



University of
South Australia

School of
Pharmacy and
Medical Sciences

Bachelor of Biomedical Research (Honours)

Research Booklet 2019



IHBY Bachelor of Biomedical Research (Honours)

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Why the IHBV Bachelor of Biomedical Research (Honours)?

Thank you for your interest in undertaking the IHBV Bachelor of Biomedical Research (Honours) within the School of Pharmacy and Medical Sciences of the University of South Australia.

Undertaking an Honours program with the School of Pharmacy and Medical Sciences will allow you the chance to work one-on-one with a research-active academic or within a research group and to participate in the research culture of the School. It will also provide you with the opportunity to contribute to the development of knowledge in your area.

The program is designed around project based, hypothesis-driven research. As an Honours student you will enjoy access to our **state of the art facilities**, and to a wealth of knowledge from our research-active academic staff.

The School has established an international reputation for high quality research aimed at improving human health outcomes. Our academic staff, honours students, and postgraduate students contribute to a great variety of scientific study, aimed at helping to find solutions to the major health challenges facing our planet. From cancer treatment to infectious diseases, nutrition to health policy and education, DNA and gene technology to complementary therapies, our researchers' interests are many and varied, but they all share a spirit of cooperation and a desire to improve human health outcomes through innovative research.

In this document you will find a description of potential Honours supervisors within our School, their respective research groups, projects and contact information.

If you would like to know more about the program, your options and the support available to you, please do not hesitate to contact us.

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For a general overview of the main research themes across the School, please refer to:

<http://www.unisa.edu.au/Health-Sciences/Schools/Pharmacy-and-Medical-Sciences/Research-in-School/>

Acute Leukaemia Laboratory

Acute Myeloid Leukaemia (AML) is the most common form of acute leukaemia in adults. AML results from the accumulation of immature myeloid cells in the bone marrow and peripheral blood, and is heterogeneous in nature, with many different subtypes classified according to molecular aberrations. Overall survival for adult AML is still only 30-40%, and certain subtypes are particularly resistant to therapy, resulting in a median overall survival for these patients as low as 10 months. The molecular basis for many subtypes is still largely unknown, and there is a clear need to improve patient stratification in order to select the best available treatment for each patient, and also to develop new therapies targeted to the specific patient groups which are currently associated with poor outcomes.

Our major focus is understanding the mechanisms underlying normal blood cell development, and the changes associated with disease, in particular AML and related blood diseases (including Myeloproliferative neoplasms and bone marrow failure syndromes). A significant research focus of the Group is the investigation novel genetic changes that lead to altered DNA repair or metabolism in pre-cancerous cells, and the identification and testing of novel therapeutics that target these changes. We also use genomic and epigenetic approaches to identify genes and pathways that contribute to myeloid malignancy.

We have identified a number of genetic changes associated with childhood AML and new projects in the laboratory will further investigate the role of these, and the potential of these as targets for therapy.

Project 1: Testing New Therapies for Acute Myeloid Leukaemia (AML)

AML is a heterogeneous cancer both in terms of genetics and patient response to treatment. While most patients respond to chemotherapy and achieve remission, the majority will relapse within 3 years and prognosis is dismal once relapse has occurred. There is therefore great need to develop novel and more selective treatment approaches targeting individual AML subtypes and relapse patients who currently face very poor outcomes on standard therapy. This project represents a cross-disciplinary collaborative initiative (with Prof. Thomas Gonda; Sansom Institute, UniSA) investigating the clinical potential of novel inhibitors of the Myb oncoprotein in AML.

Project work includes:

- Testing the activity, sensitivity and mechanism of action of novel MYB inhibitors on a panel of AML cell lines and primary patient samples, and to determine the effect of these inhibitors on healthy bone marrow stem and progenitor cells.
- Use an established xenograft mouse model of MLL-AML to test lead inhibitors selected based on the assays above.

Project 2: Acute Myeloid Leukaemia (AML) Genomics

The leukaemogenic process is characterised by the accumulation of acquired somatic mutations and epigenetic changes in haematopoietic progenitor/stem cells, which result in the deregulation of cell proliferation, survival and maturation. An increasing number of genetic alterations have been identified in AML and many of these have important impacts on outcome following treatment with conventional chemotherapy. The use of high-resolution molecular methods, particularly high-throughput (next-generation) DNA sequencing in AML patient samples, is proving to be a powerful approach to identify leukaemic mutations and pathways. This can lead to the development of new markers for classification, prognosis and may also identify molecular targets for novel therapeutics. We have recently performed whole exome capture and high-throughput microarray-based sequencing on a panel of 171 AML patient samples.

Project work includes:

- Identification and characterization of recurrent molecular changes identified in our AML cohort, including germline variants associated with DNA repair.
- Bioinformatics and molecular biology approaches to investigate the genetic changes that drive predisposition and pathogenesis of childhood AML.

Project 3: Understanding the clinical and functional significance of GADD45A silencing by methylation in Acute Myeloid Leukaemia

GADD45A is a tumour suppressor gene that plays cell-type dependent roles in cellular stress coordinating DNA repair and de-methylation, cell cycle arrest, and pro-apoptotic or pro-survival responses. Methylation of four discrete CpG (CpG1-4) residues in the distal promoter of GADD45A is a hallmark of many solid tumours and has been associated with impaired cell stress signaling and reduced drug response. In AML, GADD45A silencing is widespread but poorly characterised. We have shown that hypermethylation of the distal promoter of GADD45A (CpG1-4) is a common event in AML, occurring in 93 of 222 (42%) patients. GADD45A hypermethylation is associated with poor survival in AML overall (median OS: 10 vs 25mths; $p=0.03$) and in the intermediate risk group of patients (median OS: 11 vs 33mths; $p=0.04$).

This project aims to determine the functional significance of silencing of GADD45A in AML with a particular focus on the mechanism of silencing, and also the effect of silencing on the response to chemotherapeutics.

Project 4: Molecular characterisation of Myeloproliferative Neoplasms (MPN)

MPN are a group of late onset and progressive malignancies characterised by the clonal hyperproliferation of stem and progenitor cells, increased output of mature cells of one or more myeloid lineages, and disease progression to bone marrow fibrosis and AML. Activating mutations in the tyrosine kinase JAK2 in particular are a key feature of MPN, but recent studies indicate that additional, JAK2-independent events contribute to the altered cell signaling and MPN phenotype. Furthermore, treatment with JAK2 inhibitors has shown little evidence of disease-modifying effect. It is important now to identify pathways that can be targeted in conjunction with JAK2 to develop more effective therapy that may alter the long-term natural progression of MPN to dramatically improve patient quality of life and survival rates.

Future work on this project will include:

- Investigation of other genetic events contributing to MPN pathogenesis.
- Testing the effects of other signaling pathways in MPN patient samples.

Our research methodologies include: genetics, genomics, gene expression analysis, bioinformatics, signal transduction analysis, cell and molecular biology and *in vitro* and *in vivo* models of AML. Projects would be suitable for students with knowledge in these areas and with an interest in developing further skills.

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Australian Centre for Pharmacometrics (APC) Research Group

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Our research is primarily focused on identifying the pharmacokinetic and pharmacodynamic factors which govern variability in drug response. This work employs pharmacometric analysis (modelling and simulation) as a tool to translate basic and clinical research into improved pharmacotherapeutic use. Pharmacometrics is the science which deals with the quantitative description of disease, drug effects and variability. This field quantifies drug, disease and trial information to aid efficient drug use, development, and regulatory decisions. The strength of such analyses is the ability to integrate knowledge from prior understanding, related compounds and biology, together with the ability to include both richly sampled data and more limited/incomplete data typically unusable in traditional statistical approaches. This quantitative understanding plays a key role in the selection of treatment strategies for the optimisation of clinical use and drug development decisions.

Areas that we are specifically interested in developing further include using physiologically-based pharmacokinetic modelling including the oral absorption of drugs, modelling the cardiovascular system, the use of pharmaceuticals in the veterinary sphere, improving our understanding of pain and its treatment, and therapeutic drug monitoring using Bayesian forecasting.

For more information on the Australian Centre for Pharmacometrics (APC) Research Group

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Bone Growth and Repair Research Group

Musculoskeletal conditions including osteoporosis, fractures and arthritis are major health burdens and they have been identified as a national health research priority area in Australia. Childhood bone health is critical for ensuring healthy development, and the peak bone mass achieved in adolescence also profoundly influences adult bone health.

The Bone Growth and Repair Research Group explores the mechanisms and regulation of children's bone growth, bone growth defects, growth plate and bone injury and repair, cancer chemotherapy and ageing-induced bone loss. The Group's research is aimed at understanding the underlying pathobiology and developing biological treatments that impact on children's bone growth, bone mass accumulation and adult bone health.

Using in vivo, ex vivo and in vitro models and a wide range of histological, cellular and molecular techniques, the Group's research activities can be classified into two areas:

Growth plate cartilage injury responses, repair mechanisms, and growth factor and/or stem cell-based approaches for regeneration: Trauma injury of children's growth plate cartilage (which is responsible for bone growth) remains a key challenge as it is a common and significant problem with 20% of fractures in children involving the growth plate. The injured growth plate is often repaired by faulty bony tissue leading to life-long bone growth defects, for which the underlying mechanisms require further investigations and there are no biological treatments. Our group aims to increase our understanding of the pathobiology, and to develop progenitor cell/growth factor-based regenerative therapy, for growth plate injury-induced faulty repair & growth defects.

Pathobiology for and prevention of cancer chemotherapy-induced bone defects: Cancer chemotherapy-induced bone defects (bone growth arrest, bone loss, excess bone marrow fat, and fractures) have become more prevalent due to the greater success of cancer chemotherapy regimens and a growing population of cancer survivors. Currently mechanisms for chemotherapy-induced bone defects remain unclear and there are no effective and safe therapies. Our group aims to establish the mechanisms for, and prevention of, cancer chemotherapy-induced bone loss, bone marrow defects and bone pain.

Current projects within the Bone Growth and Repair Research Group include:

1. Roles of matrix proteins glypicans in regulating skeletal cell formation and bone growth;
2. Roles of neurotrophic factors in regulating skeletal cell formation and bone remodelling;
3. Roles of neurotrophic factors in regulating bone healing;
4. Altered expression of matrix proteins in growth plate cartilage degeneration;
5. Roles of matrix proteins in bone injury repair;
6. Mechanisms for injury-induced growth plate cartilage degeneration;
7. Development of growth factor/hydrogel composites for growth plate cartilage regeneration;
8. Pro-inflammatory cytokine – NF- κ B signaling in osteoclast formation and bone loss after cancer chemotherapy;
9. Roles of Wnt/ β -catenin signaling in cancer chemotherapy-induced bone loss and marrow adiposity;
10. Bone marrow stromal stem cell damage and regeneration after cancer chemotherapy;
11. Roles of oxidative stress in bone loss following cytotoxic chemotherapy;
12. Osteocyte apoptosis and molecular signals for osteoclastic bone resorption following cancer chemotherapy;
13. Mechanisms for and prevention of bone loss caused by breast cancer chemotherapy;
14. Potential action of nutraceuticals in preventing or reducing cancer chemotherapy-induced bone loss.

For more information on the Bone Growth and Repair Research Group:

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Centre for Cancer Biology

<http://www.centreforcancerbiology.org.au/students/research-opportunities/>

Student Research Opportunities

The Centre for Cancer Biology (CCB) is a Medical Research Institute which carries out a world-class program of innovative research, making breakthrough discoveries in fundamental biology, the processes underpinning cancer, and translating these discoveries into new ways to prevent and treat life-threatening cancer.

The CCB is an alliance between SA Pathology and the University of South Australia and boasts the largest concentration of cancer research in South Australia, currently hosting 22 full-time research group leaders and their teams.

CCB laboratories carry out research across a broad spectrum of solid and blood cancers, focusing on the specialised areas of gene regulation, molecular signalling, tumour microenvironment, translational oncology and cancer genomics. In addition to these laboratories, our ACRF Genomics Facility provides access to state-of-the-art genomics research equipment, computing technology and bioinformatics expertise to the Centre for Cancer Biology and the wider research community.

Translation of new discoveries into clinical practice is strengthened by the co-localisation of the laboratories within a single centre, as well as its proximity to the Royal Adelaide Hospital along with its clinical resources, the University of South Australia and the University of Adelaide, with which it shares key research facilities.

The CCB is a hub of internationally recognised cancer research excellence, aiming to achieve tangible outcomes for patients with cancer. A key platform within this goal is to foster high quality postgraduate studies to build a new generation of world-leading cancer researchers.

Scholarships

A range of scholarships are available for students wishing to undertake Masters or PhD studies at the CCB. Both the University of South Australia and the University of Adelaide administer Australian Postgraduate Awards (APA), and offer a limited number of University Postgraduate awards (for Australian students).

Scholarships are also available for international students through both Universities. Externally-funded scholarship opportunities may also be available for some laboratories and projects, please contact the relevant laboratory head to enquire what opportunities are available. The Universities also provide scholarship opportunities to assist students in specific categories including indigenous students, students who have experienced socio-economic disadvantage, students from rural areas and students with disabilities.

Cancer Research Laboratories

Each CCB laboratory offers exciting opportunities for research studies at Honours, Masters and PhD level, as well as undergraduate summer student placements. For full laboratory details visit our website: <http://www.centreforcancerbiology.org.au/research/laboratories-overview/>

Acute Leukaemia Laboratory led by Professor Richard D'Andrea and Dr David Ross

Studies the genetic and epigenetic mechanisms involved in normal blood cell development and the changes associated with acute myeloid leukaemia and other haematological malignancies. New therapies for these diseases are investigated and tested in clinical trial to ultimately improve patient treatment outcomes.

Cell Signalling Laboratory led by A/Professor Yeesim Khew-Goodall

Understanding what turns a benign cancer cell which remains local and treatable to a metastatic cell capable of spreading to multiple organs.

Cytokine Receptor Laboratory led by Professor Angel Lopez

Seeking to understand the mechanism of cytokine receptor activation in health and disease to support the development of new drugs for unmet clinical needs.

Gastroenterology Research Laboratory led by A/Professor Andrew Ruzkiewicz

Engaged in research activities spanning aspects of gastroenterology pathology including cancer precursor lesions and malignancies of the colorectum, oesophagus and pancreas.

Gene Regulation Section Laboratory led by Professor Greg Goodall

Focused on molecular mechanisms regulating cancer cell metastasis, including mechanisms involving microRNAs, circular RNAs and gene transcription. The Section includes research groups headed by Dr Cameron Bracken, focusing on microRNAs and their targets and Dr Philip Gregory, investigating the regulation of alternative splicing in cancer.

Inflammation and Human Ailments Laboratory led by Professor Vinay Tergaonkar and Dr Nirmal Robinson

Understanding the molecular mechanisms that regulate human ailments like cancer, inflammatory diseases like allergy and metabolic syndrome and the interplay between these (collaborative effort with Prof Tergaonkar's laboratory at the Institute of Molecular and Cell Biology (IMCB) in Singapore).

Leukaemia Unit, Molecular and Genetic Pathology Laboratory led by A/Professor Susan Branford

Investigating the molecular response to therapy of patients with chronic myeloid leukaemia and the mechanisms of drug resistance.

Lung Research Laboratory led by Professor Paul Reynolds

Focusing on a range of projects involving lung cancer, pulmonary vascular disease and airway inflammation, includes gene and cell therapy strategies and the use of conditionally replicative viruses as cancer therapies.

Lymphatic Development Laboratory led by A/Professor Natasha Harvey

Understanding how the lymphatic vasculature is "built" during development and how lymphatic vessel growth and development is dysregulated in pathological settings including cancer, lymphoedema and inflammation.

Molecular Pathology Research Laboratory led by Professor Hamish Scott

Identifying disease causing genes and mutations in humans and the study of the molecular pathogenesis of diseases, including familial cancer syndromes and rare genetic diseases.

Molecular Regulation Laboratory led by Professor Sharad Kumar

Focusing on the cellular and molecular biology of disease. We study how cell death and ubiquitination control cell homeostasis during development and in disease.

Molecular Signalling Laboratory led by Professor Stuart Pitson

Examining how defects in lipid metabolism contribute to cancer (including brain tumours, acute myeloid leukaemia and multiple myeloma), and how this can be targeted for therapeutic benefit.

Neurovascular Research Laboratory led by Dr Quenten Schwarz

Advancing understanding of the molecular development of the neuronal and vascular systems.

Tissue Architecture and Organ Function Laboratory led by Dr Guillermo Gomez

Understanding how the cell's capacity to generate physical forces and sense the biomechanical properties of its environment contribute to the architecture and function of organs, and how this is affected in different types of cancers

Translational Oncology Laboratory led by Professor Michael Brown

Focusing on the preclinical and clinical development of novel antibody and T-cell-based methods for the diagnosis, monitoring and treatment of cancers, particularly of the skin, lung, and brain.

Tumour Microenvironment Laboratory led by A/Professor Michael Samuel

Discovering the molecular toolkit that cancers use to exploit and modify the capabilities of other cells and tissues around them (the microenvironment) to promote their own growth and spread. The laboratory's specific aim is to uncover targets for new classes of therapies against cancers that are difficult to treat.

Vascular Biology and Cell Trafficking Laboratory led by A/Professor Claudine Bonder

Investigating the contribution of the blood vasculature to disease. Examination of how the blood vessels form and are activated during disease progression may provide new treatment options for cancers such as melanoma and breast cancer, organ transplantation to cure diabetes and provide valuable information to overcome allergies.

ACRF Cancer Genomics Facility

This state-of-the-art facility is headed by Mr Joel Geoghegan and Dr Andreas Schreiber and provides opportunities to pursue studies in genomic medicine and bioinformatics.

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Centre for Drug Discovery and Development

The Centre for Drug Discovery and Development was established by UniSA to fast-track the discovery and development of new drugs. We follow a multidisciplinary approach to discover new small molecule probes and drug-candidates, and understand their actions *in vitro* and *in vivo*. The Centre is located at the Reid Building (City East Campus) and enjoys state-of-the-art facilities. These facilities include Computational Modelling (industry-standard software for high-throughput virtual screening and inhibitor design, protein-ligand simulations, QSAR, pharmacophore modelling and etc.), Synthetic & Analytical Chemistry (Discovery Microwave Reactors, IsoleraFlash & FlashMaster Purification Systems, HPLC, AB SCIEX TripleTOF™ 5600 LC/MS/MS System, AVENCEIII 500MHz NMR and etc.), Biochemistry and Cell Biology (Envision multi-mode reader, Gallios™ Flow Cytometer, Auto-Western Blotting System and etc.), and pre-clinical Pharmacology. The Centre is led by [Professor Shudong Wang](#), the Chair of Medicinal Chemistry, who has an international reputation in Drug Discovery and Medicinal Chemistry, and includes a multidisciplinary team of scientists (Assoc. Prof. Bob Milne, Senior Lecturers Dr. Hugo Albrecht, Dr. Matt Sykes and Dr. Cobus Gerber, and many postdoctoral and postgraduate researchers), who are working towards the discovery of new medicines for a range of therapeutic applications, particularly for cancer treatment.

Our main focus is to modulate kinases, a critical group of regulatory proteins that are implicated in many diseases. Kinases are the most popular drug targets for innovative drug discovery. Blockbuster cancer drugs such as Gleevec® and Palbociclib are kinase inhibitors and have revolutionized the treatment of some forms of the disease. Nevertheless, being an extremely complex group of diseases, cancers are in dire need of new treatments. As such, our research projects are focused on the discovery and development of novel protein kinase inhibitors as cancer therapeutics. This involves the structure-guided design, synthesis and optimization of inhibitors that target relevant kinases with high potency and specificity, and their biological and pharmacological evaluation. All of our research projects are highly multidisciplinary, and students will work alongside medicinal chemists, cell biologists, and pharmacologists.

The following projects are specifically designed for students with a strong desire to pursue a career in the fields of drug discovery, medicinal chemistry, cancer biology and pharmacology:

1) Discovery and preclinical development of cyclin-dependent kinase 4 inhibitors as anti-cancer agents

Hartwell, Nurse and Hunt discovered cyclin-dependent kinases (CDKs) as key regulators of the cell cycle, which earned them the 2001 Nobel Prize in Physiology & Medicine. CDKs catalyze the phosphorylation of substrate proteins by transferring phosphate from ATP via their serine or threonine residues. Tumour-associated cell-cycle defects are mediated by alterations in CDK activity. Although many CDK inhibitors have been identified, little progress has been made in the discovery of mono-specific inhibitors of CDK4, a kinase that is dysregulated in several cancers. High specificity will reduce off-target activities of the inhibitors and allow them to be minimally toxic. The aim of this project is to design, synthesise and evaluate a novel class of drug-like molecules that specifically targeting CDK4, and are cytotoxic to cancer cells.

2) Mechanistic investigation of Mnk inhibitors against metastatic cancers

Eukaryotic translation initiation factor 4E (eIF4E) regulates mRNAs that encode proteins involved in cell growth, angiogenesis, invasion, and survival. MAPK-interacting kinases (Mnk1 and Mnk2) phosphorylate and activate eIF4E. Our Mnk inhibitors have been shown to block eIF4E phosphorylation and subsequently inhibit cancer cell growth. This project will further investigate their inhibitory mechanism of colonization, invasion, and migration in metastatic breast and lung cancers.

