THE UNIVERSITY of ADELAIDE

School of Medical Sciences

PostGraduate Handbook

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Introduction

The School of Medical Sciences offers a dynamic research-intensive environment that fosters excellence in interdisciplinary research and nurtures the development of our students to reach their full potential. The School encompasses the disciplines of Anatomy & Pathology, Pharmacology and Physiology and focuses on:

Investigating the morphology of the human body at the macroscopic and microscopic levels to illustrate how structure relates to function. Investigating functions of the body with a particular emphasis on the human body. Understanding the causes and mechanisms of disease and its consequences. Establishing how drugs may be used to improve health and quality of life, as medicines to treat and prevent diseases or, as a research tool to further explore the function of the human body. Understanding the acute chronic physiological responses to exercise and physical activity. Together, these disciplines provide the foundation for careers in medicine, dentistry and the allied health sciences.

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Anatomy and Pathology – Bone and Joint Research

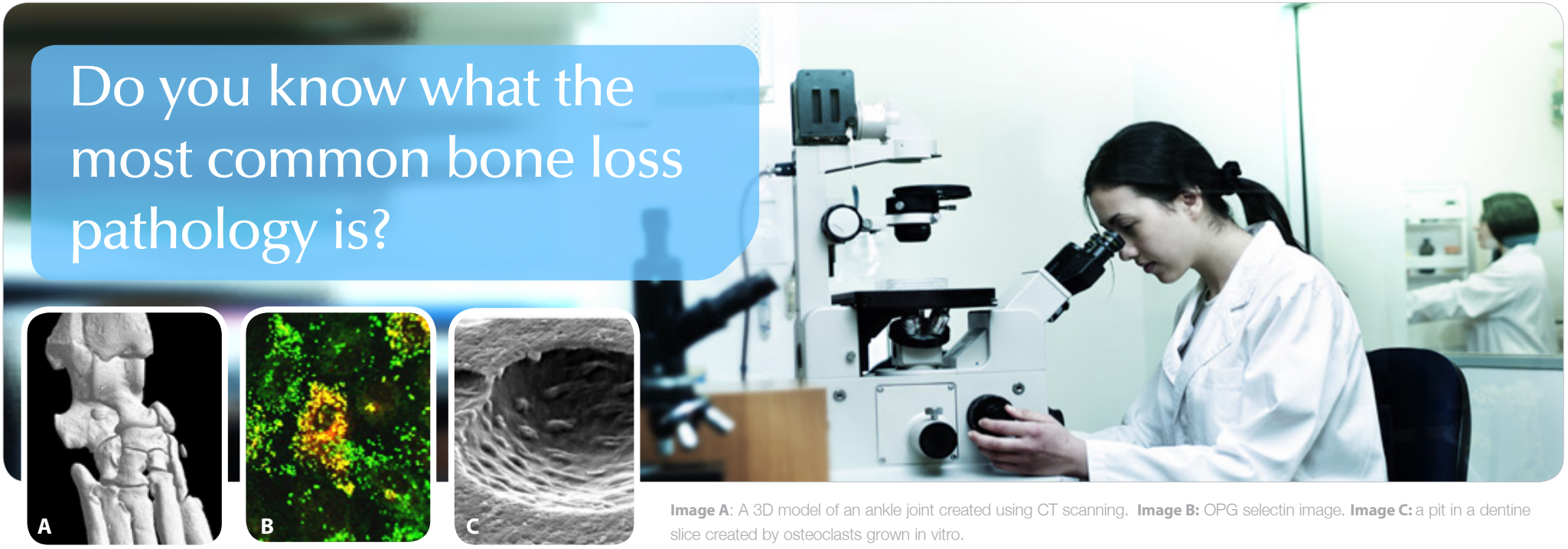

Image A: A 3D model of an ankle joint created using CT scanning. **Image B:** OPG selectin image. **Image C:** a pit in a dentine slice created by osteoclasts grown in vitro.

If you thought osteoporosis or osteoarthritis think again.

Gum disease or Periodontal disease which affects the structures supporting your teeth is one of the most common bone loss pathologies in the world, affecting up to 60% of the population.

This along with rheumatoid arthritis and bone loss around hip replacements (peri-implant osteolysis) are the major diseases which are researched by Associate Professor David Haynes and the members of the Bone and Joint Laboratory.

The Bone and Joint research group uses "state of the art" facilities currently available at the University and surrounding campuses including Confocal microscopy, electron microscopy, CT, micro CT scanning and various immunological and molecular techniques to understand the process of bone loss and how it can be treated. The unique access to human tissue samples obtained from surgeries allows them to further investigate the inflammation and bone loss processes in disease.

The Haynes Lab are looking at exciting new treatments which target epigenetic regulation via regulating gene expression and inducing programmed cell death (apoptosis) in the bone resorbing cells – the osteoclasts!!

Other work includes researching the relationship between periodontal disease and rheumatoid arthritis. They have excitingly shown in recent publications that pre-existing periodontal disease can result in more severe arthritis using models of disease. This work is being conducted with researchers from the Colgate Dental Research Centre at the University of Adelaide.

The work is being conducted with their local, national and international collaborators.

Research Projects:

> Bone Cell Metabolism is regulated by the interaction of osteoclasts (break down bone) and osteoblasts (form new bone). Projects are looking at new treatments that regulate gene expression to be able to reduce bone loss by the osteoclasts.

> Biomaterials are one of the fastest growing fields of medical research. Projects include an international study that is looking at the coating of artificial implants and how they interact with the bone cells.

> Apoptosis is an important process regulating many diseases. Studies are looking at new drugs that cause programmed cell death (apoptosis) of the osteoclast and inflammatory cells.

> Vascular Disease is associated with many inflammatory diseases.

Anatomy and Pathology – Bone and Joint Research

Projects are looking at the relationship between the vascular system and diseases, particularly looking at important molecules in osteoclasts that also expressed by the blood vessel lining cells poptosis is an important process regulating many diseases. Studies investigate how apoptosis may regulate several inflammatory diseases.

Skills

Models of disease – periodontitis, arthritis and peri-implant osteolysis (bone loss around hip implants), cutting edge methods for bone analysis – including live animal micro CT scanning, mimic bone loss in vitro by growing up osteoclast cells that resorb bone.

Career Possibilities

Postdoctoral research, research assistant positions, working in industry, academic positions.

Web Links and media related articles

Bad gums link to Arthritis

http://www.adelaidenow.com.au/news/south-australia/university-of-adelaide-researchers-find-bad-gums-link-to-arthritis-in-mice/story-e6frea83-1226497333830

http://freshscience.org.au/2012/arthritisgums

Bone Researcher

http://blogs.adelaide.edu.au/alumni/2013/01/06/bone-researcher-promotes-offshore-experiences/

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Melissa Cantley – Postdoctoral Fellow

My PhD project was focussed on novel treatments of pathological bone loss particularly looking at a class of anti-cancer drugs – histone deacetylase inhibitors and their effects on inflammation and bone loss in rheumatoid arthritis and periodontitis.

Completing my PhD allowed me to learn a range of new and exciting research techniques in the area of bone research including live animal micro CT scanning. I was also very fortunate to be able to attend local, national and international conferences throughout my studies to allow me to present my work and gain feedback from experts in the field.

I have received a NHMRC Peter Doherty Early Career Fellowship to work with Professor Andrew Zannettino, looking at 'The effect of histone deacetylase inhibitors on the bone environment in multiple myeloma' at the University of Adelaide.

What currently incurable group of diseases is caused by excessive matrix production ?

Few people have even heard of these diseases which cause as many fatalities as breast cancer.

Excessive extracellular matrix production is called fibrosis and it can cause fatal disease in a number of tissues and organs such as lung, liver, heart and kidney. Fibrosis is considered to contribute up to 45% of deaths in the industrialised world. Currently there is no effective treatment for the condition. Fibrosis is usually the result of repeated insult or injury to a tissue where the normal repair process becomes disrupted.

TGF-beta and fibrosis. The mechanism of fibrosis is complex but activation of a growth factor called TGF-beta is central to the process. TGF-beta is stored in inactive (latent) form within normal tissue matrix and is activated following tissue injury. It stimulates cells within the tissue to produce some new matrix during normal repair processes, and excessive matrix in fibrosis. Thus understanding how production and activation of TGF-beta is controlled will identify targets for therapeutic intervention to slow or reverse fibrosis.

Elastic fibres and fibrosis. Latent TGF-beta is stored on matrix structures called elastic fibres which have been the focus of our research group. Elastic fibres are complex in structure and our lab has identified and sequenced a number of their molecular components. Our lab is using a wide variety of molecular and morphological approaches to elucidate the role of elastic fibre components in the fibrotic mechanism.

LTBP-2 and fibrosis. Currently, we are determining the function of an elastic fibre component called LTBP-2 which is a member of a family of TGF-beta binding proteins. Interestingly LTBP-2 does not directly bind TGF-beta but it causes cells to greatly increase TGF-

Research Projects:

- **LTBP-2 in fibrotic diseases.** We are studying the expression patterns and tissue location of LTBP-2 in a variety of fibrotic disorders. We next aim to use selected animal models of specific fibrotic diseases to determine how LTBP-2 is upregulated and establish where LTBP-2 fits in the molecular pathway to fibrosis.
- LTBP-2 and upregulation of TGF-beta. We are determining how LTBP-2 upregulates TGF-beta production by fibroblast cells. The research involves elucidation of LTBP-2 interactions with cell surface receptors and intracellular signalling pathways.
- LTBP-2 and Fibroblast growth factor-2 (FGF-2). FGF-2 is a potent stimulator of TGF-beta production and a fibrogenic agent. LTBP-2 binds and inactivates FGF-2. We are determining the significance of this molecular interaction in wound repair and in

Anatomy and Pathology - Extracellular Matrix Research

the fibrotic mechanism.

- ***LTBP-2 and elastinogenesis.*** Elastin is the major component of elastic fibres which confers stretch and recoil on tissues such as lung, arteries and skin and this elasticity is disrupted in fibrotic diseases. We have shown that LTBP-2 is a negative regulator of elastin assembly into extracellular matrix. We are determining how LTBP-2 accomplishes control in normal tissues and in disease processes.

Skills

A wide variety of molecular and histological techniques are routinely used in the research including, immunofluorescence and confocal microscopy; electron microscopy; bacterial and mammalian cell culture; molecular cloning and sequence mutagenesis; recombinant protein production; molecular binding assays; protein, DNA and RNA analysis, quantitation and purification; PCR and QPCR etc.

Career Possibilities

Post-doctoral Research in Universities, Government Research Institutions and Industry; Academic Teaching; Research Administration; Government Advisory and Information Institutions; Health Services. Australian and Overseas Positions.

