAT reanalysis.

Potential projects include:

1. Reanalysis of an influential RCT of an antidepressant and cognitive-behaviour therapy
2. Reanalysis of an RCT of an antipsychotic

> Psychotropic drug use by older people

There are high levels of polypharmacy (use of multiple prescribed drugs) among older people. This includes psychotropic drugs (particularly antidepressants, benzodiazepines, and antipsychotics), as well as other drugs that can have psychoactive effects (e.g. dizziness). Much of this drug use is off-label (for non-approved indications). The number of prescribed drugs is the single most important predictor of adverse drug events in older people.

Potential projects include:

1. Pharmacoepidemiological investigation of adverse events associated with psychotropic use.
2. Patterns/drivers of psychotropic prescribing to elderly people in residential aged care.
3. Patterns/drivers of psychotropic prescribing to elderly people living independently in the community.

> Antipsychotic prescribing

Antipsychotics should not be prescribed unless benefits exceed harms, which include rapid weight gain and metabolic disorders. However, prescribing rates have increased greatly. There is substantial inappropriate off-label prescribing (for unapproved indications) and prescribing without adequately trying first-line approaches, as well as diversion for recreational use.

Antipsychotics are being prescribed for sleep problems, for which behavioural strategies would generally be more appropriate. Many elderly people are prescribed them, despite evidence of potential harms, including increased mortality. Children/adolescents are prescribed them, mainly for unapproved indications such as behavioural problems, for which there is very limited evidence of effectiveness, and substantial evidence of harmful effects.

Potential projects include:

1. Investigation of GPs'/specialists'/nurses' prescribing practices and attitudes
2. Investigation of influences on prescribing

> Deprescribing of psychotropic and other drugs

Doctors are trained to prescribe drugs but historically have not been trained to discontinue them. Deprescribing is the systematic process of identifying and discontinuing drugs for which existing/potential harms outweigh benefits, within the context of an individual patient's circumstances/preferences. Medications are tapered/stopped in order to minimise polypharmacy and improve patient outcomes. However, there are potential barriers, including fragmented care, time constraints, guidelines developed for patients without multimorbidity, anticipated withdrawal effects, patients' perceptions, and carers' concerns.

Potential projects include:

1. Investigation of GPs'/specialists'/nurses' deprescribing practices/attitudes.
2. Investigation of patients' attitudes towards deprescribing of drugs.
3. Investigation of carers' attitudes towards deprescribing of drugs for elderly relatives.
4. Development and trialling of deprescribing protocols.

> Social determinants of mental health

Social determinants of health (including unemployment, poverty, food insecurity, inadequate housing, discrimination, and other forms of disadvantage) are significant contributors to mental health/illness. However, there has been inadequate research on the influence of social determinants on mental health, treatment access and utilisation, treatment effectiveness, and longer-term outcomes. Furthermore, relatively few prevention strategies target social determinants.

Potential projects include:

1. Investigation of relationships between a broad range of social determinants and children's mental health status/diagnoses
2. Investigation of relationships between a specific social determinant (e.g. food insecurity) and mental health status/diagnoses
3. Investigation of impact of social determinants on longer-term outcomes after treatment
4. Investigation of the feasibility/acceptability of prevention strategies focusing on one or more social determinants.

> Overdiagnosis of mental disorders

Overdiagnosis is common in medicine. It frequently results in inappropriate prescribing of potentially harmful drugs, and unnecessary procedures, including surgery. Overdiagnosis is caused by multiple factors, including widening of disease definitions, lowering of thresholds, and increasingly sophisticated diagnostic techniques.

Early diagnosis is intuitively appealing, and is sometimes appropriate, but there is increasing evidence that detecting mild/early cases of disease paradoxically carries harms that may outweigh benefits. This is increasingly recognised in relation to physical diseases such as prostate cancer, but mental health professionals are lagging in awareness of overdiagnosis.

Potential projects include:

1. Drivers of overdiagnosis in mental health (generally, or specific disorder(s)).
2. Development and trialling of prevention strategies.

Honours projects

> Overdiagnosis of mental disorders

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Potential projects include:

1. Investigation of doctors'/medical students'/other health professionals' awareness of overdiagnosis.

> Psychiatric drug use by children and adolescents

Treatment of Australian children and adolescents with prescribed psychotropic medications (psychiatric drugs), by both psychiatrists and general practitioners, has increased substantially in recent decades. Prescribing rates vary considerably in different Australian jurisdictions and regions, adding to concerns about possible over-prescribing and/or under-prescribing.

Potential projects include:

1. Analysis of variations in prescribing rates in different states/territories and regional/metropolitan areas.
2. Investigation of sociodemographic factors that contribute to variations, including geographic isolation, family income, education, and ethnicity.
3. Investigation of health system factors that contribute to variations, including: availability and models of delivery of mental health services; prescriber characteristics; access to other health/welfare professionals.

> Psychotropic drug use by older people

There are high levels of polypharmacy (use of multiple prescribed drugs) among older people. This includes psychotropic drugs (particularly antidepressants, benzodiazepines, and antipsychotics), as well as other drugs that can have psychoactive effects (e.g. dizziness). Much of this drug use is off-label (for non-approved indications). The number of prescribed drugs is single most important predictor of adverse drug events in older people.