3) Targeting CDK9 for the treatment of prostate cancer

Apoptosis is a cell suicide program essential for regulating and ultimately preventing tumorigenesis. Evading the apoptotic program is a hallmark of cancer and is often mediated by the up-regulation of anti-apoptotic proteins. Metastatic castration-resistant prostate cancer (CRPC) is an incurable condition characterized by impaired apoptosis and the increased expression of anti-apoptotic proteins. We have shown that inhibition of CDK9, a key regulator of RNA polymerase II (RNAPII) transcription, can induce CRPC cell apoptosis. This project aims to identify CDK9 inhibitors for treating metastatic castration-resistant prostate cancer.

4) Targeting CDK8 for the treatment of colorectal cancer

The Wnt/ β -catenin signalling pathway is frequently down-regulated in most colorectal cancers. Cyclin dependent kinase 8 (CDK8) has been identified as having both direct and indirect roles in regulating the β -catenin-driven oncogenic transformation. Therefore, inhibiting CDK8 in such cancer may be of appealing clinical value. In fact, it has been shown that colon cancer cell proliferation is suppressed by depleting CDK8 expression in cell lines with high levels of CDK8. The goal of this project is to discover and develop novel, highly selective and potent CDK8 inhibitors that would be effective candidates for clinical drug development. In the process we also aim to understand more about the involvement of CDK8 in various cellular events and cancer.

5) Discovery of novel inhibitors of CDK5 for treating cancer

Long considered to have an important role in the development of diseases of the central nervous system, CDK5 is now recognized as being important for a number of other diseases, including cancer. The aberrant production of CDK5 and its activators has been observed in multiple solid tumours and haematological malignancies. It appears to regulate directly proteins important in the cell cycle and indirectly by modifying the transcription of proteins important in the proliferation of cancer cells. It may also have an important role in the self-renewal and differentiation of stem cancer cells, thereby allowing them to persist and contribute to the emergence of resistance to anti-cancer therapy. Hence, targeting CDK5 may allow the discovery of new drugs that may circumvent the drawbacks of the current therapies including emergence of drug resistance and toxic effects to healthy tissues. The CDK5 project focuses on utilizing structure-based and ligand-based drug design principles along with cell biology techniques to identify novel CDK5 selective inhibitor for target validation and drug development.

6) Developing novel inhibitors of FLT3 for treating leukemia

FMS-like tyrosine kinase-3 (FLT3) transfers a phosphate from ATP to a substrate *via* a tyrosine residue. It is recognized as important in the function of normal lymphohaematopoietic stem cells and mutation in the *FLT3* gene represent one of the most common and clinically challenging mutations in childhood and adult leukaemia. The development of small-molecule inhibitors is seen as a valuable opportunity for treating different types of acute and chronic leukaemia. Our Centre is attempting to develop inhibitors that can be used in combination with other anti-leukaemic drugs to achieve greater remission and reduce the incidence of resistance.

7) Repurposing existing drugs for cancer treatment

Drug repurposing is an alternative strategy in drug development. Some already approved drugs that are currently used to treat non-cancer conditions, may also show efficacy in cancer, and do so more quickly, safely and at a much lower cost. This project seeks reposition existing non-cancer drugs for targeted cancer therapy.

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Centre for Pharmaceutical Innovation and Development (CPID)

Through the Centre for Pharmaceutical Innovation and Development (CPID), I would like to welcome students to our exciting translational drug development research projects. Majority of my projects are in partnership with pharmaceutical industry, local and international collaborators, and research foundations. Following are my research interests:

Anticancer drug delivery and nanomedicine: local and systemic tumour targeting, applications of nanoscience to drug development; intracellular drug targeting.

Infections: novel antibacterial compounds and formulations for resistant pathogens (Superbugs) in human and veterinary applications.

Translational drug development and delivery: Preformulation, physico-chemical characterization, solubility and stability assessment and improvement, patentable non-infringing platform technologies: nanotechnology, solid, semisolid and liquid dosage forms; reverse engineering, cosmetics and

complementary medicines.

Novel veterinary delivery systems: for cattle, horses, cats, dogs, pigs and fish.

Pharmaceutical analysis, quality control and regulation: analysis of drugs, metabolites and excipients in the pure form, formulations; stability indicating analytical method development and validation; Good Laboratory Practices (GLP); quality assurance and control (QA and QC); regulatory documentation; registration dossier preparation and evaluation; Intellectual Property (IP) issues.

Extemporaneous compounding: shelf life assessment and improvement, formulation improvement.

Following are examples of some projects on offer for 2018:

- Novel intracellular drug targeting systems for tuberculosis, HIV, and Cancer
- Solubility improvement of a novel antibacterial compound and its evaluation
- A novel antibody based topical system for wounds
- A novel sustained release delivery system for otic treatment in dogs
- Stability assessment and improvement of an extemporaneously compounded hospital preparation

In addition, I am happy to tailor a project, matching your interests and dreams.

Student requirements

Students with a dream to achieve something big, enthusiasm to explore new ideas and opportunities, commitment for intelligent hard work, and unlimited stock of smile are invited to discuss opportunities. Our projects will provide opportunities for interacting with research sponsors and partners, helping with career progression.

For more information on the Centre for Pharmaceutical Innovation and Development (CPID):

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Early Origins of Adult Health Research Group

Our research is in the area of pregnancy and fetal development, with a focus on the early origins of adult health and disease. Our research aim is to determine the mechanisms underlying the early programming of adult disease, with a focus on the impact of a poor environment before and during pregnancy in determining cardiovascular and metabolic health in adult life.

[Professor Janna Morrison](#) is Head of the [Early Origins of Adult Health Research Group](#) in the Sansom Institute for Health Research at the University of South Australia. Prof Morrison was been funded as a fellow by the Heart Foundation from 2004-2013 and is currently a NHMRC Career Development Fellow. Her current research centres on how the fetal cardiovascular system responds to changes in nutrient supply before conception and during pregnancy. Initial work focused on understanding how the small baby maintains its' blood pressure in utero and if these mechanisms might lead to an increased risk of hypertension in adult life. With the aid of an American Physiological Society Career Enhancement

Award, she began interrogating the effects of being small on heart development. More recently, she has looked at the effects of maternal obesity on heart development. After completing her PhD at the University of British Columbia, Janna held postdoctoral positions at University of Toronto and the University of Adelaide before joining the Sansom Institute for Health Research in 2006. Among her numerous awards and achievements, Janna received a South Australian Tall Poppy Science Award (2006) in recognition of her work examining the link between low birth weight and heart disease in adulthood.

Current Projects

Does the preterm male fetus have greater cardiovascular vulnerability due to delayed cardiomyocyte maturation?

Prof Janna Morrison and Prof Doug Brooks

In Australia, 7% of babies are born preterm. Males are more vulnerable during the transition to living outside the womb. They experience more cardiovascular instability. We hypothesise that there is a delay in the maturation of the heart muscle cells in male fetuses that put the preterm male fetus at increased risk of cardiovascular collapse. We have shown that there is a delay in the terminal differentiation of cardiomyocytes in male fetuses. This is important because terminally differentiated cardiomyocytes can only get bigger. They can't make more cardiomyocytes. But the undifferentiated cardiomyocytes, that can make more cardiomyocytes, can't create as much force with each contraction of the heart. The growth of cardiomyocytes is regulated by a range of growth factors including the insulin-like growth factors (IGFs). We hypothesise that there is a lower IGF-1 and -2 gene expression in hearts from preterm male fetuses and thus less activation of the IGF-1 receptor signaling pathway. This study will use real-time PCR, Western blots and immunohistochemistry to analyse gene expression as well as protein expression and distribution.

The role of microRNA in cardiac proliferation

Prof Janna Morrison

When adults have a heart attack, there is very limited capacity for cardiac repair because cardiomyocytes (heart muscle cells) cannot proliferate after birth, they can only grow via increasing their volume (hypertrophy). The number of cardiomyocytes that an individual will have for life is set at birth. This number is influenced by the amount of proliferation, apoptosis and autophagy that occurs in the heart during late gestation. After birth, there is very limited proliferation and as a result there is limited cardiac repair after injury. Recent studies have demonstrated that cardiomyocyte cell cycle withdrawal and multinucleation may be regulated by microRNAs. Understanding how microRNA orchestrates this process will therefore allow us to increase proliferation and thus cardiomyocyte endowment. This will allow us to develop an intervention to improve cardiac health after injury and provide insight into ways to promote proliferation in the adult heart. To address this question we will use microarray and real-time PCR to measure the expression of microRNA and genes that are important in cardiomyocyte proliferation, as well as test the effectiveness of microRNA on cardiomyocytes in culture.

Does maternal supplementation with resveratrol in late gestation alter insulin signalling in the mother or the fetus?

Prof Janna Morrison and Prof Doug Brooks

Resveratrol a polyphenol (found in the skins of red grapes) is often used as a dietary supplement to help weight loss and correct blood sugar levels. It is a potent antioxidant and has the ability to act upon many cell signalling pathways, both directly and indirectly. Although the dietary supplementation of resveratrol has many positive health consequences, the implications of exposure during pregnancy on both mother and fetus are not completely understood. We hypothesize that maternal exposure to resveratrol in late gestation will alter both maternal and fetal insulin signalling pathways. This project will use techniques such as Western blot to determine the protein abundance of molecules within key insulin signalling pathways.

Epigenetic basis of left ventricular hypertrophy in the small baby

Prof Janna Morrison

Human studies show that babies whom are born small are at increased risk of cardiovascular disease, including hypertension and left ventricular hypertrophy, in adult life. However, we do not yet understand the molecular basis of this association. Until we understand the molecular basis we cannot implement effective intervention strategies. In a sheep model of fetal growth restriction resulting in a small baby, we have shown that small fetuses have fewer cardiomyocytes (hearts muscle cells) in late gestation and an increase in IGF2 and IGF2R gene expression. In the low birth weight lamb, there is an activation of the IGF2R signaling pathway in the heart due to increased histone acetylation of IGF2R and this results in left ventricular hypertrophy (a major risk factor for cardiovascular disease). We have recently shown that in early gestation, there is an increase in oxidative stress and this may be the underlying cause of the hypertrophy because there is more apoptosis and an increase in molecules that increase histone acetylase. Now that we have identified these changes, we are developing intervention strategies that we will test using real-time PCR to measure gene expression, Western blot to measure protein expression and cell culture to prevent histone acetylation or hypertrophy. When we find a suitable strategy to prevent left ventricular hypertrophy in the growth restricted fetus, we may be able to curb the proportion of low birth weight babies that go on to develop cardiovascular disease in adult life.

Are small babies at increased risk of exposure to drugs?

Prof Janna Morrison and A/Prof Michael Wiese

Many pregnancies that require drug treatment are complicated by illnesses such as preeclampsia, preterm delivery, and maternal obesity, all of which may affect fetal growth. Fetal growth is a key indicator for fetal outcomes as babies born smaller are at risk of adverse neonatal outcomes such as respiratory distress syndrome and hence more likely to require drug treatment. There is human and animal evidence showing hormonal and metabolic changes occur in both the mother and the fetus as a result of poor maternal nutrition and low fetal growth. These changes in the mother could affect maternal, placenta and fetal expression of drug metabolising enzymes and drug transporters and hence alter fetal drug exposure. Using a sheep model of fetal growth restriction, this project will explore the effect of poor fetal growth on the expression of drug metabolising enzymes, such as Cytochrome P450, and drug transporters in the placenta, fetal liver and brain.

Impact of cortisol on drug exposure in the fetus

Prof Janna Morrison and A/Prof Michael Wiese

Preterm birth affects more than 20,000 births in Australia. Glucocorticoids are routinely used to reduce the risk of respiratory distress syndrome in preterm births by promoting lung maturation. However, the use of glucocorticoids during pregnancy has been associated with adverse fetal outcomes including low birth weight. In addition, glucocorticoids also regulate the expression of Cytochrome P450 enzymes, a class of enzymes involved in drug metabolism, and drug transporters such as P-glycoprotein. Therefore, using a sheep model, we propose that infusion of the endogenous glucocorticoid, cortisol, in late gestation will alter the expression of drug metabolising enzyme and drug transporters in the placenta, fetal liver and brain.

Heart development in preterm and term babies

Prof Janna Morrison and Dr Max Berry (Univeristy of Otago)

In Australia, 7% of babies are born preterm. These small babies are at increased risk of cardiovascular disease in adult life. In sheep, the small fetus has fewer cardiomyocytes than the normally grown fetus and thus these fewer cardiomyocytes must get bigger to maintain heart growth. However, the fetal heart development in preterm and term piglets is not fully understood. Glucocorticoid administration has been shown to have a beneficial impact for lung maturation and a successful transition to extrauterine life, however its impact on fetal heart development is less clear. Therefore, we will use real time RT-PCR to investigate a range of genes and signalling pathways involved in proliferation, hypertrophy, apoptosis,

autophagy and metabolism in preterm, preterm with glucocorticoid treatment and term piglets and/or guinea pigs.

Investigating changes in fetal lipid profiles in response to changes in maternal nutrient supply

Prof Janna Morrison, Dr Sally Plush and Prof Doug Brooks

Lipid metabolic and biosynthetic pathways are implicated in a wide range of chronic diseases. Maternal diet can have a significant impact on how lipids are metabolised by offspring, and subsequently their health in later life. However, the exact mechanisms behind this are yet unknown. Methods for measuring and localising lipids in tissue can provide insight into how factors, such as maternal overnutrition, result in changes to lipid profile in the fetus. This project explores methods for analysing lipids in sheep tissue, for example epifluorescence and confocal microscopy, and high-performance liquid chromatography (HPLC), and will expose students to various laboratory techniques and analytical methods. Students will have the opportunity to gain skills in histology and tissue sample preparation, image acquisition and data analysis.

Small babies, endothelial progenitor cells and increased risk of hypertension in adult life

Prof Janna Morrison, Dr Claudine Bonder

Babies who are born small have an increased risk of cardiovascular disease in adult life. These include an increased risk of hypertension and left ventricular hypertrophy. We speculate that the small baby has a smaller pool of endothelial progenitor cells in fetal life due to a decrease in the supply of oxygen and nutrients to the fetus. A decrease in the pool of endothelial progenitor cells reduces the capacity for the development of endothelial cells and this may result in altered vessel formation. This altered vessel formation may lead to an increased risk of cardiovascular disease in adult life. We will use a model of placental insufficiency in sheep to study the gene expression of specific markers of endothelial progenitor cells in the heart, bone marrow and blood vessels in the fetus during late gestation.

Role of nutrition on surfactant development in the fetus

Prof Sandra Orgeig and Prof Janna Morrison

This project is a collaboration between two research groups in the Sansom Institute for Health Research - the laboratory for Molecular & Evolutionary Physiology of the Lung and the Early Origins of Adult Health Research Group. In the placental restriction model, the growth restricted fetus experiences both nutrient and oxygen restriction (i.e. under-nutrition & hypoxia). We hypothesise that hypoxia has the dominant effect on surfactant maturation. To determine the contribution of under-nutrition alone, we wish to examine surfactant maturation in mid- to late gestation sheep. Fetuses exposed to maternal under-nutrition. In this project lung tissue and plasma from control and undernourished sheep fetuses will be analysed for alterations in surfactant protein and gene expression and plasma glucose and cortisol concentrations. Furthermore, babies born preterm or born small for their gestational age are at an increased risk of developing respiratory distress. We wish to establish the mechanisms and timing of surfactant maturation during late gestation in relation to environmental factors that lead to intrauterine growth restriction. We hypothesise that intrauterine growth restriction in the guinea pig induced by maternal under-nutrition or maternal hypoxia will reduce surfactant protein and gene expression in the lung of the late gestation guinea pig fetus. In this project lung tissue from control and intrauterine growth restricted guinea pig fetuses will be analysed for alterations in surfactant protein and gene expression.

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Molecular Neurogenomics Research Group

Associate Prof Leanne Dibbens

Our group studies a variety of neurological disorders including epilepsy, intellectual disability and autism spectrum disorders. These disorders each have a strong genetic basis. We employ a number of different methods to identify the genetic cause of these disorders in patients. Some of these patients are from families with a history of the disorder while others are isolated cases. The strategies we use include genetic linkage, genome and exome sequencing and targeted re-sequencing of specific genes along with bioinformatics analysis. We have discovered a number of genes involved in neurological disorders including *PCDH19* in epilepsy and intellectual disability in females, *KCNT1* in focal epilepsy with psychiatric features and *DEPDC5* in focal epilepsies with or without brain malformations. We also use animal models including *Drosophila* to understand the biological processes by which mutations in these genes lead to neurological disorders. Such knowledge will assist in developing improved treatments for patients.

Project 1: Identifying new genes in neurological disorders

We have a large number of families and patients affected with various forms of, for example, epilepsy where we have not yet identified the gene responsible. In this project multiplex families will be analysed by next generation sequencing and bioinformatics analysis to identify the causative gene. Once a gene is identified we confirm the finding by looking for further mutations in additional patients with a similar phenotype. We can then begin to investigate any genotype-phenotype correlations and begin to explore the biology of the disorder.

Project 2: Using *Drosophila* to understand the biology of neurological disorders

Drosophila melanogaster is a powerful model organism which allows sophisticated genetic manipulation directed at revealing the function of uncharacterised genes. This project will utilise *Drosophila* to overexpress, knockout or alter expression of a particular gene of interest. This allows us to explore the role of our newly identified genes in neurological disorders to identify which gene pathways they act in and how perturbation of their function results in human disease. We also use *Drosophila* carrying these disease causing gene alterations as a means to screen for new drugs to treat these diseases.

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Experimental Therapeutics Laboratory

The Experimental Therapeutics Laboratory (ETL) is a collaborative venture between scientists from the Sansom Institute for Health Research (University of South Australia), the Hanson Institute and the Cancer Clinical Trials Unit (Royal Adelaide Hospital Cancer Centre). We perform diverse basic, translational and clinical research that aims to improve chronic and acute health outcomes by exploring novel immunotherapeutic approaches to treat and prevent allergy, chronic and acute infections, uncontrolled inflammation in sepsis and the body's response to biomaterial implants. We exploit the specificity and power of the immune system to design, develop and implement cutting edge approaches to new diagnostic and therapeutic agents. Industry and clinical links ensure that our research has a strong potential for commercialisation and improved therapeutic outcomes for patients.

Professor John Hayball (Group Leader; Sansom Institute, UniSA)

<http://people.unisa.edu.au/John.Hayball>

Professor Hayball has an interest in understanding the fundamental mechanisms involved in controlling the mammalian immune response, particularly those involved in the development of an early innate immune response. He is using this information in rational approaches to develop new therapeutics for the treatment and prevention of diseases such as cancer, infection and allergy. Professor Hayball supervises a number of Honours and PhD students involved in basic research, as well as research undertaken collaboratively with industry partners and across disciplines.

Dr Kerrilyn Diener (Collaborative partner; NHMRC Early Career Research Fellow, UA)

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Dr Diener's interests lie in understanding the early innate immune mechanisms behind antigen recognition and presentation, particularly those relating to viral infection and pregnancy. Dr Diener's research focus investigates the effect that viral infection within the reproductive tract has on reproductive outcomes, and whether early infection can have long term effects on behaviour in offspring, including the induction of autism after pre-pubescent vaccination.

Dr Paul Howley (Industrial collaborative partner; Adjunct Senior Lecturer, UniSA; Chief Scientific Officer, Sementis Ltd)

<http://people.unisa.edu.au/Paul.Howley>

Dr Howley's interests lies in vaccine research and development, from antigen discovery, design and delivery modes to immunological mechanisms and correlates of immunity pertinent to vaccine efficacy. Special interest lies in the field of therapeutic vaccines for the treatment of cancers, allergies and chronic viral and bacterial diseases and preventative vaccines for new emerging viral and bacterial diseases.

Dr Tamara Cooper (Postdoctoral Research Fellow)

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Dr Cooper is interested in how viruses can be used to modulate immune responses and exploited to provide protective immune responses to a range of disease types. She is currently involved with the pre-clinical development of novel vaccine technologies. This work involves engineering a safe and effective viral platform with antigens that could be used to treat a variety of diseases with current projects aimed at allergy, emerging infectious diseases and cancer.

Dr Liang Liu (Postdoctoral Research Fellow)

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Dr Liu has a main research interest in developing new vaccine platforms. By using cutting-edge genetic engineering tools, safer and more efficient vaccine vectors are being created. The new platform can be applied into various diseases' vaccine development, such as HIV, peanut allergy, cancer vaccines. Dr Liu also has an interest in the novel mechanisms of innate immune signaling involvement in neurological disorders, particularly drug addiction and chronic pain.

Dr Preethi Eldi (Research Associate)

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Dr Eldi's interests lie in the field of host-pathogen interactions and vaccine development. Her current research focus involves the modulation of T helper responses as a strategy to induce desensitization to peanut allergens. This work is directed towards the development of a safe, therapeutic vaccine against peanut allergy.