Web Links and media related articles

Mark Gibson directory listing

http://www.adelaide.edu.au/directory/mark.gibson

More detail on fibrotic diseases

Pulmonary fibrosis

http://www.youtube.com/watch?v=fTNTTvgQ5Ws

Scleroderma

http://www.youtube.com/watch?v=7zh1IcuCu1c

Myocardial fibrosis

http://www.youtube.com/watch?v=tK4wy3-mWYg

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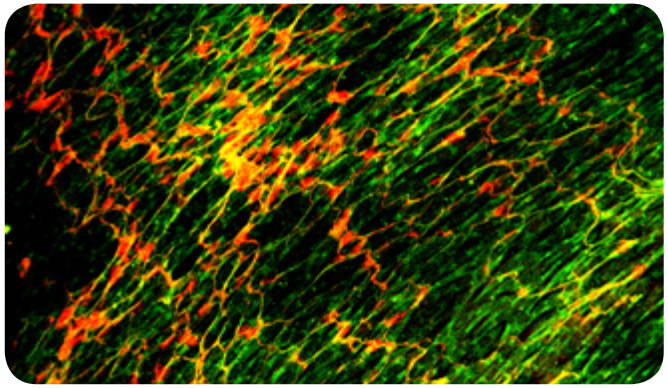
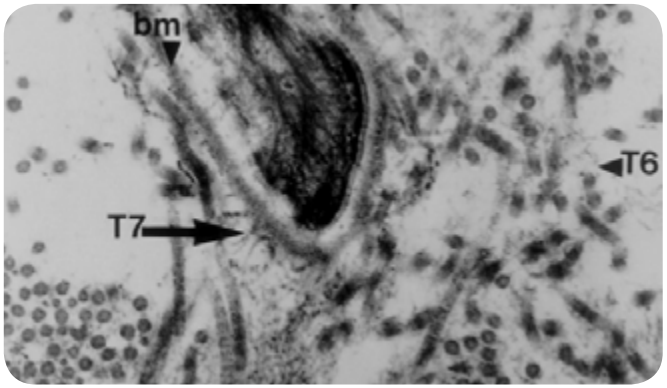
Mohammed Arshad Sideek – Current PhD candidate

My PhD project is focused on the mechanisms of fibrotic diseases specifically on the dysregulation of growth factor activity and characteristic signalling changes caused by latent transforming growth factor-β binding protein (LTBP-2). My research training has equipped me with a range of research skills in the area of extracellular matrix such as immunofluorescence, recombinant protein production, molecular binding assays and intra-cellular signalling analysis.

The Medical School provides substantial supports including access to the high quality facilities, equipment and materials necessary to produce research of the highest standard internationally. The research environment and PhD journey are a great experience to keep me motivated and prepare for a promising future research career.





Anatomy and Pathology - Reproductive Biology Research

Coming together of the male and female gametes, the eggs and sperm, at the time of fertilisation is the key to the formation of a new individual and hence the continuation of life on this planet. This is my area of research and the questions I am interested in asking are

Research Projects:

> Why do males produce so many sperm and yet females so few eggs? – and what are the factors that determine the differences of gamete numbers across species?

> Why are there such differences in the form of the male gamete across mammalian species and what are the co-evolutionary events that have taken place between eggs and sperm?

> How have the native mammals of this country adapted to the diverse environments in which they occur and what effects has this had on their reproductive strategies?

> Many species of Australian mammals are unfortunately now greatly reduced in their abundance and distribution. How can we manipulate the reproductive biology of these mammals to minimise the chances of extinction of these species taking place?

> Human populations continue to rise dramatically in most countries on earth today and are having an ever increasing negative effects on natural ecosystems and the plants and animals therein. About 10% of pregnancies are “unplanned” even in a supposed enlightened country like Australia. How can we reduce the numbers of unwanted pregnancies in this and other societies?

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Anatomy and Pathology - Gut Microbiome Research Group

Chemotherapy-induced gut toxicity (CIGT) or mucositis is unfortunately extremely common, occurring in a large percentage (40-100%) of cancer patients. CIGT is a significant burden on patients' quality of life, and causes substantial additional health care costs.Patients with mucositis typically experience severe symptoms including but not limited to oral ulceration, vomiting, diarrhoea and constipation. Of greater clinical importance, CIGT often necessitates reductions and / or treatment breaks in chemotherapy, overall compromising patient survival outcomes. Unfortunately there are few treatments and currently no prevention options for mucositis; this is where our laboratory comes in. We are investigating ways in which the gut is damaged following cytotoxic chemo- and radiotherapy so we can understand how this leads to mucositis. The overall goal of our research is to discover new underlying mechanisms of mucositis we can appropriately target new treatments.

Research Projects:

- ***Targeting TLR4 to prevent mucositis:*** Chemotherapy-induced gut toxicity is a major health issue impacting on patient care. We wish to understand how a patient's immune response and genetic variability alters toxicity severity. These research outcomes will demonstrate the importance of patient immune response in determining toxicity after chemotherapy and identify patients genetically predisposed to toxicity.

- ***Tight junctions as key regulators of mucositis:*** Research in our laboratory has identified tight junction defects in both the small and large intestine. We now wish to understand how underlying mechanisms for these tight junctional defects and how they lead to mucositis. Clinically, this has the future potential to result in a fundamental change in the approach to preventing this toxicity.

Anatomy and Pathology - Gut Microbiome Research Group

Skills

We use a range of different skills in our research ranging from pre-clinical animal models of mucositis; State-of-the-art histopathological analysis; and other molecular and functional assays.

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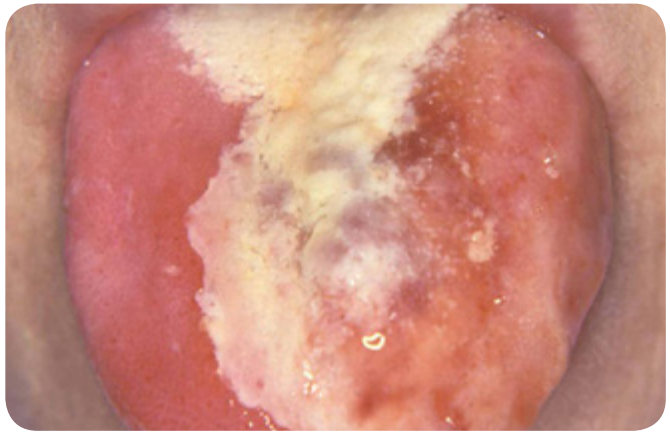
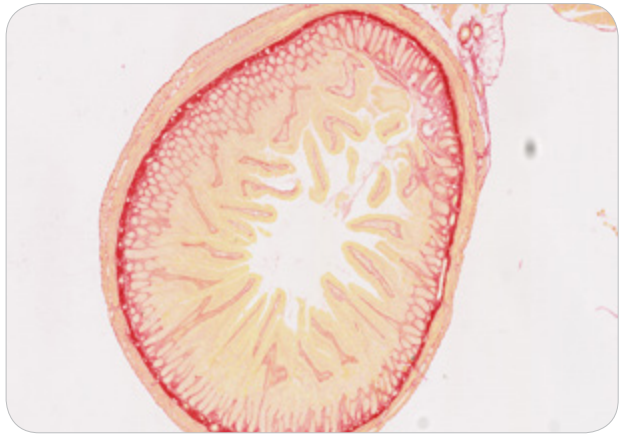


Oral Mucositis in a patient undergoing chemotherapy

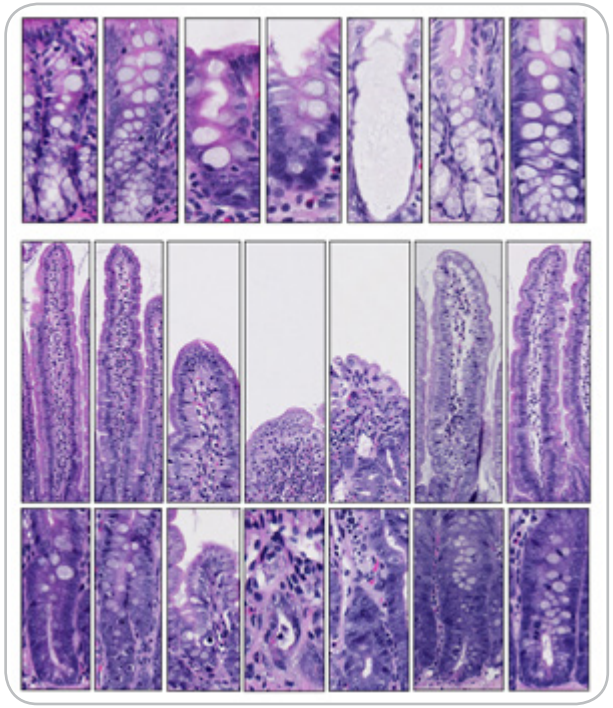


Red Duodenum

Hannah Rose Wardill - Current PhD Candidate

As part of the Gut Microbiome and Mucositis Research Group, my PhD primarily focuses on gut toxicity caused by chemotherapy and other anti-cancer drugs. Currently, there is a mentality that in order to achieve a 'cure', patients must endure severe side effects such as debilitating diarrhoea. By unraveling the pathological mechanisms responsible for chemotherapy-induced gut toxicity, my PhD aims to identify both predictive markers of toxicity and therapeutic interventions to reduce or prevent the side effects of anti-cancer treatment.

•My PhD has already equipped me with a range of new and exciting skills from novel research techniques to transferable skills involving critical thinking and problem solving. I have also been fortunate to be able to attend local, national and international conferences, which have enabled me to gain networking experience and confidence in presenting my research.



Histopathology changes following chemotherapy

Pharmacology - Neurogastroenterology and Neuroprotection

Image A: Neuronal cells displaying dendritic processes and long axonal projections. -amyloid tends to cause axonal degeneration in initiating neurotoxicity. **Image B:** Markers of cell proliferation staining in human colonic mucosa, alone **Image C:** following proinflammatory cytokine incubation. Such cytokines may induce proliferative signalling in mature epithelium, which may make them more susceptible to damage from pathogens or

Few people know this, but we have a 'little' brain in our gastrointestinal tract. Our gut has layers of nerves that control its own function (try 500 million of them), but also sense what we ingest and relay these signals to the brain. The gut also harbours bacteria; in fact it has been estimated there are more bacteria in our lower gut than cells in our own body! Because of this, we also need a large cohort of immune cells in close proximity and an epithelial lining (mucosa) to keep everything in the right place. Sounds like an interesting community of residents. Mostly they all get along, but sometimes the balance is perturbed. In inflammatory bowel diseases, bacteria interact with the immune system and gut (enteric) nervous system in a way that initiates and supports inflammation and pain. How they all interact with each other is a question we'd like to know, because understanding this has implications not just for intestinal disease, but may also be fundamental to understanding inflammation, infection and even neuronal degeneration in the brain, such as occurs in Alzheimer's disease.

Our lab's interests centre on how disease affects both gastrointestinal and central nervous system integrity, particularly understanding how the neuroimmune axis regulates mucosal and enteric structure and function, but also how molecules can interact to alter protein misfolding that occurs in some neurodegenerative diseases like Alzheimer's disease. As pharmacologists, our ultimate aim lies in developing new medicines that may be used to treat diseases as diverse as Crohn's disease and Alzheimer's disease.