Potential projects include:

1. Patterns/drivers of psychotropic prescribing to elderly people in residential aged care.
2. Patterns/drivers of psychotropic prescribing to elderly people living independently in the community.

Behavioural neuroscience group



Lead researcher:

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a strong interest in the neurobiological basis of individual differences in behaviour and mental health. She works on the intersection between psychology, physiology and behaviour using a translational approach. She has proposed a new theory about the effects of early life experiences on the developing oxytocin system and the impact this has on later drug use. Her research group is using a range of techniques to test the impact on infants of observed early life environment.



Dr Femke Buisman-Pijlman

For additional information see:

researchers.adelaide.edu.au/profile/femke.buisman-pijlman

Research projects

> Improving child outcomes through play

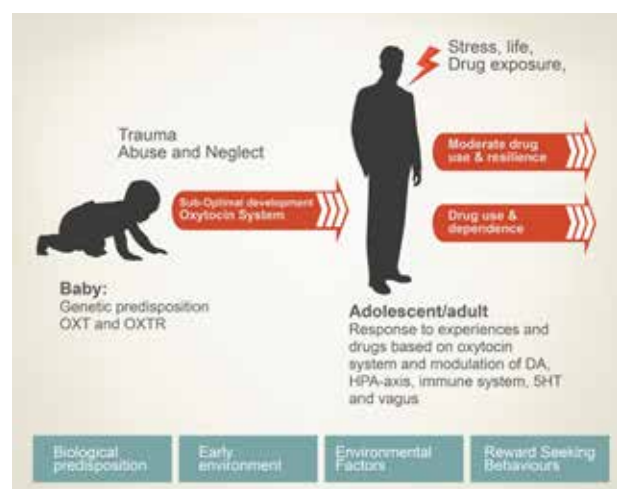
Play and social interaction are vital for babies and children. They learn how to behave and how the world works. But does play and social interaction impact on our body through our hormones as well? Kids with early adversity can be at increased risk of developing mental health and addiction problems. Does the experience, or lack of positive experience, affect the developing brain and hormone systems? What makes some people so resilient? We will start answering these questions using behavioural observations and hormone measurements.

Honours projects

> A responsive early social environment is vital for development.

But does play and social interaction impact on our body through our hormones as well? We will use different techniques to start answering these questions.

We have found that collecting new human data is not feasible in an Honours project. However, secondary data analysis of birth cohort data can be very useful to answer sub questions.



Hypothesised model of the impact of early environment on the developing oxytocin system and later drug use (Buisman-Pijlman et al, 2014).

Lead researcher:

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Centre for Traumatic Stress Studies research team



L - R : Director of Centre, Prof Alexander McFarlane,
Director of Research, Dr Miranda Van Hooff

The Centre seeks to improve evidence-based practice by informing and applying scientific knowledge in the field of trauma, mental disorder and wellbeing in at risk populations. The Centre has expertise in the aetiology and epidemiology of mental/physical disorders, disasters, accidents, early life stress and occupational health (including military and first responders) and has five streams: Trauma and adversity across the lifespan, Military mental and physical health,

Research projects

> Trauma and adversity across the lifespan

Exploring the impacts of lifetime trauma on mental and physical problems across the lifespan. Data are derived from four longitudinal datasets with multiple time points. Exposures include accidents, disasters, environmental exposures, childhood trauma and injuries. Projects examine predictors of ICD-10 mental disorder, physical health, socio-economic outcomes, PTSD, somatic symptoms, personality, risk taking behaviour, functioning, emotional regulation and family structure and relationships. The role of cumulative and repeated trauma exposure is a key focus.

Key projects:

- A 26-year study of 1532 children exposed to the 1983 Ash Wednesday Bushfires.
- A 30-year study of the relationship between lead exposure, early child development, cognitive functioning and adult health in a birth cohort (N=723) from Port Pirie SA.
- The long-term mental and physical impacts of major injury (childhood burns N=1101 and traumatic injury survivors N=1084).

> Military mental and physical health

This large research program examines the mental and physical health of Australian Defence Force personnel (ADF) specifically civilian and military (incl. deployment) predictors of health and performance. Key themes: ICD-10 mental disorder, mental and physical health, mTBI, screening, substance use, help seeking, resilience, support, combat exposures and lifetime trauma.

Neuro-biological and physical impacts of conflict and service including environmental exposures, illness and injuries are priorities

Key projects:

- Prevalence and predictors of mental disorder and psychological distress in the entire ADF (N=50049): 2010 ADF Mental Health Prevalence and Wellbeing Study.
- Deployment to the Middle East (MEAO): The MEAO Prospective Study of 1324 personnel pre-post deployment.
- The Transition and Wellbeing Research Programme (N=103049). Mental and physical health of current and ex-serving ADF members and their families: the role of transition and combat.