Dr Pablo Garcia Valtanen (Research Associate)

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Currently, my research focus is on the rational design and development of therapeutics to treat cancer and viral diseases. In a joint venture between ETL and ConCa Pty Ltd (a South Australian owned company), I manage the day-to-day research operations of a project to generate polyclonal antibodies for the treatment of oesophageal cancer and its precursors. Furthermore, I study potential molecular targets in white adipose tissue to find treatments for herpesvirus infections. As part of my mentoring roles at the ETL I am co-supervising two PhD research projects, one on the role of adipose tissue-resident regulatory B cells during pregnancy and another on the development of dissolving microneedles to deliver virus-vectored vaccines.

Dr Martin Sweetman (Research fellow)

<http://people.unisa.edu.au/Martin.Sweetman>

Dr Sweetman's research is linked closely with an industry partner, focused on the development of new technologies for water treatment and monitoring. The detection and removal of organic and pathogenic contaminants is crucial for providing safe water to individuals. His current research involves the design and construction of a point of use sensor for monitoring water quality pre and post filtration. Following on the same theme, Dr Sweetman is also interested in developing advanced materials for improved water filters. Research in this field will help to ensure efficient and sustainable use of this scarce resource into the future.

The Experimental Therapeutics Laboratory currently has opportunities for students in the following areas:

Development of a Multi-purpose Vaccine Platform

The ETL in collaboration with Sementis Ltd are developing a vaccine vector platform. The genetically modified virus is designed to encourage the body's own immune system to fight disease. This proprietary technology is being designed to not only be safe but to also be extremely effective through superior immune stimulation.

From this platform, an array of immunotherapeutics are being developed against allergies, infectious disease and cancer.

Emerging infectious diseases

Recent years have seen the re-emergence of a number of infectious diseases including Zika, Ebola and Chikungunya viruses. Globalization and climate change have increased and extended the geographical reach of these threats and effective vaccines are greatly needed.

The ETL research group in collaboration with Sementis Ltd are working on preventative vaccines for an array of infectious diseases, based upon its proprietary viral vector platform.

Reproductive Immunology

The ETL research group has an interest in studying the innate and adaptive immune systems within the female reproductive tract. This is in an attempt to understand their role in dictating the outcome of many conditions including the response to vaccination, infection and pregnancy. The group are currently investigating the role of infection, tolerance and plasmacytoid dendritic cells during different stages of the reproductive cycle and pregnancy to determine whether early infection, or depletion of plasmacytoid dendritic cells throughout pregnancy, can adversely affect the outcomes of implantation and pregnancy and ultimately fetal growth and survival.

Tasmanian Devil Facial Tumour

The ETL research group is currently developing cancer therapeutics to treat the Tasmanian devil facial tumour disease and also to treat cancer in dogs. The new therapeutics will be developed based on

cancer therapeutics that have already been proven to be effective in treating human cancer. This project has the potential to help save an endangered species, develop new veterinary therapeutics that could become widely used in veterinary medicine, and shed light on how cancer evades the immune system. Students involved in cancer therapeutic design will develop basic molecular biology, immunology, cell culture, genetic engineering skills that will prepare them well for a career in the biomedical sciences.

Peanut Allergy (allergic disease)

Despite the risk of potentially fatal allergic reactions, there is currently no method available in routine clinical practice for treating peanut allergies. The ETL research group have established a robust murine peanut-induced anaphylaxis model that will be used to test an immunotherapeutic approach which aims to selectively inhibit the production of peanut allergen-specific antibodies and decreases the risk of anaphylaxis during the desensitization process. This type of immunotherapy could have broad application in treating allergic diseases.

The ETL research team is currently working in partnership with clinical immunologists in order to investigate potential therapeutic avenues to treat peanut allergy, and other allergic disease that will readily translate to human clinical medicine.

Sepsis

Sepsis, defined as systemic inflammatory response to an infection, is a significant health burden with increasing incidence in Australian hospitals. Current treatment involves providing supportive care and broad-spectrum antibiotics. High Mobility Group Box protein 1 (HMGB1) is considered a late mediator of this systemic inflammatory response, released after the acute phase of the 'cytokine storm' and drives further immune activation. The ETL research group is trying to establish a clinical role for HMGB1 neutralising antibody in sepsis.

T cells and Vaccine responses

T cells are immune cells that are crucial for an effective vaccine. The T cell is able to respond to infected cells by binding them and releasing enzymes that can destroy these potentially harmful cells. T cells also divide rapidly to form an 'army' to increase the fight. But one of their most important qualities is that they can become memory T cells - a population of cells that hang around in your body, 'remembering' the previous threat, so if it sees it again, it's ready for the fight. Only this time, it's faster and stronger. Vaccines are used to train your immune system on how to respond appropriately to these infections. Put simply, good T cell response, good vaccine. But getting a T cell to respond appropriately can't occur without controlled intracellular processes that direct the T cell to perform its functions. The ETL research group is interested in assessing one of the most crucial processes: the release of calcium ions. The ETL group has developed a method for quantifying the rate of calcium release as a function of the strength of T cell activation. It is hoped to use this method to assess the quality of vaccines ex vivo as a quick and more sensitive assay than current methods.

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Healthy Environments, Healthy People Research Group

Ecosystem determinants of human health: Healthy environments provide the foundations for human health. Through studies of both terrestrial and aquatic ecosystems, the determinants of human health are investigated in order to develop novel public health interventions. Particular areas of focus are medical entomology, invertebrate biodiversity, and aquatic system health. Citizen science is also employed as an overarching approach to research that connects, empowers and educates.

Projects on offer for Honours students

- Salinity tolerance and climate adaptation in Australian frogs: adaptive benefit of salinity tolerance
- Toxin tolerance and predator prey interactions in aquatic animals

- Exotic predators, exotic prey: can an introduced frog (*Litoria cyclorhyncha*) control an introduced beetle (*Blaps*)?
- The impact of climate change on mosquito vectorial capacity

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Infectious Diseases and Microbiology Research Group

Superbugs are costing the medical and veterinary industry billions of dollars a year and antibiotic resistance is one of the world's most pressing health problems. Research in the Infectious Disease Group is predominantly focused on understanding and treating antimicrobial resistance and at addressing issues such as multidrug resistance.

Dr Rietie Venter (Head of Microbiology)

<http://people.unisa.edu.au/Rietie.Venter>

We have projects aimed at measuring antimicrobial resistance in a variety of organisms from clinical and environmental origin and projects aimed at understanding the mechanisms that underlie multidrug resistance. Other projects focusses on antimicrobial drug discovery and development.

Antimicrobial Drug Discovery and Development

Surveillance by the World Health Organization has identified that globally bacterial resistance to antibiotics has reached alarming levels. With pharmaceutical industry-led development in this area lagging, there is an urgent need for discover new antibacterial agents that have a novel mechanism of action especially against drug-resistant Gram-negative organisms that are on top of the WHO's list of most critically dangerous & drug resistant pathogens.

Project 1: Reversing multidrug resistance with efflux pump inhibitors

Central to antimicrobial resistance is the expression of efflux pumps, through which bacteria extrude drugs. These efflux pumps are also implicated in bacterial virulence and biofilm formation. Moreover, functional efflux pumps are necessary for the selection of drug-resistant bacteria.

Due to the critical role that drug efflux pumps play in resistance and virulence efflux pump inhibitors (EPs) will (a) synergise with currently used antibiotics, (b) restore the efficacy of antibiotics to which resistance has arisen, (c) reduce the emergence of drug-resistant pathogens, (d) reduce the ability of pathogens to infect the host as the inhibition of efflux attenuates the bacterium and (e) prevent the development of highly drug resistant biofilms. This project aims to identify and develop new inhibitors against drug efflux pumps from Gram-negative bacteria.

Project 2: The cell division machinery as novel drug target in antibiotic resistant bacteria

FtsZ (filamentous temperature-sensitive protein Z) is the major protein of the cell division machinery of the bacterial cell. It has guanosine triphosphatase (GTPase) activity. In the presence of GTP, monomers of FtsZ polymerize into protofilaments that aggregate into a structure called the Z-ring at the site of bacterial cell division. Other cell division proteins can then be recruited and a septum forms that allows a single cell to divide into two daughter cells. FtsZ is an attractive target to develop new antibacterial agents with selective toxicity to bacteria because it is essential to bacterial cell division, it is highly conserved in different bacterial species and it is not present in higher eukaryotes. This project aims to identify and develop new inhibitors targeting the FtsZ protein of antibiotic resistant bacteria.

Antimicrobial Resistance in Residential Aged Care Facilities

Project 3: Turning antimicrobial resistance in residential aged care inside-out from the patient to facility level

Populations in Australian residential aged care facilities (RACFs) are growing rapidly. RACFs are particularly vulnerable to infections and the impacts of antimicrobial resistance (AMR) due to aged-related physiology, underlying chronic conditions and the dense cohabitation. RACF antibiotic usage is well-known, but data on the level, nature and spread of AMR are absent. Using a novel blend of patient-, facility- and sewage level analyses, we will develop new knowledge to understand the risks and inform future policy needs to slow the spread of AMR in RACFs.

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Mechanisms in Cell Biology and Disease Research Group

To develop better diagnostics and treatments for major diseases we need to increase our knowledge on cell function and develop methods to monitor how potential new treatments work at the cellular level. This cannot be achieved through the application of one discipline alone, but instead needs a multidisciplinary approach. We have addressed this by developing a highly skilled multidisciplinary research grouping comprising of specialist cell biologists and synthetic chemists and this is backed by significant national (Curtin and Monash Universities) and international (Trinity College in Dublin Ireland, NIH in Washington DC USA and University of Bologna, Italy) collaborations. This interaction has led to some highly novel technology, including the development of molecular probes which can be used to image unique cellular interactions in live cells and the development of innovative detection systems for particular cancers. The Mechanisms in Cell Biology and Diseases Research Group is a collective of highly innovative research scientists who work cohesively to answer the bigger questions and develop an understanding of cell biology and diseases states, which is coordinated by a world leader in cell biology Professor Douglas Brooks.

If you are interested in applying chemistry to biology or vice versa, have an interest in understanding how cells function, are keen to answer important questions about disease biology and want to work in a team environment this grouping may suit you.

Professor Doug Brooks (Group Leader)

<http://people.unisa.edu.au/Doug.Brooks>

Professor Brooks is a Research Professor in Molecular Medicine who has over 25 years of experience in cell biology/immunochemistry and translational research, with a strong record of NHMRC funding. Professor Brooks has a strong interest in lysosomal cell biology and a desire to develop practical applications in biochemical medicine that benefit patients and the wider community.

Dr Emma Parkinson-Lawrence (Senior Lecturer; Project Leader)

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Dr Emma Parkinson-Lawrence is a senior lecturer in cell biology who has a developed passion for protein structure and function and endosome-lysosome biology in disease pathogenesis. Dr. Parkinson-Lawrence has extensive expertise in biophysical protein biochemistry and the application of immunochemistry in pathophysiology. Dr Parkinson-Lawrence has specific interests in lysosomal storage disorder and cancer pathology.

Dr Shane Hickey (Research Associate)

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Dr Hickey is a Research Associate and the senior organic chemist within the Plush Laboratory, whilst simultaneously working within the Mechanisms in Cell Biology and Disease Research Group led by Doug Brooks. His work is focused on developing organic and inorganic molecules suitable for live cellular imaging to better understand mechanisms which underpin disease. Dr Hickey also has a strong background in the development of potent antimicrobial agents and has numerous publications in this area.

Current Research Projects

1) *Defining altered endosome-lysosome biogenesis in prostate cancer*

Professor Doug Brooks (UniSA), Dr Ian Johnson (UniSA), Dr Emma Parkinson-Lawrence (UniSA), Dr Stavros Selemidis (Monash), Assoc. Prof. Lisa Butler (UniA) and Professor John O'Leary (Dublin)

Due to the high incidence of both breast and prostate cancer, there is a growing need for specific detection methods for the early diagnosis and implementation of therapy. A better understanding of the pathogenic process in breast and prostate cancer will facilitate the identification of novel biomarkers for the early detection of these cancers. Endosomes and lysosomes are directly involved in the critical processes of energy metabolism, cell division and intracellular signaling, and may therefore have a direct role in cancer pathogenesis. We are investigating endosome-lysosome biology in breast and prostate cancer. New knowledge on altered endosome-lysosome biogenesis in cancer will be used to develop diagnostic and prognostic biomarkers. Students who undertake honours in this area can be expected to become skilled in the areas of cell biology, imaging, protein chemistry, immunochemistry and mechanisms of vesicular traffic.

2) *Developing biomarkers and therapeutics for primary and metastatic lung cancer*

Prof. Doug Brooks, Prof. Sandra Orgeig, Prof. Paul Reynolds, Dr Emma Parkinson-Lawrence

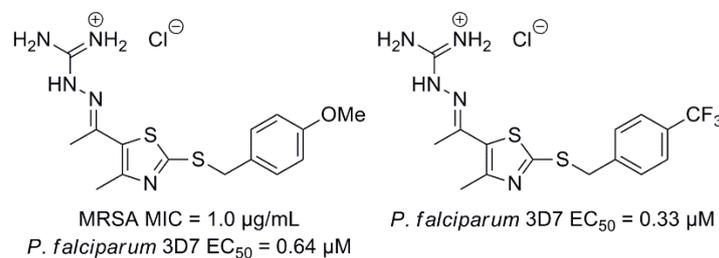
There is currently a chronic global cancer pandemic with over 14 million new cases of cancer each year and 8.2 million deaths. Lung cancer is one of the most common types of cancer, and for lethal metastatic

cancers the lung is also one of the most common sites for secondary cancer development. This makes it imperative that we understand why the lung is so heavily involved in cancer development. For prostate cancer we went back to the basic biology of the cancer, removed any confounding variables that could relate to secondary pathogenesis and searched for a cell biological pathway that was connected to the primary pathogenesis. This new project will use this groundbreaking agnostic discovery approach to provide the same outcomes for primary and metastatic lung cancer. We have assembled a multidisciplinary network of cutting-edge researchers to solve the biology of lung cancer. We will undertake a comprehensive search of older literature looking for key aspects of the pathogenesis for cancer in the lung, bioinformatics analysis on existing mRNA biobank datasets, and use this information together with current biomarkers to search for and identify potential cell biological pathways that relate to the known cancer pathogenesis in lung. Students who undertake honours in this area can expect to become skilled in bioinformatics, cell biology, imaging and immunochemistry.

3) The Synthesis of Novel Drugs to Target a Global Issue: Bacterial and Parasitic Resistance

Dr Shane Hickey (UniSA), Dr Trent Ashton (Walter and Eliza Institute of Medical Research), Dr Sally Plush (UniSA) and Professor Doug Brooks (UniSA)

Antibacterial resistance is now a critical worldwide concern. A decline in the number of pharmaceutical companies pursuing new therapeutics, in combination with the continued misuse of antibiotics has only served to exacerbate the problem. Guanidine containing thiazole compounds have recently been identified as potent antibiotics towards both Vancomycin resistant (VRSE) and methicillin resistant (MRE) strains of bacteria. This project will focus on the synthesis of guanidine thiazoles bearing benzyl substituents. These analogues are readily synthesised in two steps from a common starting material and will allow for the rapid development of detailed structure activity relationships. In addition, this compound class has recently been shown to exhibit sub-micromolar growth inhibition of *Plasmodium falciparum*, a causative parasite of malaria. *Plasmodium* parasites cause over two hundred million infections and over 438,000 deaths annually, with high mortality rates amongst infected children, and when coupled with the worrying increase in the number of instances reported of resistance to currently used pharmaceuticals, there is an obvious need for the development of new treatment options.



Students who choose to undertake this medicinal chemistry Honours project will develop compounds potentially capable of dual potency against bacterial and parasitic pathogens. The student can expect to become proficient in key skills related to synthetic organic chemistry and analytical chemistry (NMR, mass spectrometry, HPLC etc.) as well as developing an understanding of microbiology techniques and the interpretation of data from biological assays.

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<http://www.unisa.edu.au/Research/Sansoni-Institute-for-Health-Research/Research/Mechanisms-in-Cell-Biology-and-Diseases-Research-Group/>

Molecular and Evolutionary Physiology of the Lung Laboratory

The laboratory's key aim is to understand the evolution, molecular function and regulation of the pulmonary surfactant system, a complex mixture of lipids and proteins that forms a film at the air-liquid interface of the lung. Here it performs critical functions enabling the lung to inflate and deflate and in protecting the lung from foreign organisms and particles.

Currently available projects:

Honours projects are currently available as part of two newly established collaborative research programs primarily with the Mechanisms in Cell Biology & Disease Research Group as well as other investigators. The first investigates the pulmonary pathology in lysosomal storage diseases (LSD) and the second investigates the role of the lung microbiome in lung cancer.

A. Lung pathology in lysosomal storage disorders

Lysosomal storage diseases (LSD) are a group of more than 70 devastating genetic diseases. They occur because of a defective enzyme that leads to accumulation of waste products within lysosomes which are responsible for cellular waste disposal. This accumulated waste disrupts the function of cells leading to a wide variety of symptoms across different diseases and different individuals, including significant respiratory pathology. How exactly the increased storage leads to different disease manifestations is currently not understood. Specifically we aim to identify the causes and mechanisms of respiratory dysfunction and the role of the pulmonary surfactant system in LSD. We hypothesise that the accumulation of storage material in endosome-lysosome organelles disrupts the intracellular architecture and function of alveolar epithelial cells. This impacts the formation of lamellar bodies responsible for producing pulmonary surfactant which is critical for breathing and fighting respiratory infections.

Specifically, as a model of lysosomal storage disorders we have been using the mucopolysaccharidosis (MPS) IIIA mouse. MPS IIIA or Sanfillipo Syndrome is the most common of the MPS Type III LSDs, which results from a deficiency in the activity of the lysosomal hydrolase, sulphamidase. This results in the primary storage of heparan sulphate and the subsequent secondary storage of the GM2 and GM3 gangliosides and cholesterol. In the lung we have shown the accumulation of lipid droplets, the appearance of abnormal lamellar bodies, altered lung structure with increased collagen deposition in lung parenchyma, changes in surfactant lipid amounts and protein composition and a reduced ability to reduce surface tension. These alterations have the potential to lead to early subclinical changes in lung function. Such subtle changes in respiratory function may go undiagnosed and untreated because of other more obvious conditions. Hence, it is possible that the accumulating storage leads to gradual progressive interstitial lung disease, explaining the increased incidence with age of respiratory obstruction and infection. We are continuing to investigate the mechanisms in this and other models. Specific projects include:

1. *Altered secretory vesicle biogenesis and secretion underpins lung pathology in lysosomal storage disorders*

Prof. Sandra Orgeig & Dr Emma Parkinson-Lawrence & Prof. Doug Brooks (UniSA), Dr David Ketteridge (Women's & Children's Hospital)

The biogenesis and secretion of pulmonary surfactant in alveolar epithelial cells involves the endosome trafficking and exocytosis pathways which are fundamental cellular processes in all cells. The biogenesis of secretory vesicles involves the exchange of lipids and protein machinery to form mature fusion-competent vesicles, and this controls the functionality of the secretory pathway. Abnormal vesicle maturation will impact on secretory systems and this may be the molecular basis of the high incidence of respiratory pathologies in lysosomal storage diseases. We hypothesise that the biogenesis of lamellar bodies in alveolar type II cells is disrupted by heparan sulfate storage and secondary lipid accumulation, which then impacts on surfactant release. This project will determine the composition and distribution of

membrane lipid in intracellular vesicle populations using novel metal-based probes and live cell imaging as well as mass spectrometry. In addition, it will characterise alterations in the population (size and subtypes) of the different vesicles associated with the secretion of pulmonary surfactant using immune fluorescence of known protein markers with confocal microscopy.

2. *Inflammation and Collagen Changes in the Lung of Mucopolysaccharidosis (MPS) IIIA Mice*

Prof. Sandra Orgeig & Dr Emma Parkinson-Lawrence (UniSA)

As pulmonary surfactant also has a major function as part of the innate immune system of the lung, an impairment of its cellular processing through the accumulation of storage material in alveolar epithelial cells, may also affect innate pulmonary immunity. In addition, we have observed altered lung structure with increased collagen deposition in lung parenchyma. Recently, skeletal abnormalities in MPS have been associated with alterations in collagen in response to inflammation in bone. This project seeks to examine whether inflammatory changes occur in the lung of MPS IIIA mice, which may account for the observed lung pathology. The project would involve further characterising lung structure alterations as well as measuring the gene and protein expression of inflammatory cytokines in isolated lung tissue from control and MPS IIIA mice by real-time quantitative PCR, Western analysis and immunohistochemistry.