Research Projects:

- ***Intestinal organoids:*** can we build a gut from scratch? This is one of the most complex tasks, as the gut contains wide array of different cell types organised in a highly structured way. This project will focus on using pluripotent cell lines to generate a basic model of the intestine, together with other cell lines of intestinal and immune origin. Such a model would have utility in a wide variety of research areas such as colitis, enteric infection and chemotherapy mucositis**.**

- ***Enteric nerves:*** can they behave like brain nerves? Gut (enteric) nerves are many and varied, but are rich in types of nerves affected by toxic proteins found in Alzheimer's disease, the cholinergic neurons. Our gut can also be affected by amyloid proteins that share some similar features to those found in Alzheimer's disease. Amyloidogenic proteins form fibrils and can damage neurons in both our enteric and central nervous system. This project will investigate how enteric cholinergic neurons can be affected by -amyloid and whether novel drugs can protect such nerves. This may provide a useful surrogate to studying -amyloid interactions in the brain in Alzheimer's disease.

Pharmacology - Neurogastroenterology and Neuroprotection

- ***Novel drug treatments for Alzheimer's disease.:*** The number of people afflicted by Alzheimer's dementia is predicted to rise sharply with an ageing population. Despite this alarming increase, we have very few good drugs to treat Alzheimer's disease. Our projects centre on using several platforms to screen and develop new drugs that can provide neuroprotection against the toxic □-amyloid protein, including molecular modelling, neuronal and microglial inhibition and a fly (Drosophila) amyloid model to rapidly screen new inhibitors of □ amyloid aggregation.

The lab also has collaborations in cancer cyclotherapy research, anti-infective drugs and characterising cyanobacterial toxins and their effects on mucosal and neuronal health. These collaborations include groups from The Hanson Institute, Flinders University, SA Water and The University of Adelaide and different projects may arise from these networks.

Skills

A wide array of molecular and functional pharmacological approaches are utilised in the lab. Some of these include organ bath pharmacology, immunohistochemistry, western blot. We utilise cell and tissue culture of epithelial, neuronal and microglial cell lines and also utilise human tissue to maximise the translational value of our research. We are also investigating computational modelling approaches and other novel platforms for drug development in different areas such as Alzheimer's disease.

Career Possibilities

Postdoctoral research and research assistant positions working in industry and academia. Students who have undertaken research in the lab have subsequently worked for multinational pharmaceutical companies in Europe and in research institutions and universities in North America and throughout Australia.

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Benjamin Harvey - Current PhD candidate

My PhD project examines the potential role of novel cannabinoid treatments for inflammatory bowel disease. Using human colonic tissue we have been able to show a beneficial effect of these compounds against tissue damage caused by inflammatory cytokines. My PhD has also enabled me to learn and perform a number of laboratory skills ranging from western blotting to immunohistochemistry.

I also have had the opportunity to present my work at national conferences as well as an international conference in Germany. I was also fortunate to travel to the USA and Canada to visit other labs and study additional techniques.

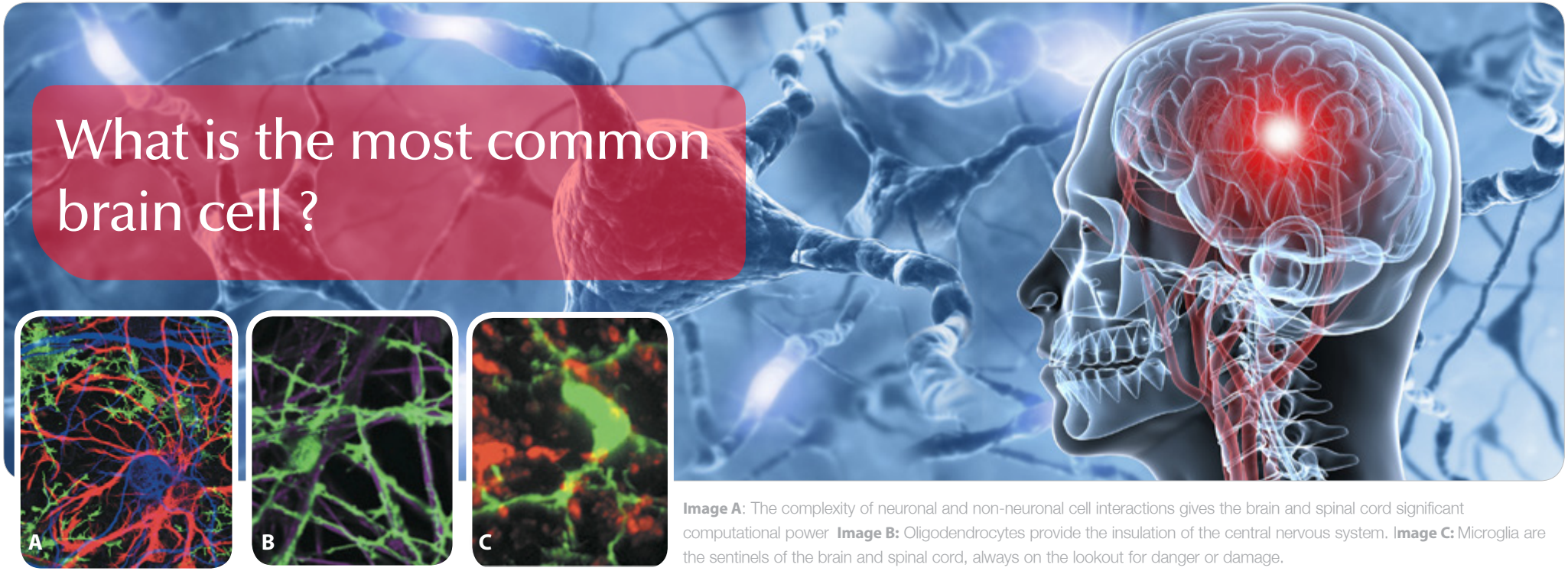

Image A: The complexity of neuronal and non-neuronal cell interactions gives the brain and spinal cord significant computational power **Image B:** Oligodendrocytes provide the insulation of the central nervous system. I**mage C:** Microglia are the sentinels of the brain and spinal cord, always on the lookout for danger or damage.

Ever wondered why we only "use" 10% of our brains?

Reality is we just haven't realised or appreciated what the other 90% is actually doing.

Fact: roughly 10% of your brains are made up of neurons. These are critical cells of our brains and spinal cords that convey the fundamental information at astonishing speeds through our central nervous systems.

Fact: the rest are immune like cells of the central nervous system, called glia. These include immune-like cells such as microglia, astrocytes and oligodendrocytes. These cells not only hold the brain together, but also make sure the central nervous system is fed, cleaned and repaired. But they do even more than this!

Ever wondered how you know you are sick? The immune cells of the brain and spinal cord help convey some of this information from your peripheral immune system to the brain and help change your behaviour when you have an infection.

BUT, the immune cells of the brain can also change behaviour in bad ways. Immune responses in the brain have now been implicated in almost every central nervous system disease including, depression and anxiety, through to epilepsy, stroke and drug addiction.

So what does the Neuroimmunopharmacology group do?: Our laboratory investigates how glia function in a normal healthy brain so we can understand when they go bad and contribute to diseases such as chronic pain, drug addiction & epilepsy. The goal of the research is to discover new mechanisms of disease so we can make new drugs or treatments that can regain control of these immune cells to prevent diseases. Importantly, this research will lead to disease cures rather than just treatments.

Research Projects:

> ***Neuroimmunopharmacology of alcohol:*** Acute and chronic alcohol action is now understood to require glial involvement. We wish to understand what alcohol is doing to glia, how alcohol is doing this and the neuronal and behavioural consequences of these immune responses. The end goal is to create a new glial targeted drug to stop alcohol's unwanted glial actions.

> ***Neuroimmunopharmacology of opioids:*** Wanted pain relief and unwanted drug actions of opioids like morphine involve glia. We wish to understand what opioids are doing to glia, how opioids are doing this and the neuronal and behavioural consequences of these immune responses. The end goal is to create a new glial targeted drug to stop unwanted opioid glial actions.

Physiology – Neuroimmunopharmacology

> ***Neuroimmunopharmacology of chronic pain:*** Chronic pain is a debilitating disease, which is at epidemic levels worldwide. Immune signalling within the brain and spinal cord contributes significantly to the creation and maintenance of the disease. Moreover, many unwanted side effects of medications currently used to treat pain are created through central immune mechanisms. Therefore, we are seeking to better understand the roles of central immune responses in chronic pain and design new drugs and treatment approaches to prevent and cure pain rather than just treating it.

> ***Neuroimmunopharmacology of sex:*** Females experience some diseases and disorders of the brain and spinal cord at far greater rates than males. Our approach has been to re-examine many of these diseases from a neuroimmune perspective to understand if sex-dependent glial contributors may be at the heart of these disorders.

Skills

Owing to the mechanistic and translational discovery of our research we rely on a breadth of experimental techniques. These range from computer simulations and bioinformatics analysis, to molecular assays protein design and quantification, to drug formulation and delivery, to neurosurgical and behavioural techniques. If there is a gold standard experimental approach out there, we want to try it in the neuroimmune domain.

Career Possibilities

Graduates from the Neuroimmunopharmacology now work around the world in China, USA, and the Netherlands; in academic, government and the private sector. Owing to the nature of the work we conduct our graduates engage with many non-academic sectors and build long lasting collaborative relationships with future possible employers. Given the translation intensive research that is conducted our graduates leave with an excellent publication track record setting them on a course to future career success.

Web Links and media related articles

http://www.youtube.com/watch?v=LTd91tYoqBM

http://www.youtube.com/watch?v=2c2fyUPcP7Y

http://www.adelaide.edu.au/news/news55261.html

http://www.adelaide.edu.au/news/news48561.html

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Jacinta Johnson – Current PhD candidate

My PhD project has involved both clinical and laboratory studies looking at how codeine might interact with the immune system to increase pain sensitivity. In addition to learning many new technical skills, undertaking a PhD has allowed me to develop a whole range of transferable skills in areas such as critical thinking, problem solving and project management, which will be valuable no matter which career path I take from here.

Physiology – Mesenchymal Stem Cell Laboratory

Image : The use of muli-fluorescence analysis to identify Mesenchymal Stem Cells

We have previously identified different mesenchymal stem cell (MSC) populations that live in adult bone marrow, peripheral fat and dental pulp tissue. These stem cells have the capacity to differentiate into connective tissue cell types and form the supportive structures of many organs. However, the precise molecular signals responsible for maintaining the stem cell pool or inducing differentiation leading to the eventual formation of bone, fat, muscle, ligament, tendon, cartilage, cementum or dentin have yet to be determined. We propose that primitive mesenchymal stem cells express critical genes that regulate maintenance of the stem cells pool and their differentiation into musculoskeletal or dental cell populations.