> Occupational mental and physical health

This stream consists of research into population rates of mental and physical disorder. Projects examine the prevalence and predictors of mental and physical health in Australian occupational settings involving repeated exposure to stress, violence, trauma and death. Representative cohort data from Emergency Service Personnel (SA Metropolitan Fire Service, Ambulance Service, State Emergency Service and Emergency Departments) is being used to investigate the role of workplace exposures, occupational stress, and lifetime trauma in the development of mental and physical symptoms over the career course.

Key projects:

- Predictors and prevalence of mental and physical symptoms in the Australian emergency services.
- Risk taking behaviour, gambling and substance use in the Australian emergency services.
- Trauma, PTSD and anger in the Australian emergency services.
- Treatment seeking, support and barriers to care in the Australian emergency services.

> Neurobiological mechanisms of traumatic stress

This research stream is focused on understanding the neurobiological mechanisms underpinning responses to stress exposure. This includes examining a range of potential risk and resilience indicators including objective neurophysiological outcomes such as emotional processing, working memory, attentional processes, and resting electrophysiology; biological outcomes such as immune response and metabolic changes; and both structural and functional brain imaging.

Key Projects:

- Investigating the dynamics of neurocognitive function in response to stress.
- Examination of physiological processes underlying the development of psychopathology.
- Identification of biomarkers of risk and resilience in highly traumatised populations.

> Intervention evaluation.

This research stream aims to identify and assess the effectiveness of novel intervention approaches aimed at enhancing performance and capacity, mitigating risk and/or augmenting existing treatments in individuals exposed to high levels of stress/trauma.

Key Projects:

- Evaluating assistance dogs as a treatment adjunct for veterans with PTSD.
- The role of mindfulness approaches in the treatment of PTSD
- Predicting and sustaining cognitive capacity in the face of the challenge of combat.

Translational neuropathology laboratory

Lead researcher:

Dr Renée Turner

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Team Neuro 2016

We use pre-clinical models to investigate the complex mechanisms of injury and disease to develop new treatments for central nervous system disorders including stroke (Dr Renee Turner), traumatic brain injury (Dr Frances Corrigan; A/Prof van den Heuvel), chronic traumatic encephalopathy (Dr Frances Corrigan), spinal cord injury (Dr Anna Leonard) and neurodegenerative diseases such as Parkinson's Disease (Dr Lyndsey-Collins Praino). We have a particular focus on translating research findings into the clinical setting. For more information please contact the individual group leaders.

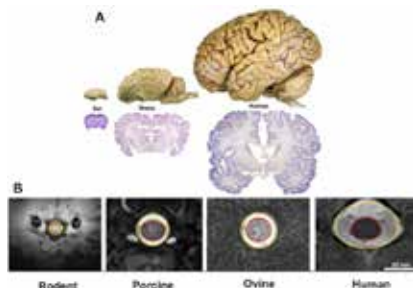
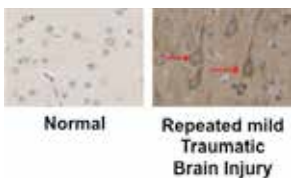
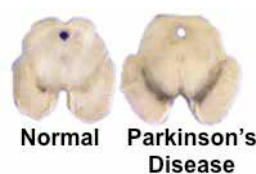


Fig.1 Differences in brain (A) and spinal cord (B) structure/size between species (Dr Renee Turner and Dr Anna Leonard).



Hyperphosphorylated tau increases in repeated mild TBI (Dr Frances Corrigan).



Loss of dopamine neurons in Parkinson's Disease (Dr Lyndsey Collins-Praino).



Centre for Neurological Diseases



Lead researchers:

Prof Peter Blumbergs

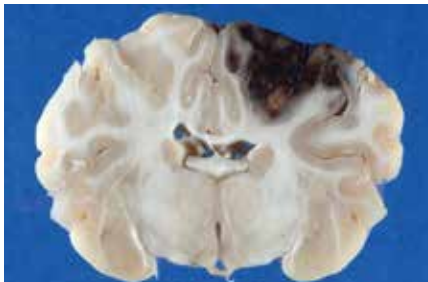
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Mr Jim Manavis

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Traumatic cerebral hemispheric impact contusion

This neurological diseases investigation group is the result of a longstanding collaboration between the School of Medicine and the Hanson Institute Centre for Neurological Diseases at SA Pathology (formerly IMVS). It seeks to

better understand the pathology and pathogenesis of a number of important neurological disorders, utilising skills in neuropathology, neurology, veterinary neuropathology, immunohistochemistry, and ultrastructural pathology.

Research projects

> Brain tumour studies

Honours projects

> Pathogenesis of traumatic brain injury

> Bacterial Neurotoxins

> Pathogenesis of neurodegenerative diseases

Neurophysiology of human movement



Lead researcher:

A/Prof John Semmler

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Our research focuses on the neural mechanisms responsible for changes in human movement throughout the life span. We specialise in the use of transcranial magnetic stimulation as a tool to painlessly and non-invasively investigate specific features of the cortical control of skeletal muscles using a number of interventions, such as ageing, exercise, training, and fatigue. The overall goal is to understand how the healthy nervous system functions to control movements following a variety of interventions, and how it may adapt in situations involving neuromuscular injury or disease.