3. *Lung pathology in the lysosomal storage disorders, Mucopolysaccharidosis I and VII*

Prof. Sandra Orgeig & Dr Emma Parkinson-Lawrence (UniSA), Dr Sharon Byers & Dr Ainslie Derrick Roberts (SA Pathology)

In order to determine whether impairment in surfactant biogenesis and secretion represents a common molecular mechanism leading to interstitial lung disease in lysosomal storage diseases, we will also characterise the lung structure, surfactant composition and biogenesis and secretory pathways in the lungs of MPS I and VII mice, through collaborations with colleagues at SA Pathology.

B. The role of the lung microbiome in lung cancer

Prof. Sandra Orgeig, Dr Emma Parkinson-Lawrence, Prof. Paul Reynolds, Dr Andrea Stringer & Prof. Doug Brooks

Lung cancer is the biggest killer among cancers, both in Australia and globally, but there is a significant stigma attached, because of the increased risk from smoking. Consequently there are low rates of research funding for lung cancer (< 5c of every cancer research \$). Significantly, the 5-year survival rate for lung cancer patients has hardly changed between 1984–88 & 2009–13, despite a reduction in smoking. The concomitant increase in the proportion of lung cancers among non-smokers suggests an underlying carcinogenic mechanism that may be triggered by other external environmental factors in addition to smoking.

Recent evidence suggests that the lung microbiome is altered in lung cancer patients. This may be critical for the establishment of a local microenvironment that leads to cancer onset and progression. We hypothesise that an altered lung microbiome plays a critical role in lung cancer. Furthermore, smoking may impact on this lung microbiome, and predispose a person to cancer development. It is well established that a disturbed gut microbiome drives intestinal inflammation and is implicated in initiation and progression of colorectal cancer. Moreover, a mechanistic link has been identified between the gut microflora and the lung innate immune defense system, which may be a key to the initiation of lung cancer. Hence, there is a very compelling rationale to investigate the role of the lung microbiome in lung cancer development. In this project we intend to investigate the molecular cross-talk between the microbiome and the blood-air barrier of the lung which may be the impetus for the discovery of new biomarkers and therapeutic targets. We aim to:

1. characterize the lung microbiome and its secretome of patient lung cancer samples using genomic/proteomic analyses
2. identify, using a systems biology approach, the altered key biological pathways and molecules implicated in cancer development (e.g. in pulmonary innate immunity, reactive oxygen species (ROS) biology and inflammation) with bioinformatics on existing human mRNA biobank datasets of lung cancer
3. confirm altered protein expression of key molecules identified with bioinformatics via proteomic and histological analysis of patient samples

Professor Sandra Orgeig (Professor in Pulmonary Biology)

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Professor Orgeig is a research leader in pulmonary biology, with >20 years' experience working on pulmonary surfactant, which is a crucial, evolutionarily conserved lipo-protein system that enables the first breath and ensures effective lung function throughout life. Her multidisciplinary research has used evolutionary, physiological and biomedical approaches, coupled with molecular, cellular, biophysical and biochemical technologies. Different members of her group are currently investigating the evolution of a group of surfactant and lung associated proteins in birds or alterations in lung and surfactant function/regulation in different animal models of disease, with a focus on fetal and pediatric disorders.

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Musculoskeletal Biology Research Laboratory

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The Musculoskeletal Biology Research Laboratory at the School of Pharmacy and Medical Sciences and runs a pre-clinical musculoskeletal Bio-Test facility providing research for the government and private-sector. Research at MBRL covers a broad area of interest with an overarching theme to develop strategies for preventing and treating bone diseases, fractures and related pathologies. Research questions are tested with a number of different models ranging from cells to humans and cover a wide range of state-of-the-art techniques.

Research Strengths:

Antimicrobial
implants for
Orthopaedic
Devices

Genetic
Disorders of
Bone Diseases

Drug Discovery
for Bone
Disorders

Cancer,
Chemotherapy,
Intestine &
Bone Health

Vitamin D,
Calcium in
Osteoporosis &
Osteoarthritis

Co-investigators:

Dr Andrea Stringer, UniSA - Cancer, Chemotherapy, Intestinal Function and Bone Health

Dr Alex Shoubridge, UniSA - Novel Antimicrobial Implants for Orthopaedic Devices

Prof Howard Morris, SA Pathology - Vitamin D, Calcium, Osteoporosis and Osteoarthritis

Prof Zhao-Peng Liu, Shandong University, China - Drug Discovery for treating Bone & Mineral Disorders

Prof Rene St-Annaud, McGill University Canada - Rare Genetic Disorders of Bone and Mineral Diseases

Novel Antimicrobial Implants for Orthopaedic Devices:

Post-operative infection from orthopaedic surgery is the major cause of prosthetic failure and morbidity. Modifying titanium surface topography to mimic the dragon-fly wing micro-structure on orthopaedic implants may be an elegant solution to create an anti-microbial surface which resists infection. Research in this area using MBRL BioTest Facility includes working with industry to perform *in vivo* osteo-integration and antibacterial safety and efficacy studies.

Rare Genetic Disorders of Bone and Mineral Diseases:

Rare genetic disorders such as X-linked Hypophosphatemia (XLH), are not fully understood and frequently do not have effective and safe treatment options. This research will aim to expand on the molecular understanding of the disease by identifying the role of target genes, such as CYP24A1, which are potential therapeutic targets to heal the bone disorder that occurs in XLH.

Drug Discovery for treating Bone and Mineral Disorders

Numerous bone and mineral disorders are associated with a lack of vitamin D activity. In many cases, such as in Chronic Kidney Disease, the only option to treat bone disorders is to bypass the usual renal vitamin D metabolism. Research in this area identifies and tests novel vitamin D analogues and competitive inhibitors of vitamin D catabolism as a safe and effective strategy for treating bone.

Cancer, Chemotherapy, Intestinal Function and Bone Health

Chemotherapy-induced mucositis is a severe toxicity associated with chemotherapy use, and affects whether patients can receive the full amount of prescribed cancer treatment. Patient quality of life, both during and after chemotherapy, is also significantly impacted by mucositis. This study will investigate whether intestinal damage associated with chemotherapy (mucositis) can be prevented or reduced by blocking the enzyme that breaks down active vitamin D and whether these treatments also improve bone health.

Vitamin D, Calcium and the Pathogenesis of Osteoporosis and Osteoarthritis

Our research vision is to contribute towards an age-friendly world by improving quality of life and enabling people to stay healthy, active and independent even at the oldest age. Osteoporosis (OP) and its consequences such as hip fractures are the leading cause of immobility in older people. Osteoarthritis (OA) is a degenerative joint disease that involves thinning or destruction of the smooth cartilage that covers the ends of bones, and produces pain, stiffness and reduced movement of the affected joints. Research in this area involves working with animals or humans to provide evidence-based approaches to adequate vitamin D and calcium nutrition to reduce the burden of these diseases. Other research includes working with novel therapeutic agents to use in conjunction with vitamin D and calcium to promote bone healing.

Neurophysiology and Human Movement Laboratory

Dr Gabrielle Todd (Senior Lecturer)

<http://people.unisa.edu.au/Gabrielle.Todd>

The control of voluntary movement engages much of the human brain. Goal-directed movements require awareness of where the body is in relation to where it intends to go, and selection of the appropriate plan to get there. Once a plan has been selected, it must be held in memory and then implemented at the appropriate time. Researchers in the Neurophysiology and Human Movement Laboratory study the structure and function of movement-related brain regions in healthy adults and in patients with movement disorders such as Parkinson's disease. The research involves studying the nervous system while people are moving, and while we quantify how they performed the movement. Researchers in the group are also interested in the neural mechanisms that underlie exercise-induced fatigue.

Current Projects

Long-term effects of illicit drug use on movement

Use of illicit drugs such as cannabis, ecstasy, and methamphetamine (or 'ice') is a huge problem in Australia. Current data suggests that over 6.6 million Australians have used cannabis and 1.3 million have used methamphetamine, a worrying number given that the total population of Australia is 24 million. Our research group has shown that use of these drugs is associated with long-lasting changes in movement and the brain regions that control movement. For example, young adults with a history of methamphetamine use have abnormal movements that resemble Parkinson's disease and changes in the neural pathway that transmits movement commands from the brain to the muscles. The aim of the current project is to further explore the long-lasting effects of illicit drugs on brain regions that control movement and motor function, and to determine how common these abnormalities occur. The results of the project will be used to make a new health message that will increase community knowledge of the long-lasting consequences of illicit drug use.

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Our group's research focuses on the three main areas

1. Neurological disorders such Alzheimer's disease, Parkinson's disease, depression, stroke and traumatic brain injury
2. Neurotrophins and their receptors as novel drug targets for treatment of neurological/metabolic/microvascular diseases
3. Cell therapy for treatment of diabetes, liver failure and Parkinson's disease

We use a variety of techniques including biochemical, immunological, molecular and histological approaches in our research projects.

Honours projects available

Project 1: Roles of p75 in the pathogenesis of ischemic stroke? A model of p75 KO.

P75 (neurotrophin receptor) and its ligands are upregulated in neurons and glia of the brain after ischemic stroke. Mature neurotrophins are known to promote regeneration and recovery after stroke. In this project, we hypothesize that the p75 signalling pathway is critical for the pathogenesis and development of neural damage and paralysis after stroke. The ischemic stroke will be induced in wild type and p75 knockout (KO) mice. Behavioral tests, pathological and biochemical examinations will be used to find the difference between wild type and p75 KO mice.

Project 2: Roles of p75 signalling pathway in the pathological and functional outcome after traumatic brain injury

P75 and its ligands are upregulated after traumatic brain injury. P75 and its neurodegenerative ligands are well known for their detrimental roles in the induction of apoptosis of neurons and oligodendrocytes, which leads to neurodegeneration, demyelination and permanent functional disability. In this project, we

hypothesize that blocking the p75 signalling pathway by genetic knockout or by pharmacological tools will ameliorate the damage of the brain and improve functional recovery after injury. The aim of the project is to 1) examine whether the p75 KO can reduce the pathology and increase functional recovery; 2) to test whether p75 antagonists are effective in the treatment of the rat/mice with traumatic injury.

Project 3: Pro-BDNF and its receptors as biomarkers and therapeutic targets for major depression

Depression is a leading cause of disability; however the current treatment options are limited. Furthermore, there are no reliable, objective biological markers for major depression. In this research we aim to investigate the role of the precursor protein of the brain derived neurotrophic factor (pro-BDNF) and its receptors, p75 protein and sortilin in depression. Two projects are available; 1) the first project will involve developing animal models of depression in mice and investigation of the effects of blocking the proBDNF-p75/sortilin signalling pathways by genetic knockout or by pharmacological tools on behavioural, pathological and biochemical outcomes. 2) the second project will involve developing animal models of depression in rats and investigation of the proBDNF-p75/sortilin signalling pathways in the brain and in the blood.

Project 4: Treatment of liver failure with human-urine derived induced hepatocyte-like cells (

Liver failure is a fatal disease if without liver transplantation. Progression in stem cell technology allows to generate human hepatocytes differentiated from embryonic stem cells or induced pluripotent stem cells. We have developed a protocol to generate human hepatocyte-like cells from human urine cells using small molecules (iUHC), which have potential for the treatment of human liver failure. In this project, we hypothesize that human iUHC can integrate to mice liver and can replace the function of mouse liver in an intoxication model. The student will generate hepatocyte cells from urine in the laboratory, characterize the cells and develop a model of liver failure for transplanting the cells to treat the liver failure.

Project 5: A role of p75 and its toxic ligands in the type II diabetes, energy metabolism and insulin resistance

p75 is expressed in white fat cells and plays a critical role in the obesity, insulin resistance and energy metabolism. P75 regulates glucose metabolism by interacting with PKA subunits. However, what ligands trigger p75-mediated obesity and insulin resistance is not known. We hypothesize that the blocking p75 signalling pathway in p75 KO mice or with its antagonists can block high fat diet induced obesity and insulin resistance. The aim of this study is to examine the role of p75ECD on obesity and prevent type II diabetes in obese mice in p75 wt and KO mice.

Project 6: Roles of p75 and its degenerative ligands in the development of diabetic microvascular complications

High glucose and hypoxia are strong stimulants for the expression of p75 in microvascular system. Diabetes can cause a number of complications due to the apoptosis of endothelial cells and pericytes, leading to a number of complications such as retinopathy, nephropathy, limbic ischemia, peripheral neuropathy, and erectile dysfunctions etc. It is hypothesized that these microvasculopathies are due to the over-expression of p75 and their degenerative ligands which causes dysfunction of angiogenesis. Here we propose that blocking p75 signal pathway in the diabetic mice is effective to alleviate the complications of diabetes. P75KO mice and p75 signalling antagonists will be used to test the hypothesis.

Project 7: roles of p75 and noxious ligands on the innate and adaptive immune responses- model of rheumatoid arthritis or model of multiple sclerosis (in collaboration with Plinio Hurtado)

P75 and its ligands are expressed in immune cells including macrophages, T and B lymphocytes in response to toll-like receptor ligands such as LPS, and CpG. P75 and its ligands proBDNF and other ligands are also upregulated in macrophages and lymphocytes after applying formaldehyde to footpad and are involved in pain. In this project, we hypothesise that p75 and its ligands are upregulated and are involved in the pathogenesis of rheumatoid arthritis and inflammation. Blocking p75 signalling pathway can ameliorate pain and damage to cartilage and bone after immune-induced arthritis. The aim of the study is 1) to build a rheumatoid arthritis (RA) model in mice and rats; 2) to examine the activation of B cells and T cells for their gene expression of p75, trks and neurotrophins by RT-PCR and flow cytometry analysis; 3) to examine whether blocking the p75 signalling pathway can ameliorate the pathology and pain in RA.

Project 8: TBI and addiction (Frances Corrigan)

Traumatic brain injury (TBI), particularly the mildest form concussions are common in adolescence. Of note evidence suggests that adolescents may take longer to recover from concussive insults and may have long lasting changes due to interruption of key maturation processes. In particular maturation of the pre-frontal cortex and related circuits continues into young adulthood, with this region important for judgement, planning and impulse control. Failure of this process may explain the proposed link between a history of concussion in adolescence and increased problematic alcohol consumption in later life. This study will investigate the link between concussive insults during adolescence on later alcohol drinking patterns, the rewarding properties of alcohol and vulnerability to relapse following withdrawal. This will utilise our mouse model of traumatic brain injury and standardised alcohol drinking paradigms including the use of operant boxes

Project 9: Effect of concussion in adolescence on pre-frontal cortex development (Frances Corrigan)

Traumatic brain injury (TBI), particularly the mildest form concussions are common in adolescence. Of note evidence suggests that adolescents may take longer to recover from concussive insults and may have long lasting changes due to interruption of key maturation processes. In particular maturation of the pre-frontal cortex and related circuits continues into young adulthood, with this region important for judgement, planning and impulse control. This study will utilise previously generated tissue to investigate changes in the pre-frontal cortex dopaminergic circuitry via investigating changes in levels of dopamine and its receptors via immunohistochemistry, western blot and RT-PCR. There is also an opportunity to assist in imaging analysis utilising MRI techniques including rs-fMRI and DTI

Project 10: Can the proBDNF/p75 signal pathway be targeted for the brain cancer therapy?

Brain cancer is one of the most devastating cancers with a short life span without effective treatment. Neuroblastoma and glioblastoma are two common forms of brain cancers. In our previous studies, we showed that proBDNF and p75 are highly expressed in glioblastoma in human. However, whether proBDNF and p75 play any roles in the proliferation and migration of glioblastoma is not known. In this project, the student will culture glioblastoma cells and examine the expression of p75 by Western blotting, and examine their growth and migration under the influence of proBDNF, BDNF and antibodies to the p75 extracellular domain. The data will have implication in the use of anti-p75 as an immunotherapy approach to suppress the proliferation and migration cancer cells in the brain.

Population Health Chemistry

Dr Cobus Gerber

<http://people.unisa.edu.au/cobus.gerber>

Substance abuse is linked to mental health, antisocial behaviour, risk taking, crime, etc. The burden on health is estimated to be several billions of dollars. Our focus as a research group is to determine the scale of drug use through wastewater analysis. Wastewater can be considered a pooled urine sample. Since compounds with abuse potential are taken by an individual, metabolised and excreted into the sewer system, wastewater can be considered a reliable resource to find evidence of drug use. The study approach has become known as Wastewater-Based Epidemiology (WBE). Our group has developed methods to isolate trace amounts of drug residues or their metabolites in wastewater. These range from illicit drugs to alcohol, tobacco and pharmaceuticals with abuse potential. Updated methods are constantly required as new substances appear internationally. Our longitudinal studies reveal spatial in temporal changes in drug use across Australia and form the basis for frequent reports for government agencies which informs policy and interventions. Dr Cobus Gerber and Prof Jason White work with a team of researchers and post-graduate students to expand the application of wastewater analysis and determine new ways to approach problems. The analytical methods are based on extraction techniques, chromatography and mass-specific detection. The expertise required in our field can be diverse, relating to analytical chemistry, drug metabolism (pharmacokinetics), pharmacology and statistics, to name a few. Much of our research include aspects of these different fields and students from different study areas are welcome to discuss potential projects.

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Quality Use of Medicines and Pharmacy Research Centre (QUMPRC)

Research at the QUMPRC is aimed at improving the way we all use medicines.

Medicines use is increasingly rapidly and impacts on the health care system and on individual consumers' quality of life. Problems with medicines use can cost millions of dollars and adversely affect millions of lives in Australia every year.

Our researchers come from a variety of backgrounds including pharmacy, psychology, health informatics, statistics, general practice, nursing, chemistry, and computer science.

At the QUMPRC we look to address the challenges of medicines safety and use by:

- Developing novel methods to enable early detection of adverse events associated with medicines and medical devices.
- Investigating innovative ways of using pharmaceutical and medical data to improve patient safety
- Pioneering better ways to work with consumers and industry partners to provide solutions to medicines issues.
- Working across the healthcare spectrum with expertise ranging from pharmacy and medicines safety to statistics, mathematical modelling, database management, health informatics, indigenous medicines, chemistry and health promotion.

- Collaborating internationally to achieve greater understanding and impact.
- Translating research into real world resources to help doctors, pharmacists and consumers better manage health care.

Research staff available to supervise Honours Students

<u>Prof Libby Roughead</u>	Pharmacoepidemiology Post market surveillance of medicines Medicines policy Health care program evaluation
<u>Dr Nicole Pratt</u>	Pharmacoepidemiology Statistical methods
<u>Dr Andre Andrade</u>	Digital health
<u>Dr Svetla Gadzhanova</u>	Pharmacoepidemiology Data mining Evaluation of change management in primary health care
<u>Dr Lisa Kalisch Ellett</u>	Medicines that cause or worsen dementia and cognitive impairment Quality use of medicines Post market surveillance of medicines Pharmacoepidemiology
<u>Dr Renly Lim</u>	Quality use of medicines Medicines utilisation
<u>Dr Anna Moffat</u>	Medicines and Autism Spectrum Disorder Pharmacoepidemiology
<u>Dr Tuan Nguyen</u>	Medicine associated dementia Access to medicines Quality use of Medicines
<u>Dr Susan Semple</u>	Australian Medicinal Plants Antimicrobials Complementary and Alternative Medicines

Current projects available:

1) *Complexity and number of changes in medicines post admission in aged-care facilities.*

Supervisors: Svetla Gadzhanova, Libby Roughead

Predictors of admission to residential care are health-related and majority of people have multiple medical comorbidities. However, residents with multiple medications have a higher risk of hospitalisation due to adverse drug events. The project will examine drug regimens on and post admission to 60 residential aged-care facilities using de-identified data containing a complete record of all medicines supplied in dose administration aids for each resident.

2) *Risk management plans for newly marketed medicines*

Supervisors: Nicole Pratt, Emmae Ramsay

This project will involve a review of recently marketed medicines and quantify their uptake onto the market. A review of each of these new medicines will identify any safety concerns requiring a specific Risk Management Plan. The project will involve a medicine utilization study using a time series analysis approach to model the uptake of the medicine and a review of TGA communication will identify which medicines were approved subject to an RMP. The RMPs will be reviewed to determine the nature of the safety concern.

3) *Product Information and the influence on prescribing*

Supervisors: Nicole Pratt, Emmae Ramsay, Lisa Kalisch

This project will involve a review of product information documents for a class of medicines Novel Oral Anti-coagulants. The project will identify differences in details provided in each of the product information documents and how these may have influenced prescribing. Data on the characteristics of newly initiated patients on the medicines will be compared to the indications and contraindications and safety concerns highlighted in product information.

4) *Development of a medicine complexity index using administrative health claims data*

Supervisors: Anna Moffat and Lisa Kalisch Ellett

A number of factors related to a patient's medication regimen have been shown to influence outcomes. Dosage frequency, number of medications and administration requirements all contribute to the complexity of the regimen. This project will explore whether it is possible to use administrative claims data to create a medicine complexity index.

5) *Can Pharmaceutical Benefits Scheme (PBS) data be used to assess chemotherapy dosing?*

Supervisors: Libby Roughead, Nicole Pratt

Following on from under-dosing problems with chemotherapy in both NSW and SA, this project would assess whether it was possible to create a measure of dose intensity standardised to doctor. Variability across doctors would be assessed.