Research Projects:

> ***Mesenchymal stem cells in skeletal tissue regeneration.*** This work investigates the molecular mechanisms controlling maintenance of osteo/chondrogenic precursor cells and skeletal tissue regeneration. Projects will focus on stem cell biology and the use of microarray analysis and proteonomic analysis for determining differences in the gene expression profiles of normal and genetically modified mesenchymal stem cell populations. In particular the role of transcription factors and epigenetic histone/DNA modifying enzymes in postnatal MSC maintenance and development will be assessed in the context of diseases and conditions that affect the skeleton including bone fracture repair, osteoporosis and osteoarthritis

> ***The role of MSC in the maintenance and support of haematopoiesis and modulation of immune responses.*** In addition to having tissue regenerative properties, MSC have also been shown to exhibit the potential to support and regulate haematopoietic stem cells the precursors of white cells, red cells and platelet producing megakaryocytes. Furthermore, MSC are capable of regulating immune cells through direct contact or via secreted factors. Projects will address the underlining molecular mechanisms (soluble cytokine/ chemokine factors, extracellular matrix components and cell surface bound molecules) that mediate MSC and blood/ immune cell interactions. These projects will focus on clinical models of haematopoiesis, bone marrow transplantation, chronic inflammatory diseases, autoimmune diseases and organ transplantation.

> ***Dental mesenchymal stem cells for tissue regeneration.*** These studies involve the identification and characterization of human, rodent and ovine periodontal ligament stem cells (PDLSC) and dental pulp stem cells (DPSC). Studies will determine the efficacy of different stem cell preparations and biomaterials to repair alveolar bone, cementum, dentin and periodontal tissues using both rodent and ovine models representative of different dental defects or following disease (periodontitis) or trauma. Projects will investigate the underlining molecular mechanisms (transcription

Physiology – Mesenchymal Stem Cell Laboratory

factors, epigenetic factors, cell adhesion molecules, soluble factors extracellular matrix components) that govern stem cell maintenance, migration and differentiation during the repair process.

Skills

Cell culture, molecular biology/ gene cloning, protein analyses, flow cytometric analyses, histology, transgenic and disease mouse models.

Career Possibilities

Postdoctoral research, research assistant positions, biotechnology industry, academic positions, media.

Web Links and media related articles

http://www.adelaide.edu.au/stemcell/members/

http://downloads.realviewtechnologies.com/Luna%20Media/RI%20Aus/Regenerative%20Medicine.pdf

http://www.mesoblast.com/

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Dr. Agnieszka (Agnes) Arthur – Postdoctoral Researcher

My PhD project was focused on stem cells isolated from the tooth, known as dental pulp stem cells which are thought to be neural crest in origin. I investigated two separate aspects of these stem cells, firstly how a family of molecules known as the Eph/ephrin molecules influence dental pulp stem cell maintenance and function, particularly, in response to tooth injury. Secondly I explored the neural potential of dental pulp stem cells in response to neural cues both in culture and in the developing brain of chicken embryos. During my PhD I was able to develop and establish new techniques, expand my research over multiple disciplines and integrate the findings. I was also fortunate to present the findings of my research at nation and international conferences and also to laboratories around the world.

The findings of the neural differentiation potential of dental pulp stem cells has led to successful grant applications with the Catholic Church investigating the therapeutic potential of adult dental pulp stem cells for Stroke studies conducted in animals. It has also led to patent applications and interest from a commercial company.

Since completing my PhD, I have been working as a Post Doc for Prof. Stan Gronthos investigating the function of the Eph family of molecules in bone marrow stem cells and how they influence these cells in bone metabolism under steady state and trauma induced conditions, including femoral fracture and osteoporosis. I have also recently become a Mary Overton Research Fellow and I am a mother of two gorgeous boys.

Physiology – Neurophysiology of Human Movement

Is the idea of "No Pain, No Gain" a myth ?

When it comes to human motor performance and training, the commonly held view is that much pain and effort needs to be devoted to a particular activity before substantial gains are achieved. However, new evidence suggests that improvements in motor performance can be achieved just by imagining performing that particular task, or by watching someone else perform the activity. This type of training highlights the important role of the nervous system in improving motor performance, and represents a key area of interest for the Neurophysiology of Human Movement Laboratory.

A major focus of research in the Neurophysiology of Human Movement Laboratory is in understanding the mechanisms responsible for normal and impaired motor function, and in the development of novel approaches to rehabilitation following damage to the nervous system. Specific areas of interest include the neurophysiology of exercise and training, changes in the nervous system throughout the lifespan, and the role of nervous system plasticity and repair in learning new motor skills.

The group uses sophisticated stimulation and recording techniques to address these issues, which include transcranial magnetic stimulation, peripheral nerve stimulation, isokinetic dynamometry, and surface and intramuscular electromyography. 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.

Research Projects:

> ***Neurophysiology of Exercise.*** The performance capabilities of the human neuromuscular system are affected by the amount and type of daily physical activity. These projects examine changes in the central and peripheral nervous system following increases (exercise, fatigue, strength training) and decreases (disuse) in physical activity and its effect on movements performed by humans.

> ***The Ageing Nervous System.*** Old age is commonly accompanied by a deterioration of brain and motor function, which can have major personal, social and economic impacts to our rapidly ageing society. These projects examine the neural mechanisms responsible for impaired motor performance in older adults, and investigate ways to rejuvenate ageing brains and enhance movement quality in the elderly.

> ***Brain Plasticity and Motor Learning.*** The ability to learn new motor skills is influenced by the capacity of the brain to reorganise its connections: a process known as plasticity. These projects examine factors that influence plasticity of the CNS and how this may improve motor learning in specific subject populations.

Physiology – Neurophysiology of Human Movement

Skills

Transcranial magnetic stimulation (TMS) is a noninvasive, painless method used to excite neurons in the brain. This technique is used to investigate the operation and integrity of the pathway between the brain and certain muscles in the body.

The activation of muscle by the nervous system is assessed with electromyography (EMG). This involves placing electrodes on the surface of the skin overlying the muscle of interest and recording the electrical activity of the muscle when it is activated. EMG can also be recorded with electrodes inserted into the muscle.

Motor performance is assessed using specific sensors that detect the force, velocity or acceleration of a hand or arm during specific goal-directed tasks.

Career Possibilities

Graduates from the Neurophysiology of Human Movement Laboratory have used their skills to become postdoctoral researchers, research managers, human movement physiologists, pharmaceutical professionals, neurophysiological applications scientists and medical sales representatives.

Web Links and media related articles

http://www.ejnblog.org/2013/06/04/patients-with-obstructive-sleep-apnea-show-altered-motor-cortical-plasticity-in-response-to-ctbs/

Contacts

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http://www.adelaide.edu.au/directory/john.semmler

Dr John Cirillo - Postdoctoral Researcher, University of Pittsburgh

My PhD research in the Neurophysiology of Human Movement Laboratory examined factors that influence the induction of plasticity in human motor cortex, such as age, handedness, genetics, and training. This research provided me with the experimental skills capable of assessing the integrity of the human nervous systems at multiple levels. I am now using these skills as a postdoctoral researcher at the University of Pittsburgh to examine the neural mechanisms responsible for impaired motor control in patients with spinal cord injury.

George MacKenzie Opie - Current PhD Candidate

My PhD is using non-invasive brain stimulation techniques in healthy human subjects to examine how the ageing process effects parts of the brain that are important for movement, and how changes in these areas contribute to age-related deficits in motor performance.

Being a PhD student is a challenging yet incredibly rewarding process. It allows you freedom and flexibility in your research pursuits and gives you the independence to make your own decisions, while developing a broad range of technical and professional skills that have real-word relevance.

Physiology – Human Exercise Performance Group

Increasing physical activity or exercise reduces cardiovascular risk and all-cause mortality. Exercise is furthermore considered an effective management strategy for a wide-range of conditions, including cancer, diabetes, psychiatric conditions and osteoporosis. Despite this, the potential application of exercise science expands much further to include healthy ageing and sporting performance.

The Human Exercise Performance Group in the School of Medical Sciences collaborates closely with clinical partners (The Queen Elizabeth Hospital, Royal Adelaide Hospital) to (1) evaluate the mechanism(s) underlying the benefits of exercise, and (2) investigate the novel application of exercise in conditions where its effects are not well defined or where there are no alternative therapies. To achieve these aims, we utilise novel exercise approaches, 'state of the art' exercise testing equipment, and cutting-edge physiological and biological measurement techniques.

Recently, we have established two novel exercise programs in patients with peripheral artery disease and coronary microvascular disorders, to evaluate how exercise may modulate the underlying pathophysiology and improve patient outcomes. We are also interested in novel approaches to increasing physical activity, such as interrupted sitting protocols, and how these approaches may have positive effects of cardiovascular and/or metabolic health.

In addition to investigating how exercise is good for you, we are also strongly interested in how too much exercise may have complications, particularly in terms of heart function and the immune system. Recent research indicates the potential of ventricular dysfunction following prolonged endurance exercise, such as marathon running. We are specifically interested in how extended endurance exercise may alter heart rhythm, potentially contributing to cardiac arrhythmias later in life. Using this approach, we are able to extend our research into the study of trained endurance athletes to compliment our work with clinical populations.

Research Projects:

> Exercise therapy for the management of patients with coronary microvascular disorders.

> Investigating the detrimental effects of endurance exercise on cardiac rhythm and function.

> The evaluation of novel approaches to increasing physical activity and their influence on markers of cardiometabolic health.

> Acute and chronic effects of antioxidant compounds on exercise performance and adaptation.

> Physiological effects of diet intervention on exercise adaptation and metabolic health.

Physiology – Human Exercise Performance Group

Skills

Exercise Testing; Prescription and monitoring of exercise programs; Biochemistry; Assessment of vascular function; cardiac monitoring; energy expenditure measurement; Expired gas analysis

Career Possibilities

Exercise Physiologist, Cardiac Scientist, Sports Scientist, Postdoctoral Research, Academic Positions, Health Promotion, Health Assessment

Web Links and media related articles

Exercise and Sports Science Australia

http://www.essa.org.au/

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Dr Adrian Elliott

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Sara Zanetti - Current PhD Candidate

My research will focus on the energy balance of athletes. It is often difficult to accurately quantify energy expenditure in this population outside of a laboratory setting and knowledge of this can help us manipulate training programs and nutritional prescription to enhance performance. In a broader sense, developing practical methods of quantifying energy expenditure can be utilised across many populations, not just athletes, and this can benefit our wider society and our understanding of the factors that contribute to energy balance.