For additional information see:

researchers.adelaide.edu.au/profile/john.semmler

Research projects

HDR projects examining the neurophysiology of human movement are available. Please contact the group head for further details.

Honours projects

> Optimising brain plasticity and motor function in older adults

Ageing is associated with a pronounced decline in many motor, cognitive, and other brain functions, but the cause remains elusive. This project will examine the mechanisms that contribute

to a decline in brain plasticity and motor function in the elderly. Using novel brain stimulation techniques, the project will develop an optimal approach to boost plasticity in the ageing brain and improve motor function in the elderly.

There will be several studies on offer in this area, which are supported by an Australian Research Council Discovery Project grant.

> Genetic influences on human brain plasticity and motor performance

Several studies have shown that a common variation in the brain-derived neurotrophic factor (BDNF) gene influences motor cortex plasticity and motor skill learning under some circumstances. Furthermore, it is well known that spaced practice is more effective for motor learning than massed practice. This study will examine how different types of practice influence motor cortex plasticity and motor performance in people with different BDNF genotypes. Results from this study may suggest that different practice structures could be tailored to optimise motor performance in people with different genetic profiles.

> Neurophysiological effects of concussion in humans.

Recent studies using transcranial magnetic stimulation (TMS) have shown that concussion results in long-term motor dysfunctions that are attributable to altered excitability and plasticity in primary motor cortex. However, TMS-EEG is emerging as a more sensitive assessment of synaptic function and cortical connectivity, providing information that cannot be obtained with any other neuroimaging technique. This project will use TMS-EEG to examine the influence of prior concussion on cortical function and connectivity. Findings from this study may lead to a more objective assessment of brain health following concussion and provide a more reliable indicator of recovery.

Human anatomy teaching research group



Lead researcher:

A/Prof Ian Johnson
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This is a collaborative project run by teaching experts in Adelaide (A/Prof Ian Johnson) and Newcastle upon Tyne, UK (Prof Steve McHanwell and Dr Iain Keenan). It will also include input by professional visual artists in Adelaide and Capetown, South Africa. Most of the group's interactions will be online, but some international travel will be required.

Research projects

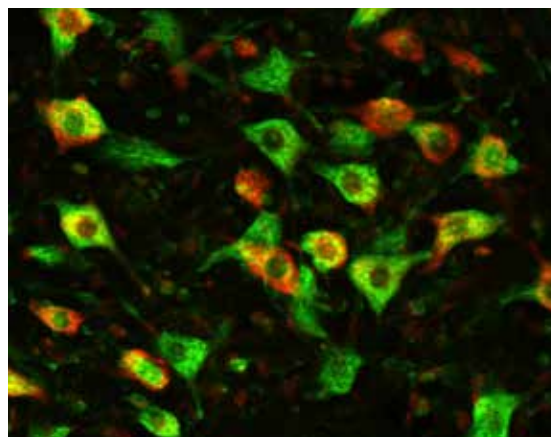
A recent study by a group in Newcastle, UK found improved learning outcomes in human anatomy and the acquisition of transferable skills for students who incorporated an online structured drawing regime in their studies. This collaborative Newcastle-Adelaide project will refine this work to incorporate online instruction in visual arts into anatomy courses at the University of Adelaide. The hypothesis tested is that observational drawing will improve students' understanding of 3-D anatomy and improve student satisfaction. The study will be supervised by anatomy education specialists in both countries, have a crossover design, input by visual artists and careful evaluation of learning outcomes in the context of contemporary pedagogical theories and current knowledge of the neuroscience of spatial memory. It will involve short periods in the UK and application of the results to inform the delivery of virtual reality into anatomical teaching at the University of Adelaide is envisaged.

Motoneurone research laboratory



Lead researcher:

Associate Prof Ian Johnson
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Motoneurons captured in a confocal laser scanning microscope image

Located in the Motoneurone Research Laboratory of the 5th floor, Medical School South we use a variety of techniques to analyse mechanisms underlying motoneuronal survival and degeneration after injury with specific reference to Motor Neurone Disease. Techniques include microneurosurgery, confocal and electron microscopy, immunocytochemistry and multiplex analyses.

For additional information see: adelaide.edu.au/directory/ian.johnson

Research projects

- > Mechanisms underlying the differential vulnerability of alpha and gamma motoneurons to injury
- > Interplay between Nissl bodies and stress granules in neuronal degeneration
- > Art, human anatomy and learning outcomes (in collaboration with Anatomy Education Specialists in the UK)

Honours projects

Two Australians per day die from Motor Neurone Disease (MND) which affects people aged 55-65. Treatments have been developed from studies of immature animals, but they have all failed (Johnson, I.P. 2015 *Frontiers in Aging Neuroscience* 7. doi:10.3389/fnagi.2015.00168). The projects will examine the possibilities that MND:

1. Could be due to age-related changes in neuroinflammation, excitation or neuroglial activity
2. Could MND be cured by a muscle-specific isoform of IGF-1 called Mechanogrowth factor (MGF).

Specifically, they will determine whether facial motoneuronal survival is affected by:

- a. Experimentally-induced neuroinflammation
- b. The balance of excitatory and inhibitory synapses
- c. The nature of the microglial and astroglial activity
- d. Delivery of MGF or inhibition of its action.