6) *Medicines and frailty*

Supervisors: Renly Lim, Libby Roughead, Lisa Kalisch Ellett, Nicole Pratt,

This research project would examine the association between medicine use and indicators of frailty. The association between individual medicine use and grip strength, activities of daily living, self-rated exhaustion, walking time/8 feet, physical activity and cognitive impairment will be assessed. The study will use data collected as part of the Australian Longitudinal Study of Ageing.

7) *Confidence in medication use following Home Medicines Review interventions*

Supervisor: Anna Moffat

Home Medicines Reviews (HMR) and Residential Medication Management Reviews (RMMR) services provided via a collaboration between general practitioners (GPs) and accredited pharmacists in Australia. Over more than a decade, the Veterans' MATES Program has conducted a number of interventions that aim to educate and promote the use of HMRs and RMMRs to pharmacists, GPs and Australian veterans. This project will look at whether confidence and understanding around personal medication regimens are increased following these interventions. Whether being targeted in multiple interventions has a cumulative effect will also be examined.

8) *General practitioner feedback following targeted health interventions*

Supervisor: Anna Moffat

The Veterans' MATES Program delivers health interventions on a variety of topics related to Veteran health in Australia. This project will use data collected as part of the program to assess the intended actions from general practitioners who are targeted in the interventions.

9) *An overview of systematic reviews of medicines with anticholinergic or sedative properties inducing cognitive impairment*

Supervisors: Tuan Nguyen, Thu Ha Dang, Libby Roughead

This research project will consider systematic reviews and meta-analyses of randomised controlled trials in healthy adults (≥ 18 years old) evaluating the effect of any medicines with anticholinergic or sedative properties on inducing cognitive impairment. The student will be trained in conducting systematic reviews and meta-analyses and will be involved in study screening, data extraction and meta-analyses.

10) *An overview of systematic reviews of medicines with anticholinergic or sedative properties worsening cognitive impairment*

Supervisors: Tuan Nguyen, Thu Ha Dang, Libby Roughead

This research project will consider systematic reviews and meta-analyses of randomised controlled trials evaluating the impact of any medicines with anticholinergic or sedative properties on worsening cognitive impairment in otherwise healthy adults (≥ 18 years old). The student will be trained in conducting systematic reviews and meta-analyses and will be involved in study screening, data extraction and meta-analyses.

11) *Using wearable accelerometer data as a proxy for physical and cognitive impairment*

Supervisor: Andre Andrade

Wearable devices present us with the possibility of using passively collected data to improve diagnostic and optimizing therapy. However, to date, the number of clinical applications is mostly focused on young and fit individuals, while the potential to improve our understanding of the elderly population remains untapped.

This research project will use data from the Remindar trial to look for association between frailty measures and wearable data. The goal is to search for patterns that can objectively measure both physical and cognitive impairment from passively collected data, such as activity (steps, energy expenditure) and sleep patterns.

12) *Identifying reasons for non-adherence of clinical guidelines for mental conditions*

Supervisors: Andre Andrade, Anna Moffat

Clinical guidelines are an important tool to optimize patient management. Guidelines are usually the result of huge efforts in analysing current evidence and consensus building, and highlight the clinical conditions when a patient is most likely to benefit from particular medicines, and when these medicines should not be used. However, adherence to guidelines vary, leading to inconsistent and, sometimes, inadequate care.

This project aims to identify and quantify the reasons for non-adherence of clinical medication guidelines for established mental conditions (cognitive and mood impairment). To do this, we'll use a Discrete Choice

Experiment (DCE), a carefully designed survey capable of quantifying the most important variables that lead to a decision.

These projects are suitable for students with an interest in:

- Medicine utilization and data analysis
- Population health
- Regulatory pharmacoepidemiology
- Quality use of medicines

For more information on the Quality Use of Medicines and Pharmacy Research Centre (QUMPRC):

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Regenerative Medicine Laboratory

Professor Allison Cowin

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The Regenerative Medicine Laboratory is part of the Future Industries Institute (FII). FII focuses on building knowledge and capacity in core future industries and develops the University's internationally competitive research capacity across four key strands: Minerals and resources engineering, Energy and advanced manufacturing, Environmental science and engineering, and Biomaterials engineering and nanomedicine. FII supports a range of scholarships for students wishing to undertake Masters or PhD studies within the FII.

Professor Allison Cowin has several main interests that seek to improve the way that wounds heal. Wounds most often affect our most vulnerable populations, the elderly, the obese, people with diabetes, children with burns and children with fragile skin. Wounds include chronic non-healing venous leg ulcers, arterial ulcers, diabetic wounds, pressure injuries, skin tears, and burns leading to hypertrophic scars. Our research is primarily focused on understanding the mechanisms involved in wound healing and developing new approaches and technologies to make wounds heal better.

Honours projects available

Project 1: New approaches for the treatment of wound infections

Prof Allison Cowin and Dr Zlatko Kopecki (FII, UniSA)

Project overview: Wound healing and burn injury are serious medical problems affecting thousands of Australians. Infection is a serious compounding problem affecting the healing of skin. Being able to fight off infections before they take hold would be a major step forward in the treatment of bacterial wound infections. This project aims to understand the contribution of actin remodelling proteins in the regulation of the innate immune responses during wound infection. The project will utilize human samples and a newly developed murine model of wound infection to assess the effect of altered levels of cytoskeletal proteins on wound infection and innate signalling responses including toll-like receptor mediated inflammation and inflammasome activation.

Project 2: Role of inflammation in diabetic wound healing

Prof Allison Cowin and Dr Stuart Mills (FII, UniSA)

Project overview: The prevalence of diabetes is exploding with 21 million diabetic and 54 million pre-diabetic patients worldwide. Approximately 15% of diabetics develop non-healing ulcers and complications lead to one major amputation every 30 seconds. While wound healing is an efficient process, progressing through established phases of inflammation, proliferation and remodelling in patients with a chronic wound this does not happen. The wound becomes stuck in the inflammatory phase and high levels of inflammation contribute to chronic non-healing wounds. This project aims to investigate how the inflammatory process is regulated in response to wounding in diabetic wounds. Monocytes and macrophages are key players in the development, persistence and resolution of inflammation. Their differentiation 1) from monocytes to M1 macrophages and then 2) their polarisation from pro-inflammatory M1 macrophage to anti-inflammatory M2 macrophage like states provides them with distinct physiological wound functions. Using genetic mouse models in conjunction with in vivo and in vitro assays, studies will be performed to investigate the role of Flightless I, a protein involved in the regulation wound healing and inflammation, has on diabetic wound healing.

In these and other available projects, students will develop skills in animal models, cell culture, microscopy, immunohistochemistry, western blotting and number of different in-vitro wound healing assays. The student will work as part of a large team of post-doctoral scientists, research assistants and PhD students and will be well supported to complete all tasks successfully. Opportunities exist for the projects to be continued and developed into PhD studies.

For more information on the Regenerative Medicine Laboratory

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Therapeutics and Pharmaceutical Science Research Group (TPSRG)

The TPSRG is an active research unit seeking to improve patient outcomes and quality of life through the appropriate and timely clinical implementation of therapeutics derived from pharmaceutical sciences and medicine. The Group's research interests cover a spectrum of therapeutics from the chemistry of drugs (including modelling, drug design and natural products), the effects drugs have on the body (pharmacology and toxicology) and the effects the body has on drugs (pharmacokinetics and drug delivery), through to how drugs can be best used to treat diseases (topical drug delivery and the quality use of medicine) for patients.

Therapeutics Research Centre (TRC)

<http://people.unisa.edu.au/Michael.Roberts>

Professor Michael Roberts (Centre Director) has several main research interests that seek to improve patient outcomes and quality of life through the appropriate and timely clinical implementation of therapeutics derived from pharmaceutical sciences and medicine. The Group's research interests cover a spectrum of therapeutics from the chemistry of drugs (including modelling, drug design and natural products), the effects drugs have on the body (pharmacology and toxicology) and the effects the body has on drugs (pharmacokinetics and drug delivery), through to how drugs can be best used to treat diseases (topical drug delivery and the quality use of medicine) for patients. Under the daily supervision of postdoctoral researchers, Dr Mackenzie, Dr Holmes, Dr Alinaghi and Dr Abdalla we offer Honours projects tailored to suit the interests of the individual student that can be patient based, product development based, animal and human toxicology or chemical analysis based. Examples of project involvement for 2017 include but are not limited to:

- Clinical and Regulatory Toxicology: assessing safety of medicines, consumer products, pesticides and herbicides and managing poisonings associated with exposure to them.
- Medicine efficiency and safety: exploring how well medicines work and if products are safe.

- Skin penetration studies to improve therapeutics delivery.
- Development of minimally invasive sampling techniques *in vivo*.
- Nanomedicines: exploring the therapeutic potential and safety for nanomedicines.
- Development of a high throughput dermatotoxicology screening platform using microscopy.
- Liver function assessment of patients using new and novel imaging techniques prior to resection in order to predict surgical outcomes.
- Burn wound repair and infection (ex vivo) using novel nanoparticles.
- Treatment of chronic leg ulcers in patients using novel therapeutics.
- Development of non-invasive techniques to detect therapeutic levels in critically ill patients.

More information on TRC:

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Dr Amy Holmes (Post-doctoral researcher in forensic toxicology)

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Which barriers work to prevent dermal exposure of pesticides?

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

Honours scholarships available

Previous Honours students studying with Dr Amy Holmes have been successful in securing a scholarships and travel grants from a range of sources, some of which are specific to the project. Scholarship sources include NHMRC Translational Australian Clinical Toxicology network, The Hospital Research Foundation and Medical Advances without Animals Trust.

Dr Timothy Barnes (Senior Lecturer, Pharmaceutics/Pharmaceutical Science)

<http://people.unisa.edu.au/Tim.Barnes>

Dr Barnes' research is focused on the development of novel drug delivery systems for the delivery of peptide/protein therapeutics and poorly soluble drugs, such as: emulsions, liposomes, mesoporous materials (e.g. porous silicon), dendrimers and nanoparticles. This work involves laboratory work to prepare the formulations which are then characterised using a range of advanced physicochemical techniques. In collaboration with other internal and external (e.g. hospital) researchers we also test the optimised formulation using animal models.

Current projects available:

1) Using bacteriophages to control bacterial infections: A formulation challenge

Collaborators: Dr James Munro (Adelaide Uni), Prof Mary Barton, Prof Clive Prestidge

Bacteriophages are virus' that specifically target bacteria, offering an alternative approach for bacterial control that does not rely on small molecule antibiotics. This project numerous potential applications, ranging from animal to human health, however, the challenge is how to deliver the phages to the host. This project involves formulating the bacteriophages into lipid-based delivery systems, the physicochemical characterization of the system as well as testing the phage viability after processing.

2) Multiple emulsions for vaccine delivery

Collaborators: Prof Clive Prestidge, Prof Sarah Hook (U Otago, NZ)

This project involves the development of novel multiple emulsions for the delivery of peptide/protein therapeutics used in vaccines.

3) Use of liquid crystal lipid for the delivery of poorly soluble drugs

Collaborators: Prof Clive Prestidge, Achal Bhatt (PhD student), Prof Ben Boyd (Monash Uni)

This project involves the development of silica nanoparticle stabilised liquid crystal lipid hybrids for the delivery of poorly soluble drugs.

These projects are suitable for a student with:

- An interest in pharmaceutical science
- Laboratory based practical work

Dr Kristen Bremmell (Senior Lecturer, Pharmaceutical Science)

<http://people.unisa.edu.au/Kristen.Bremmell>

Dr Kristen Bremmell undertakes research in the areas of formulation science, drug delivery and bio-pharmaceutical purification. General interests include novel, controlled release formulations of drugs, and protein aggregation and adsorption on surfaces which is important in areas such as biomaterials design and pharmaceutical delivery. An example of a current research project follows;

Silica-lipid hybrid microparticles for protein delivery

Biotechnology drugs such as proteins and peptides require careful formulation due to stability problems, and are mostly formulated for parenteral delivery. For administration via alternative routes such as oral, nasal and pulmonary, solid lipid systems have been investigated for delivery of peptide and protein drugs. The lipid matrix improves protein stability and releases the protein in a controlled manner. Addition of silica nanoparticles added to lipid emulsion systems have been shown to increase the bioavailability of poorly soluble drugs and will be investigated in this project for their ability to stabilise the lipid droplets, enhance protein incorporation in the lipid and to control delivery.

Dr Matt Sykes (Senior Lecturer in Chemistry)

<http://people.unisa.edu.au/Matt.Sykes>

Dr Sykes has a number of projects available which are broadly in the area of molecular modelling. Whilst the projects are broadly computational, there is the ability to incorporate some synthetic chemistry/pharmacology if you would prefer a combined project. The exact composition of these projects is open to negotiation, and can be tailored to include aspects which are most appealing to potential honours students. Current projects are:

1) Investigation of the reported interaction between fusidic acid and statins

(Associate Supervisor: Prof John Miners, Flinders University)

Fusidic acid and statins are commonly prescribed for prophylaxis against infection and for continuing treatment of hypercholesterolaemia following major orthopaedic procedures in the elderly. The interaction between these two drugs has been shown to cause rhabdomyolysis, a debilitating disease affecting skeletal muscles. This interaction is suspected to occur due to competitive inhibition at the 1B1 subfamily of Organic Anion Transporter Polypeptides (OATPs), located in the hepatocytes of the liver. Limited understanding of the mechanism of this interaction and the metabolic properties of fusidic acid and its metabolites hinders the implementation of ideal clinical guidelines to manage this situation.

This project will look at the role that OATP and other enzymes (such as P450s) play in this important clinical interaction. Computational work will also be undertaken in order to understand the theoretical basis for the drug-drug interaction. Experimental work for this project would be conducted in the Department of Clinical Pharmacology at Flinders University.

2) Identification of kinase inhibitors using structure-based approaches

(Associate Supervisor: Prof Shudong Wang, UniSA)

Kinases are responsible for many types of human cancers. Inhibition of kinase activity can provide an effective anti-cancer strategy. This project (which is in conjunction with Professor Shudong Wang) aims to: (1) design and synthesise a library of heterocyclic compounds that block kinase activity by targeting both the ATP binding site and the DFD motif; (2) develop biochemical assays to determine the potency, specificity and mechanism of ligand binding; and (3) characterise kinase-ligand binding interactions by crystallography. The outcomes of this project will significantly advance the current understanding of the structure and mechanism underpinning kinase activity. The ligands will be invaluable chemical biology tools to study the role of kinases in protein translation leading to pharmacological target validation. We are interested in a number of different kinases; students will have the opportunity to work on the most current kinase of interest.

Various other projects in the area of drug design and discovery may be available (please talk to Dr. Sykes for more information)

Please note: Students working with Dr. Sykes will be offered the opportunity to be involved in chemistry laboratory teaching.

Dr May Song (Formulation Scientist)

<http://people.unisa.edu.au/May.Song>

Dr Song has broad research interests in the development of pharmaceutical preparations:

- Novel drug delivery system development
- Formulation improvement & development
- Quality evaluation
- In-vitro & in vivo studies
- Analytical services
- Applications of the above in the pharmaceutical industry

Potential projects for students could cover any of the above topics. Students are welcome to discuss their interests with Dr Song. A couple of projects are listed below.

Controlled release capsules development

The study will investigate a non-invasive method to detect and monitor small intestinal function and the severity of mucosal damage. An oral capsule for controlled-release of ^{13}C labelled sodium acetate will be prepared using modern pilot scale equipment. The results will demonstrate that this approach can be used for the study of chemotherapy-induced mucositis and pave the way for clinical trials of the technique to evaluate procedures for control or prevention of chemotherapy induced mucositis.

A novel drug delivery system for insoluble drug with high bioavailability

High doses are often necessary to poorly water-soluble drugs which can attain therapeutic plasma concentrations after oral administration. Improving the extent and rate of its dissolution is highly desirable, since that can increase and reproduce an oral bioavailability further, accordingly reduce a clinical dose, side effect and offer a more reliable therapy. Oral administration of a drug-loaded nanoparticle in the gastrointestinal tract that leads to a satisfied bioavailability.

Associate Professor Michael Wiese (Senior Lecturer in Pharmacotherapeutics)

<http://people.unisa.edu.au/Michael.Wiese>

My research interests primarily revolve around the use of personalised medicine – using factors such as age, height, weight, organ function and our own unique genetic make-up to select medicines that are most likely to achieve positive outcomes with medicines, namely optimal efficacy and minimal toxicity. I have primarily worked in the area of rheumatoid arthritis, and collaborate closely with rheumatology units at the Royal Adelaide Hospital and Repatriation General Hospital (Daw Park).

Projects that I am involved in that I would like to develop further include the measurement of drug concentrations in blood and blood cells, and correlating this to drug efficacy and toxicity. Other projects involve investigating genetic variability in enzymes involved in drug transport, metabolism and effect, and how these relate to blood drug concentrations, drug efficacy and drug toxicity. Ultimately, these projects aim to optimise drug treatment of rheumatoid arthritis, a potentially crippling form of arthritis which affects 1-2% of Australians, and has a tremendous influence on the quality of life of affected individuals.

The skills required will vary depending upon the specific project that we undertake. Some projects are primarily office based, and for these projects a good organisational and critical thinking skills are essential. Sound computing skills and an understanding of clinical study design would also be useful.

Laboratory based projects will usually involve liquid chromatography, PCR/genotyping, SDS-PAGE and western blotting and ELISA, but other techniques will be used if necessary for a project. For these projects, confidence in a general laboratory situation is useful, and you will receive teaching in the specific techniques. Good organisational skills and willingness to work independently and with others in a laboratory environment are essential qualities for this type of project.

Dr Des Williams (Program Director, Bachelor of Pharmaceutical Science, and Program Director, Bachelor of Pharmaceutical Science and Pharmacy double degree)

<http://people.unisa.edu.au/Des.Williams>

Dr Williams' research interests relate primarily to pharmaceutical chemistry. Specific fields in this general area include the formulation of new drugs into dosage forms, assessment of their stability, pharmacokinetics and, ultimately the clinical use of dosage forms. Current projects include the use of injectable dosage forms of capsaicin that are used clinically for the assessment of neuropathic pain, response to opioid analgesics, and the bioequivalence of commonly used dosage forms.

There are two projects on offer in collaboration with CSIRO Land and Water. The Associate Supervisor is Dr Mike Williams, CSIRO Land and Water. The work will require the student or students to be located

mostly at the CSIRO Urrbrae campus.

The fate and effects of human pharmaceuticals are of environmental interest, especially since more powerful analytical techniques have allowed their detection and quantification from environmental surveys. Pharmaceuticals and their metabolites have been detected in diverse environmental compartments following therapeutic use; from sewage treatment plants, to sewage sludge applied onto the land, to surface waters such as rivers, lakes, estuaries, the open ocean and water destined for human consumption.

Work undertaken to date represents only a small fraction of those available in the marketplace. Regulatory agencies such as the US Food and Drug Administration (FDA), the European Medicines Agency (EMA) and the Australian Therapeutic Goods Administration (TGA) are interested in identifying key factors that influence the fate of pharmaceuticals and potential toxicity that may occur in the environment.

Project one, in collaboration with Dr David Foster (Senior Lecturer, University of South Australia)

Reliable dissolution of drugs from solid dosage forms in the gastrointestinal tract is essential for optimal patient response. This project will focus on the dissolution of drugs from sustained release dosage forms. A major factor of interest is the ability to formulate tablets that can be divided by patients so that dose adjustments and patient convenience may be addressed. As the surface area of a dosage form may be an important influence on release rate, it is important to consider the potential for less than optimal plasma drug concentrations achieved at steady state. The increase in surface area will depend on the dimensions of the original tablet before division. The project will be a combination of theoretical calculations relating to surface area and volume before and after splitting, the manufacture of tablets of differing dimensions and dissolution testing according to standard regulatory guidelines. There is a strong possibility of pharmacokinetic modelling if the student is interested in such research.

Project two, in collaboration with Mike Williams (Research Scientist, CSIRO Land and Water), Contaminant Chemistry and Ecotoxicology Group

Our group focuses on the environmental fate and potential effects of organic contaminants, such as pharmaceuticals, and we are involved in a number of projects assessing environmental processes, including photolysis and biodegradation, that can transform these contaminants in the environment. While this transformation can reduce the risk presented by bioactive contaminants, it is becoming increasingly apparent that a number of these transformation products (TPs) are also likely to have some degree of bioactivity as well. Furthermore, for each contaminant there are a number of TPs generated, which presents significant challenges when trying to characterise the potential risks associated with the presence of a contaminant in the environment. We are commencing a 3 year project in September 2012, where we will develop methodology to allow a high-throughput elucidation of TP structures for pharmaceuticals undergoing environmental transformations. This methodology will involve the use high resolution mass spectrometry (HRMS) techniques applied to pharmaceutical compounds subjected to laboratory simulations of environmental degradation processes. We have recently employed a post-doctoral fellow who has extensive experience in using HRMS techniques for elucidation of TPs produced under environmental conditions. Potential students would be expected to gain experience in applying HRMS techniques to elucidate unknown TPs in complex matrices, as well as a broader understanding of how this knowledge can be used to generate a methodology for screening TPs in environmental samples.