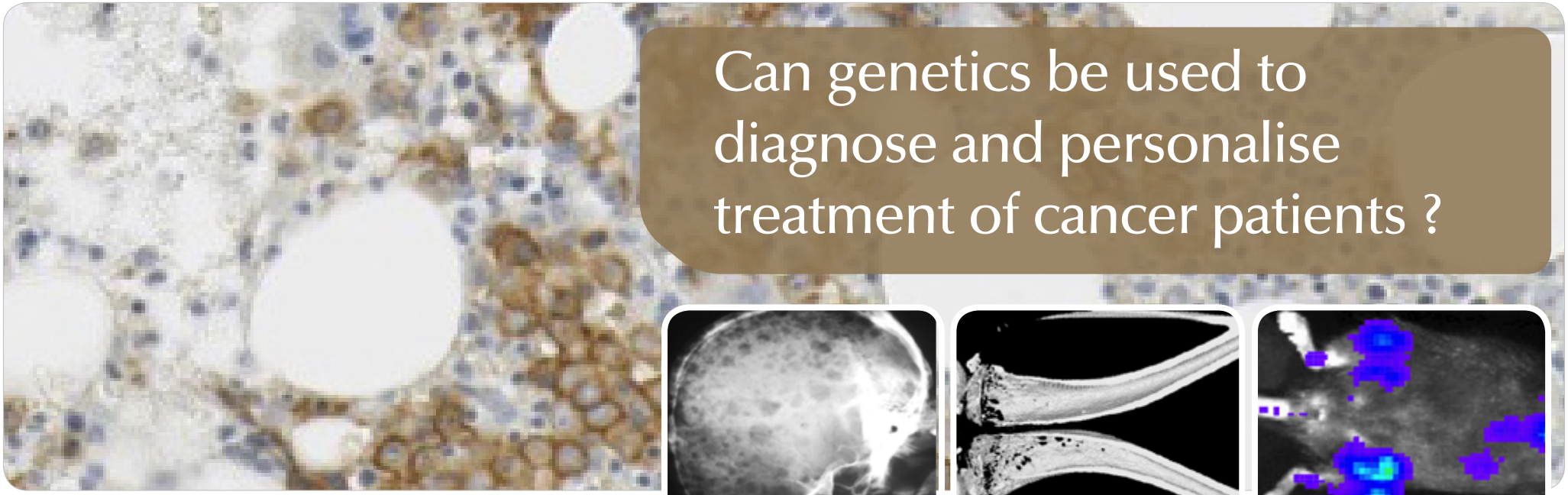

Image A: Skull with lytic lesions. **Image B:** Mouse with myeloma bone loss **Image C:** BLI mouse myeloma

Did you know that there are more than 200 different types of cancer affecting humans? In fact, cancer can affect any one of over 60 different organs in the body. While the cell type affected may differ, all cancers are genetic disorders in which the control of "normal" cell growth is lost. In other words, cancer is caused by mutations in DNA, which result in aberrant cell proliferation. These mutations often affect two classes of cellular genes: oncogenes and tumor suppressor genes.

So what does the Myeloma Research Laboratory do? Our laboratory studies the molecular and cellular basis for the development of the bone marrow cancer, multiple myeloma. Myeloma is characterised by the clonal proliferation of malignant plasma cells (an immune cell type that normally protects us against infection). Myeloma is the second most common blood cancer affecting humans, with over 1,500 Australians diagnosed each year. Despite recent advances in treatment, myeloma remains almost universally fatal with a 10 year survival rate of approximately 17%. The main clinical manifestations of myeloma are the development of osteolytic bone lesions, bone pain, hypercalcaemia, renal insufficiency, suppressed immunoglobulin production and increased BM angiogenesis (blood vessel formation). It is now widely accepted that most, if not all, cases of myeloma are preceded by a premalignant (asymptomatic) monoclonal gammopathy of uncertain significance (MGUS) stage. However, the genetic factors which trigger the progression from this asymptomatic stage of the disease to overt malignant myeloma remains to be determined. Moreover, recent studies suggest that the bone marrow microenvironment plays a central role in disease progression.

Our laboratory's research is focussed on identifying the key genes which are responsible for disease progression and the role played by the bone microenvirnment in disase pathogenesis. We believe that these approaches will enable us to identify new molecular markers of disease risk and to design drugs against novel therapeutic targets.

Research Projects:

> ***Identification of genetic factors which trigger the progression from asymptomatic MGUS to overt malignant MM.*** What causes an individual patient to progress from MGUS to MM is still incompletely understood. Our group is in the unique position of having assembled a biospecimen bank comprised of a large number of matched MGUS and MM clinical samples taken from patients at the time of diagnosis. Using a comprehensive genomics approach, we will identify structural and gene expression changes between paired

Physiology – Myeloma Research Laboratory

MGUS/MM samples and to investigate the biological roles of the candidate "myeloma genes" using established in vitro models and a mouse model of myeloma that recapitulates human disease.

> ***Defining the role of the bone marrow microenvironment in the development MM.*** There is a growing appreciation of the role played by the non-cancerous or microenvironmental cells in the development of malignancy. One area of our research is dedicated to identifying factors in the BM microenvironment that contribute to the development of MM. We have previously compared the gene expression and cellular characteristics of two strains of mice; the commonly used laboratory strain C57BL/6 and the related strain C57BL/KaLwRij. Although very similar, subtle differences have developed over time, the most striking being the susceptibility of C57BL/KaLwRij mice to the development of MM. The cause of this difference in susceptibility remains to be determined. The project is aimed at identifying genetic differences between KaLwRij and C57BL/6 mice that may underlie the propensity of each strain to succumb to, or resist myeloma disease development, respectively.

> ***Determining the effects of myeloma plasma cells on mesenchymal stem cell (MSC) differentiation.*** Lytic lesions are a common feature of MM. Notably; these lesions persist beyond disease remission, suggesting that MM PC mediate long-term changes to the normal bone remodelling process by inhibiting osteoblast function. Osteoblasts are specialised bone forming cells derived from precursor pluripotent mesenchymal stem cells (MSCs) that reside within the bone marrow microenvironment. We hypothesise that infiltration and proliferation of MM plasma cells in the BM could potentially alter the differentiative potential of MSCs leading to a deficiency in bone forming function of osteoblasts. Using gene expression profiling of MSC prior to and following exposure to MM PC we aim to identify the molecular mechanisms by which MM plasma cells influence stem cell biology.

> ***Identifying the role of the mTOR pathway in mesenchymal stem cell biology and bone formation.*** mTOR is a key signalling protein which regulates a number of cellular processes by forming one of two multi-protein complexes. These multi-protein complexes have both overlapping and distinct roles, and while most of the components of these complexes are common to both, they can be distinguished by the presence of either the Raptor protein or the Rictor protein. Recent studies from our laboratory have demonstrated that mTOR plays a crucial role in bone development, with inhibition of mTOR causing an increase in bone formation. However, due to a lack of specific inhibitors for Raptor and Rictor, we are unable to delineate which of the two mTOR complexes (or perhaps both) is involved in this process. We have developed a sophisticated animal knockout model in which either Raptor or Rictor expression is specifically knocked out in bone cells. We will use these animals to examine what happens to bone growth in response to bone-specific deletion of Raptor or Rictor. These studies will enable us to develop specific inhibitors of either Raptor or Rictor in order to stimulate bone formation in patients with myeloma-associated bone loss.

Skills

Our laboratory has assembled a biospecimen bank comprised of a large number of matched MGUS and myeloma clinical samples taken from patients at the time of diagnosis that will enable us to identify key genetic changes associated with myeloma disease development. Moreover, we have developed an array of molecular, cellular and in vivo models of myeloma disease in order to evaluate the effects of any genes we suspect play a role in disease pathogenesis.

Career Possibilities

Graduates from our laboratory now work in many outstanding medical facilities around the world and in Australia. Given the translational and internationally competitive nature of our work, our graduates leave our laboratory equipped with an understanding of cell biology, genetics, bioinformatics and an excellent publication record. These attributes equip graduates with independent research skills and the ability to forge a successful career in cancer research

Web Links and media related articles:

http://www.centreforcancerbiology.org.au/zannettino.htm

http://vimeo.com/44078438

http://www.innovation.gov.au/INNOVATION/REPORTSANDSTUDIES/Documents/MesoblastCaseStudy-

http://lifescientist.com.au/content/life-sciences/news/boning-up-on-mesenchymal-stem-cells-256479531

http://www.myeloma.org.au/MYServices/MSAG.aspx

Mary P Matthews - PhD Candidate

My PhD has involved examining the role of the Raptor gene in mesenchymal stem cell and bone biology. Undertaking a PhD has allowed me to develop skills in new and exciting research techniques. In addition to the technical aspect of my studies, my PhD has allowed me to improve a range of other skills including analytical thinking, public speaking and scientific writing. I have also had the invaluable opportunity to attend national and international conferences throughout my studies which have allow me to present my work and discuss aspects of my project with world leaders in various fields of medical

Colon epithelial cells **Image A**: Healthy cells **Image B:** Dying cells (arrows)

Personalised medicine is an emerging strategy to improve treatment for a wide range of diseases. It is based on the understanding that each individual has a unique profile of gene – host - environment interactions and this profoundly affects the way they respond to drug treatment. An area where this is critically important is cancer treatment. There is currently huge variation in inter-individual response and toxicity rates to the most common cancer treatments, and in many cases this can mean the difference between life and death.

Our research group is involved in discovery of novel biomarkers that can predict tumour response and normal tissue toxicity during treatment for cancers of the gastrointestinal tract. We are especially interested in the role gene polymorphisms play in determining an individual's risk of treatment toxicity. The laboratory is located in the Discipline of Physiology and conducts research projects in collaboration with researchers from the Disciplines of Pharmacology and Anatomy/Pathology, as well as Flinders University.

Research Projects:

> ***The SPiT study (salivary predictors of toxicity):*** Oral complications of cancer therapy are expensive and impede optimal delivery of therapy leading to poorer outcomes. Importantly, the presence of these complications is associated with a decrease in quality of life scores and can impair speaking, swallowing and sleeping. Currently there are no diagnostic markers to predict a patient's susceptibility for oral complications following chemotherapy. Given the substantial burden this places not only on patient quality of life, but also on treatment success due to an increased risk of infection and actual treatment changes (e.g. breaks in treatment, dose reductions and at times complete cessation), there is an urgent need for clinicians to be able to predict risk in their patients prior to treatment.

> A number of chemotherapy agents are considered highly toxic, with the fluoropyrimidines, fluorouracil (5-FU) and capecitabine, considered to be the worst. With use of these drugs, the risk of severe oral toxicity can be as high as 18%, with the underpinning mechanism being an increase in expression of pro-inflammatory cytokines, including interleukin-1 beta (IL-1B) via the toll-like receptor 4 (TLR4) signalling pathway. Inter-patient variability in this signalling pathway, as a result of genetic variability, is therefore likely to predict (in part) patient susceptibility to fluoropyrimidine-induced oral toxicity.

> The aim of this project is to determine the impact of genetic

Physiology – Gastrointestinal Pathophysiology

variability in the TLR4/IL-1B signalling pathway on the incidence of oral toxicity in patients following 5-FU or capecitabine treatment. Patients that have received 5-FU or capecitabine submit a saliva sample that can be used to extract DNA to look for polymorphisms in our pathway of interest. The relationship between polymorphisms and toxicity will be determined by general linear models and logistic regression.