Integrative human neurophysiology laboratory



Lead researcher:

Dr Simran Sidhu

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The research conducted in this laboratory investigates how the central nervous system coordinates the movement of our bodies and how it is reorganized as a consequence of exercise. The lab focuses on the area of fatigability and exercise intolerance in health, aging and disease. The research involves the application of various novel and non-invasive electro-physiological techniques such as Transcranial Magnetic Stimulation (TMS), peripheral nerve stimulation, and electromyography(EMG) in experiments involving human subjects.

For additional information see:

researchers.adelaide.edu.au/profile/simran.sidhu

Honours projects

- > Impact of fatiguing locomotor exercise on human brain responses

Non-invasive brain stimulation methods (i.e. conditioning-test TMS protocols) can be used to study the functional connectivity of neurons within primary motor cortex and monitor changes in responsiveness of specific intracortical inhibitory (and facilitatory) neurons during locomotor exercise. A better understanding of these pathways is significant because it would contribute to the debate on what causes people to interrupt a whole body dynamic activity in both sporting and rehabilitative contexts, and in particular if this stoppage is related to factors within the human brain. The aim of this project is to investigate the influence of functional whole body fatiguing exercise on the excitability of motor cortical circuitry.

> Neural Mechanisms underlying the impact of fatigue on the performance of visually guided movements

The aim of this project is to use various non-invasive brain stimulation paradigms including transcranial magnetic stimulation to examine the underlying neural responses, and transcranial direct current stimulation to enhance neural activity, during performance of visual tasks with and without fatigue.

Psychiatric Neuroscience Centre



Lead researcher:

Prof Bernhard Baune

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Prof Bernhard Baune

Research within the Psychiatric Neuroscience Centre in the Discipline of Psychiatry is directed into a branch of animal research and human research. Both streams use a variety of technical platforms (e.g. Imaging, genetics, -omics, animal models, genetic engineering, cell technologies) in order to study the neurobiology of psychiatric disorders and the mechanisms underlying treatments and interventions. Currently, the main research groups supporting this research centre are in the areas of basic neuroscience, behavioural animal modelling, genetic engineering of

mouse models, gene-environmental.

For further details see:

health.adelaide.edu.au/psychiatry/research_centres/psychiatric_neuroscience_centre/

Psychiatric neuroscience research group

Lead researchers:

Prof Bernhard Baune

61 8 8222 5141 or bernhard.baune@adelaide.edu.au

Dr Catharine Jawahar

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The Psychiatric neuroscience research group combines the search for psychiatric disease genes with basic studies of the nervous system. Research focuses on the genetics and neurobiology of psychiatric disorders with an emphasis on the biology of cognitive and emotional processes. Overall aim of the group is to identify candidate genes of psychiatric disorders and more subtle

phenotypes, to study the functions of these genes in pharmacological studies in relation to psychiatrically relevant phenotypes of cognition, emotion and behaviour as well as the study of the mechanisms that underlying generation.

For additional information see:

health.adelaide.edu.au/psychiatry/research/psychiatric_neuroscience_rg

Research projects

> Animal models of psychiatric disorders

Using a number of validated behavioural tests we assess for behavioural dysfunctions (mood and cognition-like) and effects of different pharmacological agents in inbred and genetically modified mouse strains of neuroimmunological interest.

> Genetics / epigenetics / gene-expression analyses in psychiatric disorders

Individual differences in susceptibility to psychiatric disorders and response to treatments have a genetic contribution. The aim of this project is identify and analyse the various gene polymorphisms that are associated with development or treatment of psychiatric disorders

> Post-mortem studies

Identification of genetic and gene expression differences between healthy individuals and people with psychiatric disorders using Laser-capture microdissection of specific group of cells from post-mortem brain tissues.

Neuroimmunology research group

Lead researchers:

Dr Catherine Toben
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Dr Catharine Jawahar
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The aim of the neuroimmunology research group is to investigate the role of the immune system in the brain ranging from normal brain function to specific neuropsychiatric disorders such as cognitive decline, depression and anxiety. Currently, the research focus is on the molecular effects of cytokines on the hippocampus, the prefrontal cortex and glia cells under physiological and immune-challenged conditions. Ultimately, the work aims at developing immune-modifying treatments beneficial for common psychiatric disorders such as cognitive decline and some forms of depression.

For additional information see: health.adelaide.edu.au/psychiatry/research/neuroimmunology_rg/

Research projects

> The role of cytokines and its receptors in cognitive function and mood

This project utilises various genetically modified mice to uncover immunological mechanisms in the brain.

> Early life stress (ELS), immune function and neurobiology in mental illness.

Immune system is increasingly implicated in mediating long-term effect of ELS on adult mental health. This project aims to understand the immune mechanisms involved in the biological embedding of ELS and its effect on behaviour of the individual

> Immune-modulating interventions with effects on neuropsychiatric disorders

Investigate effects of clinical interventions of immune-modifying agents that benefit cognitive, emotional and behavioural function in psychiatric disorders.