Student requirements

The student would need to have a good understanding of analytical chemistry, including quality assurance and quality control, and a good knowledge of organic chemistry.

Project three in collaboration with Mike Williams (Research Scientist, CSIRO Land and Water), Contaminant Chemistry and Ecotoxicology Group

Our group focuses on the environmental fate and potential effects of organic contaminants and we are currently involved in project assessing the risk associated with pharmaceuticals in freshwater systems. This project has been monitoring concentrations of a number of human pharmaceuticals being discharged into aquatic systems, although the relevance of the measured concentrations needs to be assessed to undertake a detailed risk assessment. It is already known that a number of pharmaceutical compounds can present a risk to aquatic organisms, such as fish, and this has been previously documented to occur at extremely low concentrations of exposure (ng/L). Previous work has attempted to develop models that can predict concentrations of pharmaceuticals in water that will cause an effect in fish based on principles of pharmacodynamics in humans, where plasma concentrations can be used to predict effects. Within our current project, we seek to build on this previous work by (a) assessing the water concentrations of pharmaceuticals and comparing with concentrations in plasma of exposed fish and (b) to determine whether the expected concentrations in fish plasma could be of biological relevance and (c) whether these effects are predictable based on human therapeutic plasma levels. Biological endpoints will be monitored using a combination of general biochemical and molecular markers within exposed fish, while mass spectrometry techniques will be used to quantify pharmaceutical concentrations within fish.

Student requirements

Students should have a good understanding of analytical chemistry, organic chemistry and biochemistry. For more information on project two or three contact des.williams@unisa.edu.au or mike.williams@csiro.au

Project four, in collaboration with Professor Sanjay Garg and CPIE Pharmacy Services (Andrew Sluggett): Formulation, stability and in vitro efficacy of cyclodextrin inclusion complexes with selected suitable antibiotics for 24 hour infusion in the ambulatory care setting

The hospital in the home setting is of increasing importance to reduce the length of hospital stays and allowing patients to complete intravenous antibiotic drug therapy in their own home. For this to be practical for home nursing, 24 hour infusions are administered. To be considered suitable for 24 hour home infusion the chosen antibiotic must exhibit suitable stability- a number of days under refrigeration and at least 24 hours at ambient temperature.

Clinicians would have a preference to use some antibiotics in the home setting if a suitable presentation and stability were available. Some antibiotics have poor stability profiles in compounded preparations and therefore cannot be used in the home setting. Drugs other than antibiotics will also be considered if time permits.

It is proposed that these cyclodextrin complexes will improve the stability profile of these antibiotics and render them suitable for clinical use in the home setting. Improved solubility is often another advantage of drug-cyclodextrin complexes.

Student requirements

Students should have a good understanding of drug product formulation, drug stability and analytical chemistry.

For more information contact : des.williams@unisa.edu.au, sanjay.garg@unisa.edu.au or andrew@cpie.com.au

Project five, in collaboration with Danny Slee (Manager, Organics, National Measurement Institute NSW): Investigation of emerging contaminants in environmental waters

The National Measurement Institute is Australia's peak measurement body responsible for biological, chemical, legal, physical and trade measurement. NMI's NSW Organics laboratory makes its measurement expertise available to government, industry and the community through the provision of NATA-accredited analytical services required by organisations to meet both environmental compliance and commercial requirements.

Of significant interest to NMI's NSW Organics laboratory are emerging contaminants, such as pharmaceuticals, personal care products and pesticides, commonly found in a wide variety of environmental water samples including surface water, groundwater and sewage flows at concentrations ranging from trace to ppb levels. Emerging contaminants are likely to have a significant impact on human health and the environment. Most existing toxicity data are based on tests performed on single compounds and short-term exposure. Therefore, the focus of current research has moved to understand the fate and effects of mixture of compounds, their metabolites and/or transformation by-products, as hydrolysis, photolysis and biotic transformations may lead to the formation of more toxic and persistent contaminants. At present pre-targeted screening of emerging contaminants can be performed using triple-quadrupole MS, however this technique cannot achieve sufficiently accurate mass measurement to be used for post- and non-targeted screening. Ultra-high performance liquid chromatography (UHPLC) coupled with hybrid quadrupole time-of-flight mass spectrometry (QTOF/MS) has been identified as a preferred multi-residue analytical technique for qualitative and quantitative testing and non-targeted screening of trace organic contaminants in complex environmental waters. This project would address:

- 1) Development and validation of methods suitable for NATA accreditation to permit generalized extraction of a wide range of compounds from different types of waters;
- 2) Development and validation of QTOF/MS methods suitable for NATA accreditation in elucidating the emerging contaminants and/or their metabolites and transformation by-products in an aquatic environment.

Student requirements

Students should have a good understanding of analytical and organic chemistry.

For more information please contact des.williams@unisa.edu.au or Danny Slee on 02 9449 0111 or via danny.slee@measurement.gov.au

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<http://www.unisa.edu.au/Research/Sansom-Institute-for-Health-Research/Research/Therapeutics-and-Pharmaceutical-Science/>

Independent Researchers

Dr Hugo Albrecht (Senior Lecturer in Pharmaceutical Science)

<http://people.unisa.edu.au/Hugo.Albrecht>

Dr Albrecht has a strong interest in the development of enzymatic and cell-based assay systems for pre-clinical drug discovery, with considerable experience gained in both commercial and academic settings. The developed systems are designed for High-Throughput Screening (HTS) to identify potential novel drugs, and for compound profiling at later development phases during lead optimisation. Possible projects include assay development for cancer research, and the application of established and novel genetically encoded fluorescent probes for functional monitoring of drug target activities. Within the laboratory there is an emphasis on the use of molecular and cellular biology techniques and biochemistry. In addition to this, some projects will address the development of novel nanoparticle-based formulations for specific drug delivery into cancer cells.

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Emeritus Professor Mary Barton

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Use of bacteriophage to control *Rhodococcus equi* infection in foals

Professor Mary Barton¹, Ms Carla Giles¹, Dr Gary Muscatello²

1 University of South Australia

2 University of Sydney

Rhodococcus equi is an important pathogen in horses. It causes bronchopneumonia in young foals and up to 10% Thoroughbred foals die each year. No commercial vaccine is available and treatment is not particularly effective – it involves 3 to 4 week-long courses of combination antibiotic therapy. Bacteriophages are bacterial viruses that were used to treat infections before antibiotics became available. With the emergence of antibiotic resistance there is increased interest in investigating use of bacteriophages as treatments and also to reduce bacterial contamination. Bacteriophages are already being used commercially to prevent *Listeria*, salmonella and Enterohaemorrhagic *E. coli* contamination of processed meats and as a treatment of last resort for *Staphylococcus aureus* and *Pseudomonas aeruginosa* human infections. We want to investigate the possibility of using bacteriophages against *R. equi*.

The project would involve isolation of bacteriophages from horse faeces, sewage and environmental samples. The phages would be characterised by electron microscopy, RFLP and sequencing. Their activity would be tested against *R. equi* isolates and we would assess their capacity to reduce contamination of artificially contaminated surfaces. Time permitting, it may be possible to test their effectiveness in a mouse model of *R. equi* infection.

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Dr Anton Blencowe (Biomaterials, Biotechnology and 3D-bioprinting)

<http://www.unisanet.unisa.edu.au/staff/Homepage.asp?Name=Anton.Blencowe>

My research group's main focus revolves around the development of biomaterials and bioconjugation strategies for applications in regenerative medicine, 3D-bioprinting, tissue engineering, and environmental sciences. This research is underpinned by a strong foundation in fundamental chemistry and polymer science, and a passion to develop real-world solutions to the challenges facing society and the environment. Please feel free to contact me to discuss potential research opportunities in more detail.

3D-bioprinting: In vitro 3D tissue culture models for pharmaceutical development

In vitro models for the testing of novel pharmaceutical drugs represent a prospective US\$ 17b market. 3D human-based cell models have the potential to revolutionize this field as they can reproduce in vitro the native structure and function of tissues. As drug-induced injury is the main cause of drug attrition, it is critical to test therapeutic candidates on a liver tissue model before further development. However, currently used models only consist of a 2D cell monolayer that does not represent the natural cell organization or function. Hence, a high number of therapeutic candidates fail during downstream in vivo testing as current in vitro screening is inadequate and fails to identify high-risk or toxic therapeutics. Therefore, this project aims to develop novel 3D bioprinting and culture of liver (and other) tissues as a platform for drug testing.

3D-bioprinting: Development of Bioinks for 3D Bioprinting

3D printing has emerged as an advanced manufacturing technique that has revolutionized numerous industrial sectors. In the medical and pharmaceuticals sectors, 3D printing offers the potential to rapidly generate complex tissue constructs and organs from single cells that will pave the way for advances in regenerative medicine and drug development, tackling current health care challenges. However, 3D bioprinting for biomedical applications requires specific biocompatible materials – *bioinks* – that are suited for the manufacturing process. These bioinks must have a number of important characteristics, including printability, mechanical integrity, biocompatibility, and promote cell growth and function. Therefore, the goal of this project is to develop new bioinks and methods for the 3D printing of biological tissues and organs.

Nanomedicine: Targeted Therapeutics for the Eradication of Cancer

Many types of cancer evade normal cell death cycles by switching their energy production from oxidative phosphorylation to glycolysis. This project aims to develop a therapeutic system that can reverse this process, and involves the development of a polymer nanoparticles for the targeted delivery of glycolysis inhibitors that target the metabolism of cancer cells. The nanoparticles are designed to target cancer cells and undergo disassembly and protonation at the endosomal pH, resulting in inhibitor release inside the cancer cells. The potential outcome of the project is a novel and safer approach to the treatment of multi-drug resistant cancers that are not treatable using traditional chemotherapeutic agents.

Nanomedicine: Organic Nanoparticles for Enhanced Radiotherapy

The aim of this project is to develop nanoparticles that enhance the effect of radiation (from radiotherapy) to generate reactive chemical compounds at the site of the cancer, causing cell death. The nanoparticles are designed to generate maximum killing potential at the lowest possible radiation doses, resulting in cancer cell death without damage to healthy tissue.

Nanomedicine: Nano-oxygen particles for the Treatment of Oxygen Deficiency

The aim of this project is to engineer a new class of nano-oxygen particles (NOPs) for the treatment of oxygen deficiency in medical emergencies and maintenance of transplant organ viability. The student

will focus on the development of these new NOPs, elucidation of their structure-property relationships, and their application to the treatment of disease. The potential outcome of the project is a novel treatment for oxygen deficiency, which has implications for heart failure or stroke victims, the treatment of anemic disorders and emergencies (e.g., blood loss), and oxygen staved cancers.

Frontier Biotechnologies: Biocompatible and orthogonal coupling chemistries

There is significant scope for the development of new coupling chemistries that proceed rapidly at low temperatures, don't require complex precursors or catalysts, and are specific to particular functionalities. The project will involve the development of a new type of coupling chemistry based on Diels-Alder chemistry. The aim will be to optimise the system to proceed rapidly in water, without the addition of catalysts. The coupling strategy will be used to conjugate biofactors to surfaces for guided cell growth, tag delivery devices with probes, and build 3D tissue engineering scaffolds capable of encapsulating cells.

Frontier Biotechnologies: Revolutionizing peptide synthesis and peptide therapeutics

The global market for peptide therapeutics is worth over US\$ 21 billion, and it expected to double over the next 5 years. The most widely applied method for manufacturing peptides involves the use of a technique known as solid phase peptide synthesis, and the repetitive coupling of protected amino acids. The major disadvantages with this method are the poor atom efficiency, generation of large amounts of waste by products and cost. Therefore, the aim of this project is to develop an alternative approach that is less wasteful, more environmentally friendly, quicker and cheaper.

Environmental Sciences: Saving native wildlife from predators with protective implants

Invasive species, such as feral cats, pose a tremendous threat to native Australian species and reintroduction programs. Various methods to eliminate feral cats before reintroduction of native species have been trailed with limited success, due to the cats' preference for living prey rather than baits. When species, such as quolls, are reintroduced they are naive to their predators and are an easy target for cats. Generally, it only takes a few feral cats to rapidly wipe out the reintroduced population before they have a chance to breed and establish a colony in the area. Therefore, the aim of this project is to develop innovative new implants that can be used to save native wildlife.

Environmental Sciences: Developing a cloak of invisibility for native animals

All animals have a distinctive smell as a result of the pheromones that they produce, which helps them to recognize their own species and communicate with one another. However, predators can also smell these scents and use them to track and hunt their prey. In Australia, foxes and feral cats are introduced predators that prey on our native animals, and are a major contributor to the decline (and some cases) extinction of these native animals. Therefore, the aim of this project is to develop a technology – a 'cloak of invisibility' – that hides the scent of the native animals from these introduced predators and prevents them from being hunted.

Environmental Sciences: Biosurfactants from waste streams

Many industrial biotechnology and food technology processes produce waste streams that are either sent for disposal (waste dumps) or are incorporated into other low value food (animal) and agriculture (fertilizers) products. Therefore, a number of food companies are actively looking to make more use of their waste streams by producing higher value products. Surfactants are used in a wide range of industries, and are predominantly manufactured from non-renewable resources and are non-degradable, leading to their accumulation in the environment. Therefore, this project will involve the development of a green chemistry approach for the conversion of waste streams to biodegradable and environmentally friendly biosurfactants.

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Dr Maurizio Costabile (Senior Lecturer; Project Leader)

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The immune system plays the central role in protecting us from pathogens. Of critical importance is the role the immune system plays in protecting us from cancer. We know that cancer cells evade elimination by suppressing the immune response. My laboratory has been investigating the biological activity of the enzyme, indoleamine 2, 3-dioxygenase (IDO). IDO is a central enzyme involved in tumour induced immune evasion. As a result, it is a key target for breaking the cancer mediated immune suppression, thus paving a new approach to treating a wide array of cancers. Our research aims at better understanding the biology of IDO in leukaemia. There are a diverse range of projects which are aimed at better characterizing IDO so that better treatments can be developed.

I am also affiliated with the Molecular Signaling laboratory at the Center for Cancer Biology, led by Professor Stuart Pitson. The laboratory examines sphingolipid-mediated cell signalling pathways and how they contribute to cancer and other diseases. There are a number of projects on offer which are well suited to both Honours and PhD students.

The immune system plays the central role in protecting us from pathogens that we encounter. In certain cases the immune system can become overactive and lead to allergy and autoimmune disease, while in other cases, defects in any aspect of the immune system can lead to immunodeficiency disease. The immune system also protects us from cancer. It is now appreciated that cancer cells evade rejection through suppression of the local immune response via a number of strategies. My laboratory has recently begun investigating the biological activity of the enzyme, indoleamine 2, 3-dioxygenase (IDO). IDO is a central enzyme involved in tumour induced immune tolerance. As a result, any intervention that can modulate the expression and activity of this enzyme would be useful in the treatment of a wide array of cancers. Our research aims at better understanding the basic biology of IDO in leukaemia. By understanding how it is activated and controlled, we will be in a better position to identify possible ways of inhibiting the activity of this enzyme.

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Dr Giordana Cross (Dietetics)

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Major areas of interest include:

- 1) Chronic obstructive pulmonary disease (COPD) is a major contributor to morbidity and mortality in Australia. Progressive deterioration in lung function can influence a person's ability to consume sufficient food to meet their nutritional needs, which may be increased due to their disease. This in turn can lead to the development of malnutrition and potentially an increased risk of the development of infection and hospitalisation. Optimising nutrient/ food intake is therefore important. Gaining a better understanding of the factors that influence food and fluid consumption in people with COPD who are developing difficulties with their eating is therefore important. This understanding would contribute to the development of strategies that could improve nutrient intake and thus nutritional status in this group of people. **The project in this area will build on previous work. It will involve the development, piloting and validating a questionnaire for people with COPD.** The project will develop skills in the questionnaire development and validation. It will significantly contribute to the understanding of the factors influencing food consumption in people with COPD.
- 2) Women's health focusing on weight management, PMS and appetite and the use of nutritional supplements by women. A potential project is investigating the range of supplements being used by women, the reasons for use and sources of information that lead them to this use.
- 3) Nutrition plays an important role in the development of a number of chronic diseases in Australia. Being familiar with the evidence based information in this area is important for health professionals. The research in this area focuses on gaining an understanding of firstly the nutritional knowledge of health professionals and secondly how they use this in their day to day interaction with their clients/ patients.

Students are required to have nutrition knowledge and interest in nutrition related research.

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Dr Brian Dale (Senior Lecturer in Haematology)

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Dr Brian Dale has research interests in the area of haemostasis. This encompasses the investigation of bleeding and thrombotic disorders as well as the development and application of assays for diagnosis and assessment of treatment including evaluation of the anticoagulant effects of direct oral anticoagulants. Current areas of interest that could generate Honours projects include: investigation of the thrombogenic properties of cellular microparticles in haematological malignancy; clinical applications of a recently developed Overall Haemostasis Potential assay; the role of Factor XIII and the fibrinolytic system in the coagulopathy of trauma and in thrombohaemorrhagic disease.

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Dr Chris Della Vedova (Program Director: Biosciences)

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Dr Della Vedova has two main research aims. First, to identify novel genes that play a role in the development of addiction to methamphetamine. Using an existing pool of tissue samples, we plan to test for statistical association in a number of candidate genes with an increased risk of developing addiction to this stimulant drug. We also hope to better understand the functional consequences of this variation by assessing physiological and psychological differences in response to stimulant drug administration.

The second project involves work being done in collaboration with the Department of Defence. The military is interested in understanding how fatigue impacts upon operator state - the ability of military personnel to effectively function under stressful operational conditions. Our primary research goal is to develop and validate biological markers of acute central fatigue. Ultimately these biomarkers will be deployed to military vehicles and used to determine whether military personnel are competent to operate under conditions. The current aspect of this project is using a 48 hour sleep deprivation protocol to experimentally fatigue volunteers, followed by preliminary analysis of candidate biomarkers in serum and saliva samples. These candidates will be evaluated against subjective measures of fatigue and objective measures of performance (cognitive tests and simulated driving tasks).

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Dr Permal Deo (Lecturer)

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Dr Permal Deo's main research focuses on advanced glycation endproducts (AGE) receptors (RAGE), and activation of downstream signaling mechanism including MAP kinase and NF- κ B pathways. The impact of AGEs on cell cytotoxicity, DNA damage, telomere dynamics and mitochondrial dysfunction are also explored. His research also examines AGE formation and quantification (carboxymethyllysine, carboxyethyllysine) in biological and food samples. Current studies focuses on the role of natural products on AGE-induced signaling cascade as an alternative therapeutic approach. The role of these products with high antioxidant activities and/or their potential anti-inflammatory activities enables better insight on the mechanism in preventing or delaying the onset of chronic diseases.

His other research focus is on food safety and quality, with ever increasing incidences of foodborne disease, hence continuous identification of novel peptides with antimicrobial properties. In addition, in food processing, strict monitoring process and new sanitizers are explored to reduce the microbial levels reducing the risk of foodborne outbreak. Current research in this area focuses on: (1) use of natural products as antimicrobial inhibitors in cook-chill and ready-to-eat products; (2) assessment of new food sanitizers in reducing microbial contamination in seafood, minimally processed salads and meat; and (3) monitoring and evaluation of critical control and quality control point in food processing

Project 1

Anti-glycation and anti-proinflammatory potential of Australian medicinal and food plants. (Collaboration with Dr Susan Semple and Dr Maurizio Costabile)

Plant derived medicines have received great deal of attention due to their potent antioxidant and anti-

inflammatory activities, very less side effects and economic viability. It has been reported that dietary antioxidants and free radical scavengers are able to prevent oxidation and AGE formation which can reduce the risk of diabetes. Consumption of natural antioxidants and formulation of these antioxidants in food and nutraceuticals would protect the body against various oxidative damages. The objective of this studies will be to evaluate inhibitory activities of these natural products against key enzymes relevant to hyperglycemia, protein glycation and pro-inflammation.

Project 2

Role of advanced glycation endproducts in telomere dynamics (Collaboration with Prof. Michael Fenech, CSIRO)

AGEs are a complex group of compounds formed via non enzymatic reaction between reducing sugars and free amino groups of proteins, peptides and amino acids. Accumulation of AGEs in the body is associated with ageing and with the complications of diabetes including atherogenesis, renal impairment and retinal disease. Recently, AGEs has been also associated with Alzheimer's disease. In addition, reducing sugars (glucose and fructose) are known to produce ROS mainly through the glycation process and have been attributed in cellular and genome instability. This project will extend from current research work on DNA damage and look at the role of reducing sugars and AGEs on telomere length.