> ***TLR4 knock out and irinotecan toxicity:*** Irinotecan is a drug commonly used to treat colorectal cancer. However, its' use in the clinic is impeded by severe gastrointestinal side effects and immune suppression. We expect that the innate immune receptor, TLR4, plays a key role in propagating the damage signal initiated by irinotecan treatment. As such, we will use mice with a genetic deletion of TLR4 to investigate how this signalling pathway modifies gastrointestinal injury in response to irinotecan. We will also establish human colon epithelial monolayers and test the effect of knocking down expression of TLR4 and other members of the signalling pathway on the barrier properties of the epithelial layer.

> ***EGFR inhibition and diarrhoea:*** A new class of cancer drugs called small molecule receptor tyrosine kinases inhibitors (RTKIs) have been introduced to improve treatment of a variety of solid tumours. RTKIs that target epidermal growth factor receptors (EGFR) are known to cause significant gastrointestinal side effects. In conjunction with Pfizer, we are investigating the mechanisms of intestinal damage caused by RTKIs. We are concentrating on interactions between chloride channels and RTKIs in the colon. A series of experiments will be conducted using animal and cell culture models which focus on functional changes in response to RTKI treatment. The findings will be translated to improved management of diarrhoea in cancer patients.

Skills

The Gastrointestinal Pathophysiology Laboratory uses a variety of approaches to answer specific research questions. Molecular techniques include microarray, genotyping, real time PCR and Western blot. Histological techniques include immunohistochemistry, special pathological stains, immunofluorescence and laser capture microdissection. Functional assays include cell culture monolayers, transepithelial electrical resistance, epithelial permeability and secreted protein evaluation. In addition, we apply a range of statistical modelling approaches and software programs to uncover biomarkers in complex datasets.

Career Possibilities

Postgraduate students in the Gastrointestinal Pathophysiology Laboratory are encouraged and supported to become involved in a wide range of activities outside of their specific project to enhance future employment opportunities. This includes being involved in scientific society state committees, media training and community engagement, in addition to manuscript publication and conference presentations. Postdoctoral research, research assistant positions, biotechnology industry, academic positions, media, and government are all potential career paths for graduates.

Web Links and media related articles

http://www.youtube.com/watch?v=usKYMblcB7M

(time on screen: 2:04 – 3:36)

Contacts

Dr Joanne Bowen

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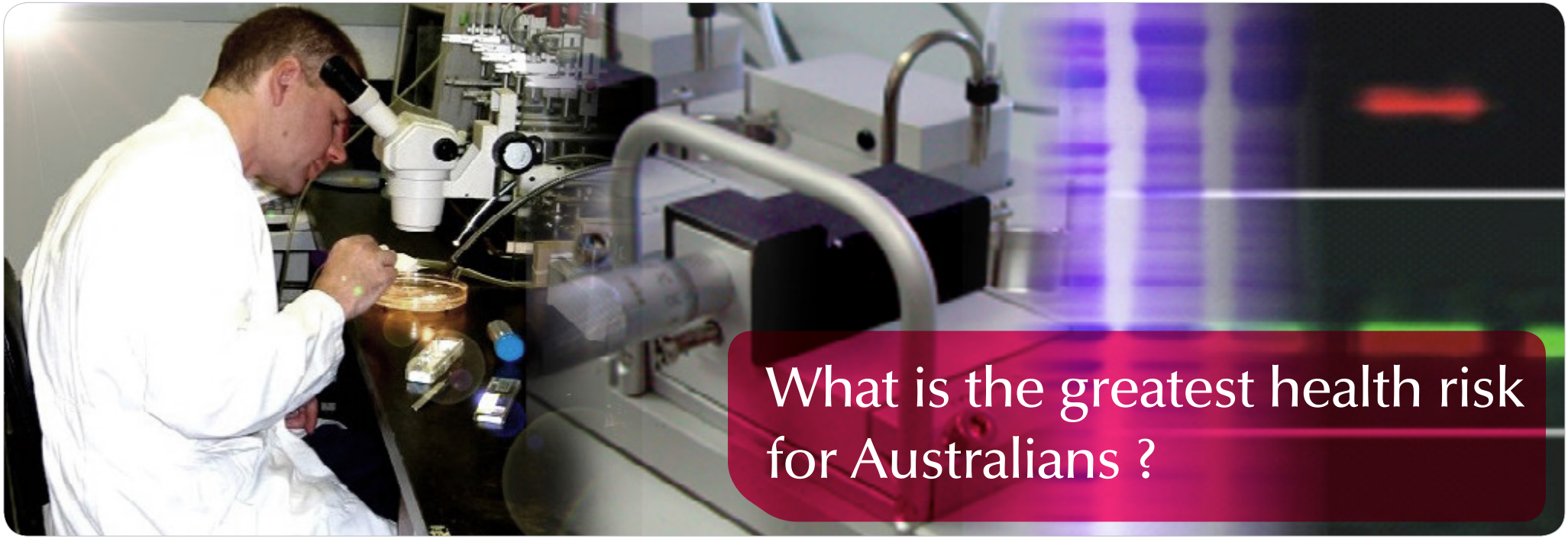
http://www.adelaide.edu.au/directory/joanne.bowen

Dr Joanne Bowen - Lab Head

I completed my PhD at the University of Adelaide, graduating in 2006. My project investigated how a family of proteins, the BCL-2 family, regulates cell death in the intestine. In particular, I found that the profile of expression of these proteins could dictate a cell's sensitivity to insult and was important in determining the degree of intestinal damage caused by different chemotherapy drugs. During my PhD I was able to travel to overseas conferences and establish collaborations with researchers in multiple countries. In addition, I became involved in the Australian Society for Medical Research South Australian Committee and found great enjoyment in helping organise local scientific meetings and networking with other scientists in Adelaide. I now balance research and student supervision with teaching as a lecturer in the Bachelor of Health Sciences Program.



If you said Cardiovascular Disease you are correct.

Many research-based innovations have been made to improve the management of cardiovascular disorders and although these have extended lifespan significantly they are not cures for cardiovascular dysfunction associated with ageing or a suboptimal lifestyle. Nevertheless, preclinical research continues to explore the causal mechanisms underlying cardiovascular dysfunction. Translational research aims to inform implementation of novel therapeutic strategies to better manage cardiovascular dysfunction.

The Clinical and Molecular of Physiology of Vascular Function Research Group is based in the Medical School and has several new and ongoing projects on offer for prospective students at the Honours, Masters and PhD level.

Research Projects:

> **Septic shock** has an associate in hospital ICU mortality approaching 40%. One of the life threatening challenges associated with this disorder is inappropriate vasodilatation and vasopressor insensitivity. This study investigates the mechanisms underlying vasopressor insensitivity and explores 3 novel translational strategies to reduce vasopressor insensitivity and reduce mortality associated with septic shock.

> **Oxidative stress mediated cardiac and skeletal muscle $Ca2^+$ insensitivity.** Myocardial infarction and claudication result in cardiac and skeletal muscle dysfunction and associated $Ca2^+$ insensitivity. This project explores the molecular basis for this dysfunction and whether this is a protective mechanism to prevent further muscle dysfunction.

> **Physical blockage of arteries can lead to life and organ threatening ischemia.** Until recently much of the research has focused on reducing the deposition of atheromatous plaque and associated platelet adherence. Our research group has ongoing research projects that focus on identifying the mechanisms and therapeutic strategies to limit, inappropriate focal vasoconstriction associated with MI, stroke and peripheral microvascular dysfunction.

> **Arteries and veins:** 70% of our blood volume is contained within the large veins while only 10% of blood volume is found within the arteries. This project explores the mechanisms underlying differential venous and arteriolar contraction. This project will inform therapeutic strategies to limit volume overload and oedema associated with $Ca2^+$ channel blocker therapy

Physiology – Clinical & Molecular Physiology of Vascular Function

Skills

Work within the Clinical and Molecular Physiology of Vascular Function Research Group, will develop research skills at the preclinical laboratory bench, including: PCR based genetic analysis, site directed mutagenesis, protein purification, immuno cyto and histochemistry, SDS –PAGE and western blot analysis, analysis of cardiac, skeletal and vascular function. Clinical studies will involve patient recruitment into clinical trials and subsequent data analysis.

Career Possibilities

Postgraduate students in the Clinical and Molecular Physiology of Vascular Function Group are encouraged and supported to become involved in a wide range of activities outside of their specific project to enhance future employment opportunities. This includes being involved in scientific society state committees, media training and community engagement, in addition to manuscript publication and conference presentations. Postdoctoral research, research assistant positions, biotechnology industry, academic positions, media, and government are all potential career paths for graduates.

Contacts

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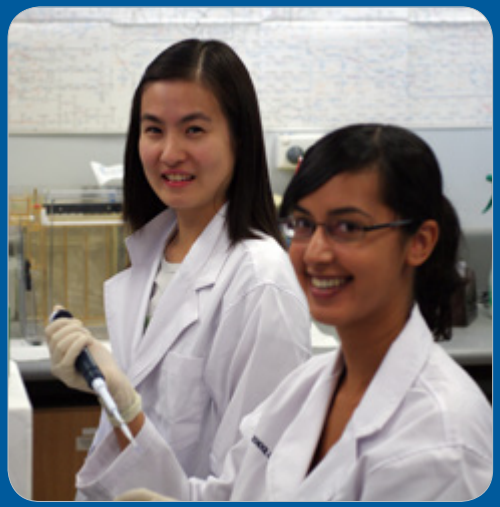

Kanchani and Yann are recent PhD graduates from our group:

Kanchani's PhD was focused on identifying mechanism of microvascular dysfunction in Peripheral Vascular Disease. While Yann explored novel mechanisms by which Ca2+ contributes to vascular contractility.

Following successful completion of their PhD both are currently pursing PostDoctoral Training in translational research within the associated Vascular Diseases and Therapeutics Research Group at the Basil Hetzel Institute for Translational Medicine that is associated with both the University of Adelaide and the Queen Elizabeth Hospital.

Pharmacology - Pain and Anaesthesia Research

Since pain is so common isn't it easy to test new drugs in people?

The answer is that it is surprisingly difficult. Pain is very common, it is true, but pain varies so much from day to day as it is highly dependent on the environment and also by patient expectation. For us to understand how we can treat pain better and especially to understand the mechanisms of chronic pain, we would like to try and avoid these confounding variables and study pain in the laboratory. We have a range of techniques in which we can safely but reproducibly induce transient degrees of clinical pain in volunteers or patients using a variety of methods. One technique which we have developed, the endotoxin/capsaicin model, is the human equivalent of some of the animal models used in the neuroimmunopharmacology laboratory. We think that this technique shows great promise to screen for new drugs which may alter the course of chronic pain. We have a dedicated clinical research laboratory for undertaking such studies. This is the Pain and Anaesthesia Research Clinic (PARC) which is located in the Royal Adelaide Hospital. This unit has a core team of physicians, nurses and trained clinical studies staff which means that, even for non-medically qualified students, they can run their own experiments in humans in a safe and well-supported manner. For more information see

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

Students who undertake their higher degree at PARC also have the opportunity to assist in commercially sponsored research studies which gives a huge edge to the CV when applying for postgraduate jobs in this sector.

Research Projects:

Is oestrogen the missing link between painful periods and chronic pelvic pain?