Neuroregeneration, neural plasticity and neural repair research group

Lead researchers:

Dr Catherine Toben
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Prof Bernhard Baune
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The study of natural mechanisms of neuroprotection, agents used as neuroprotective and therapeutic neuroprotection is an emerging area of study for their role in either preventing or supporting recovery processes of psychiatric illnesses. The aim of this research group is to identify specific agents and mechanisms relevant to neuroplasticity, neurorepair and neuroprotection with specific relevance to cognitive processes such as learning and memory, attention as well as emotional processes relevant to neuropsychiatric disorders.

For additional information see:

health.adelaide.edu.au/psychiatry/research/neuroprotection_rg/

Research projects

> Study neuroprotective agents in mouse models

Identify and investigate the effects of neuroprotective agents in animal models of neuroinflammation with hypothesised positive effects on cognitive and emotional phenotypes.

> The role of T cells in depression

Recent evidence has pointed towards T cells having an active role in the process mediating clinical depression. In this project we utilise chronic mild stress mouse models to mimic depressive like behaviour and thereby enable more defined roles of T cells to be determined.

Psychiatric-omics research group

Lead researchers:

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Dr Oliver Schubert
oliver.schubert@adelaide.edu.au



Dr Oliver Schubert

Findings from genome-wide association studies (GWAS) indicate the heritable component of psychiatric disease is comprised of genetic variation influencing gene-expression levels. There is a pressing need to integrate transcriptomic and epigenomic data with GWAS data in order to provide more comprehensive understanding of the aetiology of psychiatric disease. Further, to understand the molecular mechanisms underlying psychiatric disease, genomic, epigenomic, and transcriptomic effects on the proteome and vice-versa, and how they influence psychiatric phenotypes requires investigation.

For additional information see: health.adelaide.edu.au/psychiatry/

Research projects

> Defining the role of inflammation in depression during ageing.

Transcriptomic and genomic data integrated to predict inflammation (proteins) to define an inflammatory predictive model in geriatric depression.

> Identification of transcriptomic alterations in major depressive disorder (MDD) cases exhibiting peripheral inflammation using next generation RNA sequencing technology.

> Lithium treatment response in bipolar disorder

Functional characterisation of a genome-wide association study and a systems biology analysis using next generation RNA sequence data.

> Epigenetic mechanisms of brain dysfunction in psychotic and mood disorders.

> The Longitudinal Lifestyle of Our Kids Study.

Longitudinal study collecting genetic and epigenetic data in conjunction with psychological and physiological data investigating the role of physical activity in the primary years.

Clinical Psychiatry Research Centre

Lead researcher:

Prof Bernhard Baune
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Clinical research is pivotal to improving the mental and physical health of patients with severe mental illness. To enhance clinical research in Psychiatry, the Discipline of Psychiatry at the University of Adelaide has established a Clinical Psychiatry Research Centre. Psychiatry research within this Clinical Centre is conducted across the teaching hospitals of the University of Adelaide. The purpose of the Centre is primarily to provide high quality clinically relevant assessments and to conduct clinical studies in patients with severe mental illness. The Centre enhances clinical collaboration

For further details see: health.adelaide.edu.au/psychiatry/research_centres/clinical_psychiatry/

Cognition and functioning in psychiatry research group



Lead researchers:

Prof Bernhard Baune
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Thomas Butler
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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.

For additional information see: health.adelaide.edu.au/psychiatry/research/neuropsychology_rg/

Research projects

- > **The Cognitive Function and Mood Study (CoFaMS)**
Investigate effects of depression and anxiety on a person's mental status and 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 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.
- > **Cognition and Functioning in Depression with Peripartum Onset (PPD) Study**
This longitudinal study investigates the relationship between cognition, functioning, and parenting ability in mothers with PPD. Results will inform the personalisation of cognitive interventions to improve PPD outcomes.

Psychiatric and medical comorbidities research group

Lead researchers:

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Dr Oliver Schubert
oliver.schubert@adelaide.edu.au

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.

For additional information see: health.adelaide.edu.au/psychiatry/research/medical_comorbidity_rg

Research projects

Projects in this group aim to investigate the aetiology and clinical consequences of psychiatric conditions in both cardio vascular disease (CVD) and diabetes mellitus (primarily type 1) and vice versa (e.g., metabolic consequences of psychiatric disorder), as well as the role and impact of psychiatric, psychological, and psychosocial interventions on the course of these conditions.

- > **Mood disorder, cognitive function and cardiovascular disease.**
An investigation of the brain morphology and neuropsychiatric sequelae in patients with comorbid CVD and depression
- > **The neuropsychiatric sequelae associated with type 1 and 2 diabetes**
A study of the neuropsychiatric characteristics and consequences of type 1 and type 2 diabetes
- > **Comorbidity between depression and life-limiting illness including cancer**
Describing the relationship between depression and end-of life cancer (Conceptualisation of depression in life-limiting illnesses)

Mindfulness research group

Lead researcher:

Dr Maura Kenny
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Ongoing research in the field of mindfulness-based interventions continues around the globe. Mindfulness-based Cognitive Therapy (MBCT) for those with chronic and recurrent depression and anxiety is regularly provided through the Centre for the Treatment of Anxiety and Depression (CTAD), SA Health opening up the potential for clinical trials to be conducted on the courses provided here four times per year. Masters and PhD students are welcome to contact us if interested. CTAD also hosts regular meetings for those interested in research into mindfulness, discussing local and international articles.