Project 3

Induction into viable but non-culturable (VBNC) status of foodborne pathogens

In recent years, there has been an increasing trend in the incidence of foodborne outbreaks worldwide. In some cases, these outbreaks are associated with food pathogens that are uncommon in food; for instance, recent outbreaks worldwide, including Australia, have been associated with *Salmonella* spp. in cantaloupes and prepacked lettuce leaves. In addition, the increasing tendency of people to consume food that is ready-to-eat or food prepared outside the home is raising concerns on hygiene and food processing conditions. Owing to the possibility of direct repercussions of foodborne outbreaks on global public health challenges, sanitisation of food products is becoming a key step in their pre-market processing. The efficacy of food sanitisers has been recently challenged as most of the studies are based on the cultivation of the target microorganism. The results obtained are questionable as there are possibility of an induction of "viable but non-culturable" (VBNC) state through use of disinfectants. When the microorganism enters into the VBNC state, both the morphology and the physiology of the cell are changed, in order to allow the microorganism to survive under the adverse conditions experimented. Then, when the environmental conditions return to normality, the cell may get back to its vegetative state (culturable), through a reactivation process that is often referred to as "resuscitation". This industry based collaborative project aims at collecting data on the ability of food sanitisers (including a novel and safe sanitizer, the Ecas4 Anolyte) to induce VBNC status in foodborne pathogens. Culturable and molecular techniques will be used to assess these based on bacterial growth media and food models.

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Dr Sheridan Gentili (Lecturer in Biological Sciences)

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I am interested in prenatal programming of postnatal obesity and diabetes, specifically the impact that maternal diets high in carbohydrates have on the development of obesity and metabolic disorders in the offspring, and whether dietary interventions could play a role in alleviating such effects. Opportunities for Honours projects exist for the following project areas:

Hepatic response to elevated glucose and fructose: metabolic consequences

There is increasing evidence highlighting the detrimental effects of diets high in refined carbohydrates, specifically glucose and fructose, on the development of non-alcoholic fatty liver disease, insulin resistance and the subsequent development of type 2 diabetes. It is well established using animal models that diets high in sucrose, disaccharide made up of glucose and fructose, leads to the rapid development of non-alcoholic fatty liver disease, however the molecular mechanisms associated with this are yet to be fully described.

The adverse effects of maternal sugar consumption on the metabolic health of the offspring

Consumption of sugar-sweetened beverages is steadily increasing coincident with an increase in adult obesity and diabetes. Exposure to high glucose before birth increases the risk of childhood obesity and diabetes, however little is known on the long-term effects of sweeteners such as sucrose and high fructose corn syrup. This study will compare the impact of maternal consumption of sucrose and high fructose corn syrup during pregnancy and lactation only on metabolic outcomes of the juvenile and adult offspring.

Maternal low GI diets for improving metabolic outcomes in the offspring

There is increasing recognition of the effect of perturbations in maternal nutrition on the long-term health of the offspring. Exposure to an increased supply of glucose, as a result of maternal obesity or diabetes, has been shown to promote adipose tissue deposition in the fetus, and is associated with an increased risk of obesity and type 2 diabetes in the offspring throughout child and adult life.

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Dr Rebecca Golley (Child Nutrition)

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Affiliated with the Public Health Group within the Sansom Institute of Health Research, Rebecca's research investigates ways to work with families to improve children's nutrition and health. Rebecca utilises a range of methods including nutritional epidemiology, dietary assessment methodology, intervention and behavioural research. Her research is centred on strengthening the evidence base underpinning public health nutrition guidelines, resources and programs.

Proposed research projects include:

1) Development of a novel, short tool to measure food intake in young children

Collaborators Stewart Trost (QUT)

Dr Golley is a Chief Investigator on a National Health and Medical Research Council funded the Centre for

Research Excellence for the Early Prevention of Obesity in Childhood (CRE-EPOCH). She leads a stream of research titled “Advancing assessment of obesity-related behaviours in children under 5”. The aim of the honours project would be to evaluate the relative validity of a Short Form Measure of Diet in children 6 to 60 months of age.

2) Identifying effective public health nutrition approaches to reducing unhealthy food intake

Co-supervisor Tom Wycherley and Brittany Johnson

Excess consumption of energy-dense, nutrient-poor food and beverages is associated with increased risk of chronic disease and displaced healthy food intake. While a reduction in unhealthy food intake is a key public health target, interventions to date have been ineffective. This honours project will use data from the Australian Health Survey 2011-2012 and an established dietary simulation modelling protocol to compare the effectiveness of dietary strategies in reducing unhealthy food intake in overweight and obese populations.

3) Reducing children’s intake of unhealthy foods: what do parents want as an intervention?

Co-supervisors Brittany Johnson, Dorota Zarnowiecki and Gilly Hendrie

Children’s unhealthy food intake contributes over 30% of total energy intake. To effectively reduce children’s intake of unhealthy foods evidence-based interventions, developed in close partnership with parents, are required. This project will determine what intervention characteristics (e.g. mode/ intensity of delivery, use of technology, format, content) parents feel are needed to enable them to reduce their provision of unhealthy foods to their children.

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Dr Alison Hill (Senior Lecturer in Nutrition)

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My current research focus is on increasing our understanding of the role that diet plays in modulating risk factors for chronic disease.

Proposed research projects include:

MULTIPLE PROJECTS: Does inclusion of almonds in an energy restricted diet enhance weight loss and protect against weight regain?

Co-supervisors: Dr Alison Coates, Prof Jon Buckley

Frequent nut consumption is linked with a lower body mass index and previous studies have demonstrated the effectiveness of adding almonds to an energy restricted diet for weight loss³⁻⁶. The nutrient profile of almonds, which are rich in monounsaturated fats, protein and fibre, may assist with weight management through increased satiety⁹. Currently, data are lacking on the role of almonds in weight control diets to limit weight regain. We have recently received funding to conduct a large-scale (100+ people) dietary intervention trial to evaluate the benefits of almonds for weight loss and prevention of weight regain. We have multiple Honours projects available investigating whether inclusion of almonds in a weight loss diet:

- improves subjective and objective measures of satiety
- changes resting energy expenditure or shifts fuel selection toward fat oxidation (due to higher unsaturated fat intake from nuts)

The students involved in these projects will have the opportunity to be involved in a large scale human dietary intervention trial.

Masters projects are also available.

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Associate Professor Ivan Kempson (Biophysics)

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Associate Professor (Biophysics) Ivan Kempson leads basic and applied research in nanotechnologies for cancer therapies, combining chemistry, biology, mathematics and physics into a multidisciplinary approach to progressing experimental treatments. Much of his research involves collaborative teams (locally and internationally), engagement with hospitals and utility of the Australian Synchrotron in Melbourne. The projects below are described in very broad terms so as to tailor specific details to the skills and interests of the candidate.

‘Nanomedicines’ as DNA damage repair inhibitors.

Altering gene regulation of cancerous cells to impair their ability to recover from DNA damage is a promising target in anti-cancer treatments. This project explores the use of a novel concept to down regulate genes critical in the cells’ ability to recover from DNA damage, thus making the cells vulnerable to mechanisms of DNA insult.

Enhancing oxidative stress in cancer cells.

Hypoxia in tumour tissues correlates with poor treatment outcomes in many instances of cancer therapy. This project explores avenues to increase localised oxygenation of cells and enhance formation of Reactive Oxygen Species (ROS) that exert oxidative damage to cells to induce apoptosis. The project will identify key variables in the delivery of oxygen rich nanomaterials and mechanisms of ROS enhancement.

Targeting cancer cell sub-populations responsible for therapeutic failure.

Cancer stem cell and S-phase cell sub-populations are a negative prognostic factor, correlating with therapeutic failure. In many instances of treatment, these cells remain insensitive to therapy and are able to proliferate, leading to tumour recurrence and patient mortality. This project studies sub-populations of cells within larger populations to appreciate the role of heterogeneity in tumour recurrence and to develop therapeutic strategies in overcoming their repopulation.

Associate Professor Jennifer Keogh (Dietetics and Nutrition)

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Jennifer's is a dietitian whose research is on the dietary factors that improve and protect blood vessel health and on strategies for weight loss in people with and without diabetes. Her projects would suit students who have an interest in weight loss, diet and nutrition and have a science, food, nutrition or health sciences or background. There are a number of projects available including:

How can we help mothers who have had gestational diabetes lose weight and reduce the risk of development of type 2 diabetes?

In 2015 at least 10.9% of pregnant women in Australia were diagnosed with gestational diabetes (GDM). GDM is the highest risk factor for future development of type 2 diabetes (T2DM) and currently one in two women who have GDM will develop T2DM later in life. Lifestyle interventions that result in weight loss can reduce the risk of developing T2DM after GDM. However, weight loss can be difficult for mothers with young children given the demands of their infant, lifestyle adjustments, time constraints and inadequate sleep. Our research aims to address issues that women with young children identify as barriers to weight loss and aims to provide less burden and interruption to their daily routines.

The successful student will be involved in a qualitative project aimed to understand the experience of women who have participated in a weight loss project. Their experiences of and barriers to and facilitators of weight loss will be identified. . The student will gain experience in various aspects of the project which will include data collection, recording and analysis of interviews and abstract preparation.

Collaborators Professor Peter Clifton and Ms Kristy Gray PhD student

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Dr Evangeline Mantzioris (Nutrition)

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Current projects:

Can we improve people's omega-3 status without them eating more fish?

Collaborators: Dr Beverly Muhlhausler, University of Adelaide; Prof Bob Gibson, University of Adelaide
The importance of diet for the prevention and management of cardiovascular disease is well recognised. Health agencies across the world recommend lowering the intake of saturated fat intake by replacing animal fats with polyunsaturated vegetable oils, and increasing the intake of fish and fish-oils (which contain high amounts of omega-3 fatty acids) in order to improve heart health.

Whilst this approach is effective in individuals, many Australian's find it hard to eat enough fish, and, even if they did, there aren't actually enough fish left in the world's oceans to supply these needs for too much longer.

Luckily, omega-3 fatty acids are also found in other foods, and the amount of omega-3 fatty acids that most Australians already eat is likely to be enough to protect against cardiovascular disease if it wasn't for the high level of omega-6 fats in typical Australian diets. This is because omega-6 fats compete with omega-3 fatty acids for incorporation into tissues, which is necessary for them to have biological

effects.

This project aims to show that reducing the intake of omega-6 fats will result in increased omega-3 incorporation into tissues and protection against cardiovascular disease without the need to increase fish or fish-oil intake.

Assessing community pharmacists' knowledge of [The WHO International Code of Breast Milk Substitutes](#)

Collaborators: A/Prof Michael Wiese, University of South Australia; Prof Bob Heddle, IMVS

The WHO International Code of Breast Milk Substitutes (1981) is a voluntary code that Australia is a signatory to. It outlines the obligations and responsibilities of breast milk substitute producers and health-care workers, including pharmacists. This study will be investigating the current knowledge and practices of community pharmacists regarding infant feeding practices and The WHO International Code of Breast Milk Substitutes. It is hoped that the findings will guide continued educational program planning for pharmacists.

The project will be investigating what the current knowledge level of community pharmacists of the WHO International Code of Breast Milk Substitutes and infant feeding practices? Secondly this project will investigate if pharmacies in South Australia adhere to the advertising and display of infant formulas set out in the code (Article 5.2).

Healthy Eating for Learning and Living– A Longitudinal Observational Study in University Students

Collaborators: Dr Sze Yen Tan, Anthony Villani

Obesity is a major health concern in Australia, with 63.4% of the total adult population being either overweight or obese in the recent 2011 National Health Survey Data. Within the young adult age groups of 18-24yrs and 25-35yrs, 37% and 55% are overweight or obese respectively. However of most concern is the growing proportion of young adults over the years who are becoming overweight or obese. By analysing the age cohorts from the NHS data, those that were aged 18 years in 1995 were aged 30-31 years in 2007-08; in 1995 21% of the 18yr olds were overweight or obese, but by 2007-08 when they had aged to 30-31yrs over 50% of this cohort was overweight or obese. 20% of this age group (1.21million) are enrolled at Universities across Australia (<http://www.education.gov.au/selected-higher-education-statistics-2013-student-data>). As such Universities may be an ideal place to provide and support healthy lifestyle advice to young adults. The commencement of University for young adults represents a transition period from adolescence into young adulthood. It is a period of increased independence and decision making in many areas including lifestyle choices. In relation to health outcomes, of interest is the decision making around lifestyle choices such as the selection of meals and food, and physical activity.

This research seeks to identify what is the impact of this transition period on behaviours and choices made around diet and exercise by young adults in their first year of University, and how this may impact on nutritional intake, physical activity and anthropometric measures. Additionally the impact of the surrounding environs (the University campus and surrounding hospitality/food environment) will also be considered. This prospective longitudinal study will use mixed methods to longitudinally follow students through their first year of University. Specifically this longitudinal study will identify critical periods and areas which will then guide the formulation of appropriate interventions.

The development of a validated tool to measure consumer satisfaction with acute care adult hospital food services

This study is a collaboration with the Royal Adelaide Hospital. It involves the development and the validation of a questionnaire that assesses patient satisfaction with the foodservice provided to them in an acute care adult hospital. The questionnaire is expected to be published and used in South Australia

when this project is completed. This project involves a range of research activities such as focus group interviews and patient survey.

Antioxidant activity and antiglycation properties of whey proteins and other sports drink

Dr Permal Deo & Dr Evangeline Mantzioris

Oxidative metabolism is essential for cell survival however it generates free radicals and other reactive oxygen species (ROS) as side effect that could cause oxidative damage and are linked to the pathogenesis of many chronic diseases. Exercise has also been shown to increase oxidative stress through increased production of ROS and has demonstrated links to fatigue and muscle damage, affecting exercise performance. While the body has its own defence system against ROS, lifestyle mediated disease has been reported to significantly reduce this. Enhancements of the body's antioxidant defence mechanism through dietary supplementations are common approach in reducing the levels of oxidative stress. In recent years, the demand for natural antioxidants has increased due to the potential health effects of synthetic antioxidants.

Dairy products and their fractions have been found to have antioxidant potentials eg., milk, skim milk, whey, casein and lactoferrin. Whey protein, a by-product of fermented milk products, is recognized as valuable food ingredient with important nutritional and functional properties and gaining acceptance as functional food ingredient. Peptides isolated from hydrolysis of whey protein have shown physiological properties including antioxidant, antihypertensive, antimicrobial and antithrombotic activity but limited on protein glycation or its potential antiglycation properties. Thus this project will investigate the antioxidant activities and antiglycation properties of selected whey proteins and sports drink.

The effect of conventional cooking on phenolics and antioxidant activities of legumes

Dr Evangeline Mantzioris and Dr Permal Deo

Oxidative metabolism is essential for cell survival however it generates free radicals and other reactive oxygen species (ROS) as side effect that could cause oxidative damage and linked to the pathogenesis of many chronic diseases. Enhancements of the body's antioxidant defence mechanism through dietary supplementations are common approach in reducing the levels of oxidative stress. In recent years, the demand for natural antioxidants has increased due to the potential deleterious health effects of synthetic antioxidants.

Legumes are known to be a rich source of anti-oxidants, but little is known about the impact of different cooking techniques on the bioavailability of the antioxidants. Lentils are a common ingredient in dishes from many cultures, particularly from the Mediterranean, Middle Eastern and the Sub-continent. There is evidence of synergistic effects of when antioxidant rich ingredients are combined. The impact of other ingredients with lentils in the dishes on the antioxidant properties is not known and will also be investigated in this project.

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Dr Karen Murphy (Nutrition, Dietetics, Chronic Disease)

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Dr Karen Murphy is a Senior Lecturer, Accredited Practicing Dietitian and Sports Dietitian. Karen uses an evidence-based approach to explore the effect of whole diet and lifestyle patterns on chronic disease risk. Specifically, her research investigates the impact of the Mediterranean dietary pattern on cardiovascular disease and metabolic syndrome as well as mental health, psychological wellbeing and risk of dementia.

She is a recognized leader in research in nutrition, chronic disease and ageing and as a result collaborates with national and international researchers as well as the food industry. She offers expertise in conducting clinical trials with high compliance rates, delivery of dietetic interventions, assessment of dietary intake, measures of body composition, cardiovascular health, cognitive performance and biochemical analyses.

Karen is able to translate science and her research outcomes to clinical populations through her role as an Accredited Practicing Dietitian.

The following projects are offered:

Project Title: The cost of weight loss.

Co-Supervisors: A/Prof Jennifer Keogh and A/Prof Carol Maher (School of Health Sciences)

Project overview: Sensible and sustainable weight loss should be achieved through energy restriction, choosing a balanced diet from all food groups and incorporating physical activity. In recent years we have seen an influx of a variety of diets for weight loss including the paleo diet, South Beach diet, 5:2 diet, lemon detox diet, 8 weeks to wow, high protein diet, CSIRO total wellbeing diet, Atkins diet, meal replacements etc. But are there any real benefits in using one weight loss diet over the other? Many diets promote not only weight loss but additional health benefits, require a significant amount of food preparation and can be expensive particularly if there is a strong focus on meat protein, or meal replacements, powders or supplements. So what is the real cost of weight loss diets?

A selection of popular weight loss diets with accompanying meal plans/meal replacement plan will be chosen for this study. Each meal plan/meal replacement plan will be costed and standardised to calculate a cost of weight loss per 500g of weight. These diets will be compared and evaluated in relation to their financial cost of weight loss with consideration of any additional health benefits associated with the dietary pattern (e.g. bioactives) independent of the benefits associated with weight loss. These diets will be compared with two key dietary patterns, the Australian Guide to Healthy Eating principles – energy restriction, with consuming foods from all food groups and the Mediterranean dietary pattern for weight loss, one of 3 healthy dietary patterns recommended by the American Dietary Guidelines (2015-2020).

Project Title: Associations between lifetime dietary patterns and cardiovascular health in older Australians: the MedLey Study.

Co-Supervisor: Dr Karma Pearce, Dr Diane Hosking (AIHW)

Project overview: The Lifetime Dietary Questionnaire has been demonstrated to be a reproducible tool to assess lifetime dietary patterns across the life span. The MedLey study was a 6-month dietary intervention comparing the effect of a Mediterranean dietary pattern with habitual diet on measures of cardiometabolic health and cognitive performance in n=166 older Australians. Results showed a Mediterranean diet significantly reduced cardiovascular disease risk compared with the habitual diet group after 6 months. Dietary pattern information across the lifespan have been collected from these volunteers but not yet analysed for relationships with cardiovascular health. The project will involve the tabulation of data, statistical analyses of data to identify dietary patterns across the lifespan and their relationship with cardiovascular health.

Ref: Hosking, D & Danthiir, V 2013, Br J Nutr, vol. 110. no. 11, pp. 2069-2083.

Project Title: Development and validation of dietary and lifestyle questionnaires for use in the dynamic open prospective study: LUIISA (La Trobe University & Uni of South Australia Cohort study)

Co-Supervisor: Prof Catherine Itsiopoulos (La Trobe University)

Project overview: The LUIISA Cohort is a collaboration between UniSA and La Trobe University. It is based on the SUN Cohort and is designed to be a permanently open dynamic prospective follow-up cohort study assessing participants every 2-years. Alumni from both universities will be contacted via mail and invited to participate in this study. Upon consent, questionnaires will be posted to volunteers and subsequently invited to attend a research clinic at each university for clinic measurements. A large ongoing prospective cohort such as LUIISA will enable detailed analyses of the impact of behaviors/ exposures associated with university life on long-term health/morbidity and mortality risks. The Honours component of this project involves developing and validating a dietary questionnaire for the accurate estimation of energy, macro, micro and phytonutrient intake; and a lifestyle questionnaire which will capture information on chronic disease, behavior, physical activity, demographic etc. These will require validation prior to dissemination.
Ref: Martinez-Gonzalez MA. Public Health Nutr. 2006 Feb;9(1A):127-31.

Project Title: South Australian MedDiet Adherence Study

Co-Supervisor: Prof Jon Buckley (School of Health Sciences)

Project overview: The Mediterranean dietary (MedDiet) pattern is reported to reduce total mortality, mortality from cardiovascular disease and reduce risk of dementia. It is predominantly a plant-based diet, characterized by fruits and vegetables, legumes, nuts, olive oil, wholegrains and fish with moderate amounts of red wine, dairy foods, red meat and is very low in discretionary foods. We have an opportunity to explore relationships between cardiometabolic health outcomes and adherence to a Mediterranean diet using a database with volunteers who have participated in trials within ARENA. Trial participant data will be included if there is dietary data from either a food frequency questionnaire or weighed food record (to calculate a MedDiet adherence score) and cardiometabolic data including: BMI, waist circumference, % body fat, WHR, lipids, glucose and blood pressure. Statistical analyses will be undertaken to explore relationships between MedDiet adherence and cardiometabolic outcomes.
Ref: Murphy KJ et al. Nutrients 2013, 5, 4665-4684; doi:10.3390/nu5114665

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Dr Karma Pearce (Senior Lecturer in Nutrition)

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Current research interests include:

- 1) The use of lifestyle modification and supplements to improve fertility outcomes
- 2) The influence of diet and lifestyle in disease prevention in socially disadvantaged communities

1) Fertility– With Repromed

Supervisors: Dr: K. Pearce, Prof K. Tremellen

Infertility affects up to one in six couples within Australia and is a rapidly growing area of research. Dr. Pearce and Prof. Tremellen have just edited a book on Nutrition, Fertility and Human Reproduction and are looking at the use of specific supplements to improve fertility. As 1 in 10 couples experience difficulty conceiving a child this is a growing area of research.