> This research program investigates the link between the female hormone oestrogen and the development of chronic pelvic pain. Women bear a disproportionate burden of pain but in general little research has been done into women with pain problems.

Can we develop a blood test for pain?

> We have made exciting progress in the use of blood tests of immune function which predict chronic pain. We now plan to use these tools to see whether these tests are useful to diagnose or to choose treatments.

Clinical Trials in Pain and Headache

> We run a range of clinical trials in various painful conditions and have a special interest in headache. Some of these projects are with local collaborators, e.g. the Robinson Institute, but also internationally.

Pharmacology - Pain and Anaesthesia Research

Skills

Students will have the opportunity to learn about the conduct of research in humans in a safe, ethical, high quality environment. Students will learn to write protocols for submission to ethics committees.

Career Possibilities

Graduates with experience of research in humans are particularly highly sought by the pharmaceutical industry but many career paths are possible.

Web Links and media related articles

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

Contacts:

Team Leader – Professor Paul Rolan

http://www.adelaide.edu.au/directory/paul.rolan

PARC
Pain & Anaesthesia Research Clinic

From left: James Swift, Helie Kwok and Nicole Sumaracki

Nicole Sumracki - PhD Candidate

My PhD project investigated whether a novel experimental thermal pain model may be a useful tool to investigate the efficacy of analgesics that are poorly detected by conventional experimental pain models. Undertaking a clinical based PhD project at the Pain and Anaesthesia Research Clinic has allowed me to coordinate and execute clinical research projects at a commercial level standard, work within a team based environment, collaborate with other PhD candidates, further my knowledge in Good Clinical Practise and work with numerous patient populations, all of which are invaluable experiences for my future career prospects. During my PhD, I was fortunate to present my work at local, notional and international meetings, as well as at world renowned clinical based research laboratories. This allowed me to gain valuable feedback on my work and network with experts in the field.

Heilie Kwok (centre) - PhD Candidate

My PhD project investigated potential biomarkers for chronic pain, looking at new candidates that have been identified as we now have a better understanding of how neuro-immune interactions influence pain processing. During my PhD I had a really good time developing new research skills, networking with researchers from all around the world, attending and presenting at conferences to share and learn more about cutting-edge research! The learning experience for PhD is unique and it's definitely worth every moment!

Anatomy and Pathology - Translational Stroke Group

Stroke is a devastating condition, affecting over 15 million people worldwide each year, leaving 2/3 dead or permanently disabled. Over the past few decades over 1000 agents have been shown to be effective in improving outcome and limiting brain damage following stroke in pre-clinical models. But unfortunately we only have one approved therapy for the treatment of stroke, tissue plasminogen activator (tPA). The Translational Stroke Group, headed by Dr Renée Turner, is seeking to improve the clinical translation of agents developed in the lab for the treatment of stroke into the clinic. Through the development and implementation of new and more appropriate pre-clinical models of stroke this group is changing the way that pre-clinical stroke research is conducted.

The Translational Stroke Group operates within the Neurological Diseases Group. Several other specialist groups also operate within the Neurological Diseases laboratory, including, the Traumatic Brain Injury Group, the Chronic Traumatic Encephalopathy Group, and the Neurodegeneration Group.

The neurological diseases laboratory uses pre-clinical models of neurological diseases to investigate the mechanisms of injury and to develop new treatments for these conditions. The Neurological Diseases laboratory studies a wide variety of central nervous system disorders including stroke, traumatic brain injury, chronic traumatic encephalopathy, spinal cord injury, brain tumours, Alzheimer's disease and Parkinson's disease.

Research Projects:

Unravelling the changes in the blood-brain barrier following stroke

> The blood-brain barrier is a critical structure that regulates the entry of substances into the brain. However, following stroke this barrier can be significantly disrupted which leads to a cascade of negative events including brain swelling and inflammation. This project will seek to unravel the changes in the blood-brain barrier and subsequent brain swelling and oedema that occur following stroke to better understand these injury processes so that they may be targeted with therapeutic intervention.

Anatomy and Pathology - Neurological Diseases Laboratory

Intracranial pressure and brain swelling following stroke

> Brain swelling and the subsequent increase in intracranial pressure (ICP) are common and life-threatening complications of stroke. This project is focuses on studying the development of swelling following stroke, how this leads to changes in pressure within the brain and how this may be treated.

Assessing long-term outcome following stroke

> The number one goal of stroke treatment is to restore blood flow to the affected brain tissue but what happens next? Not only is it important that patients survive their stroke event but it is essential for their daily living that they have meaningful function. This project uses the new pre-clinical stroke model developed by the Translational Stroke Group to look at the long-term functional consequences of stroke and to evaluate the effect of novel therapeutic agents.

Developing a new model of pre-clinical stroke

> This project will develop a new pre-clinical model of stroke that allows for the study of the injury mechanisms which occur both when an artery within the brain is blocked and when blood flow is restored. This will most closely mimic the human stroke situation and allow for the testing of novel therapeutic agents for the treatment of stroke.

Skills

Novel pre-clinical models of stroke

Physiological monitoring including blood pressure, intracranial pressure, brain tissue oxygenation, blood gas analysis

Magnetic resonance imaging

Lesion volume assessment

Immunohistochemistry

Behavioural assays

Scientific writing

Career opportunities

Graduates from the Neurological Diseases laboratory are well-suited to take on research positions in academia, industry and government. Given the collaborative nature of our work, our graduates leave with an excellent publication track record and strong collaborative relationships, which will serve them well as they embark on the next stage of their research careers.

Web link and media related articles

http://www.adelaide.edu.au/news/news73002.html

https://radio.adelaide.edu.au/new-stroke-research/

http://www.2ser.com/component/k2/item/11217-new-developments-in-stroke-research

https://www.facebook.com/video.php?v=761677923896956

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University webpage: http://www.adelaide.edu.au/directory/renee.turner

Google Scholar Page: http://scholar.google.com.au/citations?user=cAx5aTMAAAAJ&hl=en&oi=ao

Dr Adam Wells - PhD graduate

As an apprentice Neurosurgeon I had the opportunity to take time off from my clinical studies for higher degree research. I ultimately spent 3 years working in the University of Adelaide Neuroscience laboratory, and completed a PhD characterising a large animal model of middle cerebral artery stroke in the sheep, supervised and supported by Professor Robert Vink and Dr Renee Turner. It was an amazing experience, completely different from the sort of clinical work I had been doing previously, and extremely rewarding. Even more than that, the new skills and thought processes that I developed from working in the team have helped me immensely in my return to clinical work. I still have a keen interest in basic science research, and I am sure that I am a better and more inquisitive clinician because of the research work I have done. Having a higher degree by research in the Adelaide Centre for Neuroscience Research is probably the most important single thing I have done that will shape my future career, and I highly recommend it for anyone interested in a career in neuroscience.

Visual Physiology & Neurobotics Laboratory (VPNL)

We study these questions with an ideal animal model system - flying insects. For example, consider a dragonfly hunting prey amidst a swarm, a dog leaping at a Frisbee or a human catching a ball. In all these scenarios, brains both small and large have evolved the ability to focus attention on one moving target, whilst completely ignoring distracters. As animals track, intercept or avoid targets, an underlying network of brain cells establishes predictive principles of 'expectation' and 'attention'. Such neurons underlie your ability to watch and catch a ball so effortlessly, even in highly cluttered environments. During this task we change our eye, head and body position, resulting in changes to the visual input. This complexity makes biological eyes different from traditional video cameras used in computer vision applications. Understanding these differences may have profound consequences for improving vision on robotic platforms and artificial systems. For example, one day the brain of blind patients may be stimulated with a neuronal prosthetic based on such a vision system.

To investigate these processes of vision, expectation and attention, we study flying insects at several levels - behavioural, computational and physiological.

> In natural settings, we capture video of flying insects pursuing prey and mates, with a gantry that holds multiple high-speed cameras. This quantifies how insects strategically use their head and body position during pursuits and estimates the visual input during such chases.

> Back in the visual physiology lab, we use electrophysiological techniques to record inside neurons that respond only to specific features – one such neuron even responds to a single target, when in the presence of distracters (i.e. an attentional 'focus'). We also fill these neurons with intracellular dyes to describe their underlying morphology.

> In the neurobotics lab, we develop computational models for use in artificial vision systems that are 'bio-inspired' from this underlying neurobiology. We develop autonomous robots capable of visually perceiving and interacting with targets in an unstructured environment, which has applications in health, surveillance and defence.

The multidisciplinary Visual Physiology & Neurobotics Laboratory (VPNL) crosses fields of neuroethology, neurobiology, computer vision and engineering. Members of our laboratory come from diverse backgrounds, including electrical and mechanical engineering, computer science, psychology and medical sciences.

Visual Physiology & Neurobotics Laboratory (VPNL)

Potential projects:

(1) 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, dye-filling and computational modeling)

(2) 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.

(3) Seeing in low light: neural summation in space and time.
The 100 million-fold transition in luminance from day to night places large demands on visual systems – either natural or artificial. Incredibly, despite very low light levels the brains of nocturnal animals permit them to see reliably at night. We will record from the insect brain to study motion vision at different light levels. We will apply this to several groups of insects with different eye designs but similar feeding behavior and active at variable light levels. This will allow us to determine the underlying strategies for optimal neural 'pooling' of information collected by the retina, in space and time. This research has applications for artificial vision where sensor noise is a problem.

(4) 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.

Skills:

Depending on the background and prior training of students, projects involve a combination of techniques including intracellular electrophysiology and neuronatomical analysis using fluorescent intracellular markers. Motivated students have an opportunity to learn computer graphics techniques and data analysis using Matlab. Students with a computational or engineering background may also be interested to expand project aims to the development of computational models and hardware development.

Career Opportunities:

Research output from our laboratory is recognised internationally, with the potential for publication in high-impact journals. Graduates will develop sought after skills and become experts in the fascinating area of sensory neuroscience. We train our students in a mentoring environment, providing the opportunity to leave the laboratory equipped for a successful career in many diverse fields.

Media related links:

(1) Nature's Drone, Pretty and Deadly (New York Times)
http://www.nytimes.com/2013/04/02/science/dragonflies-natures-deadly-drone-but-prettier.html?pagewanted=all&_r=0

(2) Dragonflies have human-like 'selective attention' (Science Daily)
http://www.sciencedaily.com/releases/2012/12/121220143224.htm

(3) Dragonflies can see by switching 'on' and 'off' (Science Daily)
http://www.sciencedaily.com/releases/2013/08/130815104811.htm

(4) Enter the dragonfly (The Conversation)
http://theconversation.com/enter-the-dragonfly-insect-shows-human-like-visual-attention-11439

Joseph Mahandas Fabian - PhD Candidate

In my PhD I study how visual systems can solve the challenge of detecting and tracking small targets in cluttered environments. In particular, I am interested in how neurophysiological properties of target-detecting neurons can be dynamically modulated based on expectation and attention, and the neuroanatomy that forms the basis of their neuronal network. Dragonflies posses a simple brain which hosts target-detection and pursuit systems that outperform the most complex artificial visual systems, and hence provide the ideal model system for answering such questions.