Research projects

- > **MBIs in workplace stress**
- > **MBCT for depression and shame**
- > **MBIs in Educational Settings**

For further details see: health.adelaide.edu.au/psychiatry/research/mindfulness_rg/

Lead researcher:

Prof Bernhard Baune
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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:

health.adelaide.edu.au/psychiatry/research_centres/translational/

Neuroimaging research group

Lead researcher:

Prof Bernhard Baune
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Neuroscience utilises key Imaging technologies such as MRI and PET among others to better characterise brain function and brain morphology in healthy individuals and in psychiatric conditions such as depression and schizophrenia. A significant progress in understanding the underlying biology and in identifying potential biomarkers in Neuroimaging has been made in the recent years by combining Genetics and Neuroimaging. In collaboration with experts around the world, this research group has been pioneering the Imaging Genetics approach in Depression and in Pharmacogenetics in particular.

For additional information see:

health.adelaide.edu.au/psychiatry/research/neuroimaging_rg/

Research projects

- > Neuroimaging of pharmacoresponse in depression
- > Genetic basis of functional and structural brain characteristics in healthy and pathological psychiatric conditions
- > Immunogenetics of brain morphology and function
- > Immunogenetics in Gene x Environment interaction

Biomarkers and pharmacogenetics research group

Lead researchers:

Dr Scott Clark
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Prof Bernhard Baune
+61 8 8222 4229 or bernhard.baune@adelaide.edu.au



Dr Scott Clark

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. For additional information see:

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

Epidemiology and health services research group

Lead researcher:

Dr Scott Clark
+61 8 8222 4229 or scott.clark@adelaide.edu.au

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.

For additional information see:

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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Dr Oliver Schubert

oliver.schubert@adelaide.edu.au

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.

For additional information see:

health.adelaide.edu.au/psychiatry/research_centres/translational/

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.

Molecular neuropharmacology



Lead researcher:

Dr Ian Musgrave
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Dr Ian Musgrave

The main thrust of this research is neuroprotection and neurotoxicity. This has been followed on three fronts; the role of amyloid peptides in neurotoxicity, how this neurotoxicity may be combated with natural products and the toxicity of herbal medicines. Collaborators include Dr Scott Smid (Pharmacology), Prof Roger Byard (Pathology) and Michael Bunce (Curtin University, WA).

For additional information see:
adelaide.edu.au/directory/ian.musgrave

Honours projects

- > **Protein misfolding into amyloid underlies pathologies as diverse as cataract formation and HIV infectivity.** One of the most important of these amyloidopathies is Alzheimer's disease (AD). Currently there is no mechanism based therapy for AD. As amyloid formation appears central to the development of AD. We have been investigating natural products which can prevent, and to some degree reverse, the aggregation of amyloid into its toxic forms. This project will further investigate the ability of natural products to reverse amyloid aggregation in relevant models
- > **Despite the popular belief that herbal medicines are safer compared to conventional pharmaceuticals, there continues to be reports of serious adverse reactions including hepatotoxicity following the use of herbal medicines.** The underlying biochemical mechanism of this toxicity is still unclear. This project will explore the role of drug-herb interactions in herbal medicine toxicity.

Neuropharmacology of drug abuse



Lead researcher:

Dr Abdallah Salem
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Understanding how drugs of abuse interact with the cells in our body to cause their effects is fundamental to the development of strategies to deal with many of the social and health problems associated with these drugs. This requires understanding of the chemistry of the drugs, associated neuroscience and their neuropharmacology. We use a number of methods and techniques to pursue this understanding including in vivo radiotelemetry and microdialysis. The drugs currently under investigation include ecstasy and associated amphetamines.

For additional information see:
health.adelaide.edu.au/pharmacology/research/

Honours projects

- > **Microglial activation and MDMA-induced hyperthermia.** The main MDMA-induced adverse effect is disruption of normal thermoregulation leading to life threatening hyperthermia which is exacerbated by high ambient temperature and linked to chronic neurotoxicity. Results obtained from our recent studies suggest an association between microglial activation and MDMA-induced hyperthermia. We have demonstrated that pre-treatment with minocycline, an antibiotic with glial attenuating properties, can significantly reduce the severity of MDMA-induced hyperthermia. The overall aim of this project is to extend our understanding of the underlying mechanisms leading to the disruption of normal thermoregulation and how minocycline reduces the hyperthermic response to MDMA.

Surgical and health systems innovation

Surgical evaluation group



Lead researcher:

Prof Guy Maddern
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Prof Guy Maddern

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.

For additional information see:
adelaide.edu.au/directory/guy.maddern

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

Ophthalmic research laboratory



Lead researcher:

Prof Robert Casson
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The Ophthalmic research laboratory, located in the Hanson Institute, is a well-funded laboratory comprising senior scientists, research assistants and students. We received two 4-year NHMRC Project



Prof Robert Casson, Head of Discipline of Ophthalmology

Grants in 2016 for approximately AUD\$1.5 million. We foster interdisciplinary and industry collaboration, and have developed a highly productive research program with an Adelaide-based ophthalmic laser company, Ellex Medical Lasers. We conduct world-leading basic science and translational research. All our students gain valuable experience in translational science and authoring publications.

For additional information see:

health.adelaide.edu.au/ophthalmology/research/

Research projects

> Understanding retinal ganglion cell bioenergetics

Primary open-angle glaucoma (POAG) is the most common, age-related form of chronic glaucoma. The pathogenesis of glaucomatous optic neuropathy remains incompletely understood, but there is converging evidence that energy production at the level of the RGCs and their axons is a key pathogenic component. In a recent double-blind, randomized clinical trial (RCT), we demonstrated that energy substrate delivery with glucose temporarily recovered vision in individuals with severe POAG. The research project will advance our understanding of the biochemical mechanism of this neurorecovery.

> Novel bioenergetic treatment for glaucoma

Glaucoma refers to a group of potentially blinding eye diseases united by a clinically characteristic optic neuropathy and associated degeneration of the retinal ganglion cells (RGCs). Primary open-angle glaucoma (POAG) is the most common, age-related form of chronic glaucoma. In a recent double-blind, randomized clinical trial (RCT), we demonstrated that energy substrate delivery with glucose temporarily recovered vision in individuals with severe POAG. This project assesses alternative energy substrates in experimental models as a foundation for clinical translation. We have already developed a clear pipeline from the lab to the clinic, and our Australian-based team is ideally placed to continue to lead the world in this field.

> Hyperspectral imaging of the retina

In this project we aim to utilise a novel imaging tool (hyperspectral imaging) to image the normal and diseased mammalian retina. This technique provides functional information at the molecular level. Successful application of this technique to the retina would revolutionise ophthalmic practice, allowing earlier detection and real-time monitoring of dynamic disease status, resulting in better outcomes for individuals with blinding diseases. We have formed an ideal interdisciplinary team to achieve this highly innovative goal with potentially rapid clinical translation.

Honours projects

> Immunolocalisation of glucose transporters in the retina

This project will use immunohistochemistry to localise the various types of glucose transporters in the mammalian retina. Our lab is particularly suited to this project, which is completely novel work that is likely to generate widespread interest across disciplines and result in high quality publications.

> Novel treatment for proliferative vitreoretinopathy (PVR)

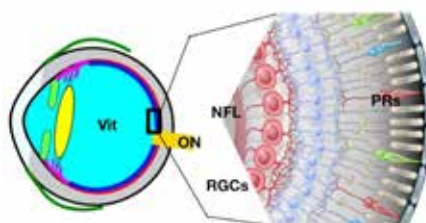
PVR is a major complication of retinal detachment surgery and the primary cause for poor visual outcomes. It is a poorly understood condition involving contracture of the retina. We have developed cell culture models of this condition and plan to test potential new treatments. This is an exciting research project that could revolutionise treatment of PVR.

> Novel microinvasive surgical treatment for glaucoma

We are collaborating with Ellex Medical Lasers and the Institute for Photonics and Advanced Sensing to develop a new technique to identify and cannulate Schlemm's canal. We are utilising a novel micro imaging device with the aim of obtaining a safe and better surgical treatment for glaucoma.

> Improving delivery and safety of a novel retinal laser

We are collaborating with Ellex on the refinement of a new retinal laser that can treat age-related macular degeneration, the commonest cause of blindness in Australia. This new laser will be the first to directly and safely treat the macula in humans. The project would include laboratory and clinical components.



In glaucoma, the retinal ganglion cells (RGCs) degenerate. Their axons in the retina comprise the nerve fibre layer (NFL) and become the optic nerve (ON). In age-related macular degeneration, the light-sensitive photoreceptors (PRs) degenerate. Loss of RGCs and PRs results in loss of vision. Vit = v

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The Department is internationally recognised as a centre of excellence in oculoplastic, lacrimal and orbital surgery. Areas of research include the management of skin malignancy in the periocular region, orbital oncology and the development of new surgical techniques in orbital surgery and eyelid reconstruction. More than 40 peer reviewed publications are generated annually by the Oculoplastics team. Prof Dinesh Selva is Head of the Oculoplastics Division and will be supervising prospective students. His publication list can be found here: publicationslist.org/dinesh.selva

For additional information see:

health.adelaide.edu.au/ophthalmology/

Honours project

The student will be actively involved in laboratory-based and clinical research projects. These include orbital tissue bank, sebaceous gland genomics and lacrimal system imaging. The student will also be writing case reports, compiling clinical case series and devising clinical protocols. The student will have the privilege to be involved in clinical activities, including outpatient clinics and assistance in surgical sessions (see oculoplastic.eyesurgeryvideos.net/). Opportunities will be provided to attend ophthalmology conferences and to assist on Sight For All charity trips.

Interested individuals please email Dr Ye Chen: dryechen@gmail.com with CV and a letter of expression of interest.

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