My project has allowed me to learn techniques such as intracellular electrophysiology, fluorescent dye injection, 3D brain reconstruction and immunohistochemistry. Additionally I have had the opportunity to spend 10 weeks overseas learning the latest neuroanatomical techniques in my field, as well as presenting my work to an international audience and discussing research ideas with my peers.

International Students Information

Information for International Applicants wishing to apply for a Masters or Doctorate Degree by Research in Medical Sciences.

The following webpage lists general information for international students: https://www.adelaide.edu.au/graduatecentre/scholarships/research-international/#rounds

Below is a list of steps which you can follow to apply:

1. PROJECTS:

Look at the projects in this handbook that are being offered by the different research groups in the School of Medical Sciences. These projects however are flexible so if there are areas that you are interested in you can email the researchers to discuss potential projects. If you are unsure of whom to contact please email medical.sciences@adelaide.edu.au and we can help to advise what researchers would be best for you to speak with.

2. MINIMUM ENGLISH LANGUAGE PROFICIENCY FOR ENTRY

This is a requirement as listed above. As English is the language of instruction at the University of Adelaide, proficiency in speaking, listening to, reading and writing English is essential. All domestic applicants for a Higher Degree by research must provide evidence of their English proficiency before an offer of a place is made. Evidence of at least one year in the last two years, or two years in the last five years study in English in tertiary education at an Australian university is generally sufficient for this purpose.

Further information of this requirement can be found using the following link:

https://www.adelaide.edu.au/graduatecentre/forms/admission/docs/hdr-english-language-requirements.pdf

3. SCHOLARSHIP APPLICATIONS:

There are a number of schemes which are available for international students to apply for. Please use the following link to access information on these scholarships https://www.adelaide.edu.au/graduatecentre/scholarships/research-international/opportunities/.

ELIGIBILITY: A number of requirements need to be met before you can be considered for international research scholarships. So it is important to look at the requirements using the following links:

https://www.adelaide.edu.au/graduatecentre/scholarships/research-international/eligibility/

Scholarship opportunities:

Scholarship opportunities:

- **International Postgraduate Research Scholarships (IPRS)**
- **Adelaide Scholarships International (ASI)**

These are competitive awards and hence publication in international peer reviewed journals is a precondition.

Please note there are four application rounds for IPRS and ASI scholarships per year

Please visit the following website to confirm deadlines: https://www.adelaide.edu.au/graduatecentre/admission/application-rounds/international/

- **Brazil Scholarship - Science Without Borders (SWB)**
- **China Scholarship Council University of Adelaide Joint Postgraduate Scholarships Program**
- **China Scholarship Council University of Adelaide Joint Postgraduate Scholarships Program**

https://www.adelaide.edu.au/graduatecentre/scholarships/research-international/opportunities/

University of Adelaide recent graduates:

The University of Adelaide offers a number of Adelaide Graduate Research Scholarships exclusively to its recent graduates to continue their education via a Masters or Doctorate degree by research. This is a competitive application process – based on both undergraduate and postgraduate (basis of honours results or the academic results from the applicant's postgraduate degree). You will need to consider the criteria of eligibility which can be found using the following link: https://www.adelaide.edu.au/graduatecentre/scholarships/research-international/opportunities/adelaide-graduate-research-scholarships/

Please take note of closing dates:

Semester 1 intake: 31 October of the year prior.

Semester 2 intake: 30 April of that year.

Support Available in Adelaide:

The International Student Centre (ISC) offers support to all international students throughout their time in Adelaide. Studying away from home and in a different country can be both exciting and challenging at the same time. The staff at the ISC are here to help you adjust to your new surroundings and to support you throughout your studies. For more information see:

http://www.international.adelaide.edu.au/life/current/

Health Sciences Postgraduate Association (HeSPA)

A student body for all postgraduate students in faculty of health sciences.

Provides an opportunity for social interaction and support from other

“Excellent Study Environment”

Zaipul Md Dom

BSc (Biotechnology), BHSc (Hons)
PhD Candidate
Discipline of Pharmacology

I am an international student from Malaysia at the University of Adelaide. I was awarded an Endeavour Postgraduate Award in 2011 and I am currently in the third year of my PhD in Medicine.

My PhD project is about investigating genetic factors that may influence the efficacy of immunosuppressant drugs and hence the incidence of rejection or organ toxicity. The findings from my research will be used to establish whether it may be possible to further reduce the risk of rejection and this study will also have the ability to reveal an important clinical tool for further individualising immunosuppressant drugs in kidney transplant recipients.

I choose the School of Medical Sciences for my PhD because of its international reputation for world-class research in medical and health sciences. The University is one of the top universities in Australia in terms of research funding and quality of postgraduate research experience. Supervisors are dedicated to their students and they provide a supportive environment in which to conduct research and I have gained great experiences working with my supervisors and colleagues. Going to Adelaide has been one of the best decisions I ever made in my life. Adelaide is a relatively smaller and more affordable than most other Australian cities. The city is very student friendly and it offers an excellent study environment for international students. What has impressed me the most is the kindness and friendliness of the people and I have met the most wonderful people of various nationalities and backgrounds. I would highly recommend anyone considering embarking on a doctoral degree to come and learn from world-leading scientists at the University of Adelaide and experience what I have - a truly rewarding and positive experience.

“Highest Standard Internationally”

Muhamad S F Zawawi (Shah)

BSc (Biotechnology), BHSc (Hons)
PhD Candidate
Discipline of Anatomy and Pathology

Given the opportunity to further my study in Australia, School of Medical Sciences at The University of Adelaide is one of the best options because of its international reputation for world-class research in medical and health sciences.

Coming from Malaysia as an international student I was nervous to see how an Australian university would be. You won’t know your worth until you take a hit, isn’t it? It has been a brilliant decision to come to Adelaide embarking a new experience as a PhD candidate. The staff and colleagues are very supportive and the environment is always positive. Sufficient facilities, equipment and materials are provided to produce research of the highest standard internationally.

Living in Adelaide with its people has been a great experience. The friendly culture, unique buildings, maintained cleanliness and a city being surrounded by parklands make Adelaide just beautiful and picturesque. I’d say Adelaide has a relaxed atmosphere without the parking and traffic hassles of other cities and this is excellently conducive for study environment. As Muslims, we could safely practice Islamic teachings. Halal foods are available and this provides decent eating and laid-back lifestyles.

My PhD research investigates the effects of NFATc1 and NF-kB inhibition on ITAM-related molecules and resorption activity in vitro and in vivo. Effects of inhibitors on gene expression, osteoclast formation and activity will be assessed in human osteoclast in vitro assays. Effects of inhibitors on bone loss and ITAM expression in vivo will be assessed in both a peri-prosthetic osteolysis calvarial and arthritic mouse models by MicroCT analysis and immunohistochemistry. We aim to provide a better understanding of how NFATc1 and NF-kB inhibition reduces osteoclast formation and pathological bone resorption, and identifies potential therapies.

Hopefully this research environment and PhD journey will be a great experience to keep me motivated and prepared for a promising future research career.

“World-Class Research”

Diana

Bachelor of Medicine and
Bachelor of Surgery (MUK)
MMedsci Candidate
Discipline of Anatomy and

I commenced my study at the University of Adelaide in August 2012. Adelaide appealed to me because of its international reputation for world-class research. I would then take my longest flight ever from Uganda to Australia.

The staff at the University are very supportive and friendly with a ‘no worries’ attitude. The University is strategically located near the malls, cafes, markets and the food is amazing!

My project investigates the potential of combining magnesium with polyethylene glycol as a potential therapy in traumatic brain injury. Magnesium is involved in all energy processes and has been found to decline following traumatic brain injury. This depletes the body of energy. While clinical trials with magnesium have been unsuccessful due to it’s poor penetration of the blood barrier, polyethylene glycol will help it get across, decrease edema and improve functional outcome!

So far, the results are exciting and hopefully magnesium polyethylene glycol will be a potential therapy for traumatic brain injury.

“Newest Experimental Techniques”

Ehsan Kheradpezhouh

PhD Candidate
Discipline of Physiology

I started my PhD in 2010 in the Ion Channels and Signal Transduction lab of A/Professor Grigori Rychkov in the University of Adelaide, after being awarded Adelaide International Scholarship. The main focus of my research is to investigate the effects of oxidative stress on liver cells and to determine the role of TRPM2 cation channels in oxidative stress-induced liver damage.

The main techniques that I’m using in my work are calcium imaging, confocal microscopy and whole cell patch clamping. Whole cell patch clamping technique allows me to investigate the changes in electrophysiological properties of hepatocytes in response to oxidative stress. The lab I am working in is one of a very few laboratories in the world measuring electric currents in primary hepatocytes; and if anybody is interested to work on liver diseases using patch clamp technique, this is one of the best choices she/he can consider. During my PhD we discovered for the first time that the redox dependent TRPM2 channels in hepatocytes are responsible for liver damage in drug toxicity and ischemia-reperfusion injury, and can be considered as a potential target to treat a range of liver diseases.

The University of Adelaide is ranked among the best 100 universities in the world. Choosing the University of Adelaide provides the opportunity to work with world-class researchers and learning the newest experimental techniques to build your career. The University of Adelaide is located in the CBD of Adelaide city with a fantastic campus area. Adelaide is one of the best cities in Australia for living. It is one of the cheapest capital cities in Australia with fantastic locations for sightseeing. The people here are very kind and welcoming. The city is multicultural, peaceful and clean. Besides, the city is very family oriented; if you are coming with family there are lots of fun places for kids, as well as for mums and dads.

“Global Reputation for Research”

Yibai Li

BSc (Biotechnology), BHSc (Hons)
PhD Candidate
Discipline of Pharmacology

I am an international student from China and currently in the third year of my PhD study. I was awarded an Adelaide Graduate Fee Scholarship in 2010. This scholarship supportedme with a living allowance during my study.

My PhD research had revealed an impact of genetic variations in drug-metabolising enzymes on the pharmacokinetics of ketamine in humans and the consequence of this impact on efficacy and safety of ketamine treatments. The finding of my research provides valuable insight to determine the appropriate ketamine dosage level for each individual patient that is critical to maximising benefits from ketamine treatment while adverse drug effects.

I chose the University of Adelaide because of its outstanding quality and global reputation for research excellence in the field of medical sciences. I have had the privileged opportunity to work with the world-leading experts in my research field and build interdisciplinary collaboration with a number of highly regarded research teams. I also received financial support from the school to assist my national and international conference attendance. Adelaide is indeed a charming city with beautiful temperate weather, vibrant sporting and entertainment events and of course friendly people. The quiet, safe and relaxed lifestyle is what makes Adelaide pleasant to live and study, especially for people like me who came from an overcrowding city.

For further enquiries

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SA 5005 Australia

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Online enquiries: adelaide.edu.au/student/enquiries

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youtube.com/universityofadelaide

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SOUTH AUSTRALIA