Project title 1: Poly Cystic Ovary Syndrome and low grade endotoxemia

Research in animals has suggested that bacteria commonly found in the gut have the ability to release toxic toxins that can interfere with ovary health, interfering with its production of hormones and oocyte quality. We have recently investigated this link in women, there have some evidence suggesting that a similar problem may exist in human reproduction, particularly in women with Poly Cystic Ovary Syndrome. The aim of this research study is to measure bacterial toxins in the blood and follicular fluid (cyst fluid) surrounding eggs and correlate those toxin levels with egg quality, ovarian hormone production and pregnancy outcomes.

Project title 2: *Helicobacter pylori* and testosterone production

Recent research has shown that infection with *Helicobacter pylori*, bacteria that reside in the gut of many people, (can interfere with sperm production. The reason for this is unclear, however, initial research has led to one theory; that this bacteria interferes with testosterone production, a hormone that is crucial in sperm development. Having low testosterone not only effects sperm production and other aspects of sexual health (such as sexual drive and erectile function), with low testosterone levels also associated with fatigue, symptoms of depression and predisposition to being overweight. The aim of this research study is to measure bacterial toxins in the blood, the presence of *Helicobacter pylori* infection, and determine if this correlates with testosterone production.

We have a number of projects exploring the influence of nutrition on reproduction including rat studies and clinical trials. If you are interested in working in this area please speak to us.

2) Healthy lifestyles for New Arrival migrants

Supervisors Dr. Karma Pearce and Dr. Giordana Cross

Acculturation of migrants under the New Arrivals program from underprivileged countries often results in the higher intake of discretionary foods. This can sometimes result in adverse health outcomes due to dietary related diseases. This project will involve mapping dietary intake to the Australian guide to healthy eating and developing education programs to assist in acculturation.

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Dr Nenad Petrovic (Pharmacology)

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Dr Petrovic offers projects that investigate molecular mechanisms by which novel drugs suppress pathological growth of blood vessels or angiogenesis. The exact projects available depend on the current research direction.

Current Project:

Prostacyclin receptor antagonists as potential drugs for suppression of pathological angiogenesis

Pathological angiogenesis or growth of new blood vessels in adult organisms (observed in cancer and diabetic retinopathy, for example) is regulated by numerous activators and inhibitors and it is directly correlated with disease progression. Important activators of angiogenesis include large family of specific lipid mediators called prostanoids. In our previous work we have compared effects of two prostanoids relevant to vasculature, prostaglandin E2 (PGE2) and prostacyclin (PGI2) on angiogenic processes in vitro. Both of those prostanoids activate corresponding G-protein coupled receptors. Four of them are activated

by PGE2 (EP1, EP2, EP3 and EP4) and one by prostacyclin (IP).

In our experiments we use Human Umbilical Vein Endothelial Cells (HUVEC) to characterize two important angiogenic processes: cell migration (with original method developed in our laboratory) and HUVEC “tube formation” (widely accepted method of assessing formation of blood vessel precursors) we have found that two prostanoid receptors (IP and EP4) mediate most of the prostanoid effects on angiogenesis. Further research will delineate precise role of these receptors in angiogenesis with ultimate aim to design specific antagonists to be used clinically for treatment of pathologically increased angiogenesis.

Student requirements

A good understanding of cell biology and pharmacology is preferred as well as high level of time management and research initiative skills. Prior experience with cell culture is highly desirable.

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Cameron Phillips (Adjunct Lecturer)

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I am a practicing pharmacist at Flinders Medical Centre with strong interests in clinical education and infectious diseases. I have recently completed a National Health and Medical Research Council Fellowship on improving the use of the antibiotic vancomycin. The research I conduct is on improving antimicrobial use in the hospital environment to ensure the best patient outcomes and limit the consequences of inappropriate use. I frequently collaborate with infectious diseases physicians and clinical pharmacologists with my research and honours projects to ensure a balanced clinical and patient based focus exists with the therapeutic content. I have had several honours students and make sure you are well supported and endeavour to see your work is published.

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Dr Sally Plush (Fluorescent probes, sensors and water purification)

<http://people.unisa.edu.au/Sally.Plush>

My group's research is focused on how small molecules interact with their local environment. This is a multi-disciplinary research group with a wide variety of collaborators ranging from postdoctoral fellows to industry partners.

Luminescent sensors for live cell imaging

To help advance knowledge in biology by developing molecules that allow researchers to visualize biological processes in real time applications to further the understanding of the pathophysiology of major disease states and develop enhanced diagnostic and therapeutic agents. We achieve this by developing luminescent metal ion complexes (transition and lanthanoid based) for live cell imaging applications. I have helped co-found the company ReZolve Scientific which manufactures and sells these molecules as live cell imaging reagents for the cell biology market.

Key personnel in this area are:

Dr Christie Bader

<http://people.unisa.edu.au/christie.bader>

Dr Bader is a cell biologist who specialises in live cell imaging

Dr Shane Hickey (see Mechanisms of Cell Biology)

Synthesis of targeted molecular probes (Dr Plush and A Prof Massi (Curtin)): Targeted molecular probes for imaging that can accurately visualise cellular processes at the molecular level in live cells, have the potential to discriminate between different tissue and cell types, map uptake and traffic within cells and/or dissect structure and function at the sub-cellular level. The aim of this project is to develop and synthesise long lived highly emissive metal ion complexes targeted to a range of biologically important molecules and pathways to provide insight into major disease states such as heart disease, cancer, infection, etc. This research is conducted in combination with researchers at Curtin University. Students who undertake honours in this area can be expected to become skilled in the areas of synthetic (organic and inorganic) and analytical chemistry (NMR, HPLC, Mass Spectrometry, Fluorescence and UV-Visible spectroscopy), cell biology and molecular imaging (live cell imaging and confocal microscopy).

Delivery systems of cholesterol tracking tools (Dr Plush and Dr Bader): Cholesterol is an important component of cellular membrane, providing stability and rigidity to the structure. Cell can synthesis cholesterol or can absorb it from their environment to ensure the correct balance is maintained. Given that cholesterol is an integral membrane component, which can be obtained from the environment, fluorescently tagged cholesterol mimics can provide a useful tools as membrane stains, aiding cell biologists to better understand membrane dynamics and trafficking. Though there are a number of fluorescently labelled cholesterols available on the market these suffer significantly from photobleaching, making them unsuitable for long term imaging experiments. Thus employing fluorescent tags which are more resistant to photobleaching may provide a better product for cellular membrane staining than is currently available. With this in mind ReZolve Scientific chemists have utilized the patented rhenium fluorescent platform as a tag for cholesterol, which in theory will provide a more photostable molecule which may associate with the cell membrane. One of the key challenges faced by biologists is developing a cellular delivery system for this hydrophobic new cholesterol compound, without interfering with the fluorescent output of the tag. A number of lipid and protein based delivery systems will be developed using common drug delivery approaches, these systems will then be assessed using a range of molecular and cellular imaging techniques. This will allow you to gain a range of technical expertise highly sort after in cell biology and biomedical sciences and may contribute to the commercialization of a new cellular imaging tool.

Improving water quality through advanced materials

Access to clean drinking water is a basic human right and appropriate purification of water for consumption is one of the key steps in providing this. Water impurities range from cancer causing chemicals to deadly water borne pathogens, at this stage removal of these impurities is costly. There is a need to develop new materials that deliver improved and cost effective water filtration. Together with Puratap, a local industry partner, we will develop/design and manufacture new materials that remove harmful contaminants.

Key personnel in this area are:

Dr Martin Sweetman (Research fellow)

<http://people.unisa.edu.au/Martin.Sweetman>

Dr Sweetman's research is linked closely with an industry partner, focused on the development of new technologies for water treatment and monitoring. The detection and removal of organic and pathogenic contaminants is crucial for providing safe water to individuals. His current research involves the design

and construction of a point of use sensor for monitoring water quality pre and post filtration. Following on the same theme, Dr Sweetman is also interested in developing advanced materials for improved water filters. Research in this field will help to ensure efficient and sustainable use of this scarce resource into the future.

Develop enhanced filtration device (Dr Plush, Dr Sweetman and Prof Hayball): This project will investigate different chemical modification/treatments of activated carbon filters that will improve the capture of both dissolved organic matter and water borne pathogens from water. The key aim of this research is to deliver a more efficient carbon filter for dissolved organic matter whose manufacture and chemical treatment can be easily upscaled from in-house to full production in South Australia by Puratap. Further, we will draw on specific expertise within the research team and will focus on advanced self-sterilising materials/surfaces that can be integrated into filters for neutralizing/removing water borne pathogens. This is of significant interest to Puratap and the research team in the scope of providing active rainwater/raw water filters for remote and isolated communities.

Detection and remediation of water contaminated with perfluorinated substances (Dr Plush, Dr Sweetman, Prof Hayball and Dr Chalker (Flinders): This project will introduce cost-effective technologies for sensing and removal of perfluorinated alkyl substances (PFAS) from water. Defense forces commonly use fire fighting measures that release PFAS into the environment, so cost-effective technologies are needed to remove it from water. This project will build on preliminary results that provide new filtration technology for use by defense forces and the general public. Commercial production with industry partner Puratap is envisioned. There are a couple of avenues for projects in this area one will involve the synthesis of novel sorbent, the incorporation and manufacture of filtration blocks for ease of use at contamination site and evaluation of PFAS capture, this knowledge will then be fed back to produce more efficient filtration. Second options is to work on the real-time and on-site sensing of PFAS, this work will look at developing enhanced sensors through the use of optical fibre laser technology. These projects work closely with Flinders University and field work is expected to be part of this project.

Development of in-field sensors (Dr Plush, Dr Sweetman and A Prof Vahid): This project will see the synthesis of graphene quantum dot (GQD) embedded hydrogels, combined with fibre optics for the development of in water sensors. The incorporation of GQD hydrogels with fibre optics to develop sensing devices presents as an innovative approach to synergistically marry these cutting-edge materials and technologies to provide solutions to real-world applications. The robust nature of the GQDs (to resist photobleaching) and the ability to design remote and real-time sensing devices using fibre optics could mean that sensing technology superior to that currently used, can be realised. The development of such devices would have immediate impact in the water industry, where accurate and continuous monitoring of contaminants is vital.

Professor Clive Prestidge (Pharmaceutical Science)

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Prof. Prestidge's group is focused on the development of novel drug delivery systems, in particular the application of particle and nanoparticle based vehicles to improve the absorption, safety and efficacy of pharmaceutically active agents. The group is a node in the ARC Centre of Excellence in Convergent Nano-Bio Science and Technology (<https://www.cbns.org.au>), is also supported by NH&MRC projects and has well established academic and industry collaborations both in Australia and overseas. In addition to establishing smart biomaterials for improving drug delivery through the oral, dermal, topical and inhalation routes, there is a strong philosophy to understand the mechanisms of action for such delivery systems. Our research is also inspired through unmet clinical needs in chemotherapy, anti-psychotic

medicines, bacterial biofilms, antibiotics resistance, cardiovascular medicines, lung therapy, biopharmaceuticals and oral vaccines. Dr Nicky Thomas (NH&MRC fellow) and Dr Hanna Gustaffson are senior scientists in the group and lead a number of the research projects.

Project 1: “Next Generation Silica Lipid Hybrid (SLH) Formulations and their Pharmaceutical Applications”

Poorly water-soluble drugs account for 40-70% of newly discovered chemical entities. Our research aims to investigate nanostructure and hybrid materials for controlling the action of gastro-intestinal enzymes to improve the solubilisation of poorly water-soluble drugs in the gastrointestinal tract and the oral bioavailability of a range of active pharmaceutical ingredients. A particular focus is the development of hybrid silica-lipid nanomaterials, and the understanding of internal structure to control the *in vivo* performance and improve the oral delivery efficiency.

Project 2: “Novel Approaches to Improve Oral Protein/Peptide Delivery”

Peptide/protein drugs (biopharmaceuticals) have become increasingly important in modern pharmacotherapy; however, the harsh gastrointestinal tract (GIT, *i.e.* presence of degradative enzymes) and the low permeability of such large molecules across the intestinal mucosa limit their oral delivery efficiency. To overcome the oral delivery challenges, nano- and micron- size carriers with abilities to protect the biological payloads from the harsh environment of the GIT are of great interest. Our research aims to improve the understanding of the uptake and transport of such particulate-carriers through the intestinal epithelium, which will provide important information for advancing the development of efficient delivery systems for oral protein/peptide delivery.

Project 3: “Improving the Oral Delivery of Anti-Psychotic Drugs – Advanced Pharmaceutical Formulation Approaches”

Many of the currently available and new pharmaceutical agents used in the treatment of psychotic conditions (e.g. schizophrenia and depression) are poorly soluble and poorly absorbed upon oral administration. One negative outcome of these drug properties is that the associated medicines are required to be taken either with or within food; this introduces extreme compliance challenges. This project is focused on developing novel solid dosage forms based on lipid encapsulated in porous excipients; these drug carriers optimise the pharmaceutical food effect and facilitate oral medicines without a food effect and hence will potentially increase compliance for patients with psychotic disorders.

Project 4: “Novel Antibiotics – Formulation and Mechanistic Understanding”

Superbugs, in another word, bacterial pathogens resistant to multiple antibiotics, have emerged as one of the pre-eminent public health concerns. Our research aims to develop novel antibiotics which will lower the threat of superbug infections that are not curable by antibiotics commercially available on the market. Two novel antibiotic compounds have been developed, which have shown great potency against Gram-positive and Gram-negative bacteria. The project will focus on the fundamental understanding of the compounds in terms of physiochemical properties, as well as developing prodrugs and advanced delivery systems to facilitate further clinical studies of the optimal novel antibiotics and future clinical applications.

Project 5: “Hybrid Particle Carriers for Antibiotics - Eradication of Bacterial Biofilms”

Biofilms- aggregates of bacteria embedded in slime -are the major cause for recurring diseases such as chronic wound infections, chronic otitis and osteomyelitis. Standard oral antibiotic therapy frequently fails to completely eradicate the biofilm due to the extreme tolerance of bacteria within the protective slime. In this project we combine the benefits of controlled drug release from hybrid polymer/silica based drug delivery systems to target biofilms for their eradication. See additional projects below by Dr Nicky Thomas.

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Email: Clive.Prestidge@unisa.edu.au**Dr Stephanie Reuter Lange (NHMRC Australian Clinical Fellow)**<http://people.unisa.edu.au/Stephanie.ReuterLange>

I am a translational pharmacologist; my research portfolio broadly focuses on using pharmacological principles to inform the optimal use of medications. Through this I work with both pharmaceutical industry and regulatory agencies in the development of new drug entities, as well as clinicians and pharmacists to improve the use of existing drugs for better management of patients in practice.

The success of a drug is dependent on its profile in three primary, inter-connected areas: pharmacokinetics, pharmacodynamics and clinical outcomes. The clinical outcomes of a drug are perhaps the most important, with the balance between the drug's ability to treat the disease/condition whilst maintaining a low incidence of side effects critical to its success in practice. However, this is largely influenced by how the drug interacts with the body's biological processes (i.e. pharmacodynamics), which is in turn affected by the movement of a drug into, through and out of the body (i.e. pharmacokinetics). The selection of treatment strategies for the optimisation of these processes is key for the quality use of medicines; however, for the most part current dosing protocols are largely empirical. My research uses computer-based modelling (pharmacometrics) to characterise drug pharmacokinetic-pharmacodynamic-outcome behaviour, from which highly informed decisions (such as identifying optimal dosing strategies) can be made.

For the most part, my research aims to address the medication issues associated with the sub-optimal use of anti-infective agents and develop rational, evidence-based guidelines for the appropriate prescription of these drugs in clinical practice. However, my research interests extend beyond this to also include cancer chemotherapy, anti-malarial agents, cannabis and caffeine.

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Email: Stephanie.ReuterLange@unisa.edu.au**Dr Julie Stevens (Gastrointestinal Physiology)**<http://people.unisa.edu.au/Julie.Stevens>

My research interests relate to the study of normal and disordered gastrointestinal motility in health and diabetes, with a particular focus on oral drug absorption and glycaemic control. Much of my work has focused on investigations of pharmacological and nutritional interventions on gastric emptying rate, antropyloroduodenal motility and glycaemia in humans, particularly in patients with diabetic gastroparesis. My research incorporates a diverse range of medical imaging methods, including scintigraphy, ultrasonography and manometry, in the measurement of gastrointestinal motility. Other areas of research include pharmacokinetic studies of orally administered agents and their potential use as alternative measures of gastric emptying rate. More recently, my research has concentrated on the physiology of the incretin hormones (GLP-1 and GIP) and the mechanisms by which incretin-based therapies (GLP-1 agonists and dipeptidyl-peptidase-4 inhibitors) improve glycaemic control in diabetes mellitus.

Current projects:

1) Effects of sitagliptin on postprandial glycaemia, incretin hormones and blood pressure in type 2 diabetes – relationship to gastric emptying

The proposed study is designed to (i) evaluate the acute effects of the dipeptidyl peptidase-4 inhibitor, sitagliptin, on gastric emptying, postprandial plasma glucose, insulin, glucagon and 'incretin' hormones (i.e. glucagon-like peptide-1 (GLP-1) and glucose-dependent insulintropic polypeptide (GIP)), blood pressure and heart rate after a high carbohydrate meal, and (ii) to determine whether the magnitude of the effects of sitagliptin on postprandial glycaemia and blood pressure is related to the rate of gastric emptying, in patients with type 2 diabetes.

2) Comparative effects of low-carbohydrate-, full-strength- and low-alcohol beer on gastric emptying, alcohol absorption, glycaemia and insulinaemia in health and type 2 diabetes

Low-carbohydrate beers have become increasingly popular, particularly amongst the young and those of middle-age (with a high prevalence of type 2 diabetes and hypertension) in an attempt to reduce caloric intake, in some cases for health reasons, such as weight loss and/or lowering blood glucose. The rate of stomach emptying is a major determinant of alcohol absorption and the glycaemic response to a meal. The aims of the study are to determine the rate of gastric emptying, blood alcohol concentration and glycaemic response in healthy subjects and patients with type 2 diabetes following ingestion of low-carbohydrate, full-strength and low-alcohol beer.

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Dr Andrea Stringer

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The Mucosal Injury Research Group, currently led by Dr Andrea Stringer, explores primarily the digestive system, and its role in healthy and diseased states. The focus of the group is the toxic effects of cancer treatments on the digestive system, including the role of oral and intestinal microbes, and analysis of new agents to combat these toxic effects.

We can develop projects around the following topics, and can also develop any new ideas:

- *The role of vitamin D in the development of chemotherapy-induced mucositis (Assoc Prof Paul Anderson, Ms Bronwen Mayo)*
- *Development of phytochemicals as anti-inflammatory agents in chemotherapy-induced mucositis (Dr Susan Semple, Dr Brad Simpson, Prof Sanjay Garg, Ms Bronwen Mayo)*
- *Developing beneficial microbial combinations for improving cell damage following chemotherapy (Prof Rachel Gibson, Ms Bronwen Mayo)*
- *The role of gut microbes in neurological disorders (Dr Larisa Bobrovskaya)*
- *The mechanisms of repair following chemotherapy induced mucosal injury*
- *The effect of chemotherapy (CT) on the intestinal microbial ecosystem*

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Dr Vijay Suppiah & Dr Libby Hotham

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Like most developed countries, Australia's population is ageing as a result of sustained low fertility and increasing life expectancy. A "greying" population has many implications, one of which is the impact on healthcare provision. A collaborative and interdisciplinary research approach into healthy ageing, chronic diseases and quality use of medicines in the geriatric population is important now so that we are adequately equipped to meet the challenges for this cohort.

We work collaboratively with Dr Cath Hall from the School of Nursing and Midwifery on various health-related projects in geriatric populations. Our industry partner, Helping Hand, is a major provider of aged care services in South Australia. Currently Helping Hand provides services to over 7,000 older Australians, including residential aged care, retirement living, home care packages, home and community care services.

Impact of global metabolising phenotypes on drug efficacy and adverse events

This project aims to determine the practicalities and feasibility of translating global metabolising phenotype profiles for a common class of medication into personalised care (drug selection and dosing) and the impact on drug efficacy and drug related adverse events. It is proposed that this work would be carried out on elderly Helping Hand residents on multiple medications where it is hypothesized that the clinical utility of global metabolising phenotype profiles would have the greatest impact.

Decision making process in the identification of non-verbal pain cues

In a number of consensus/clinical guideline documents pertaining to the management of pain in older people with cognitive impairments, lists of behavioural/physiological signs of pain such as verbalisations/vocalisations, increased heart rate, sweating, noisy breathing, grimacing, restlessness and agitation, have been reported in order to assist recognition of pain or distress in people who cannot communicate. The aim of this project is to find the evidence base (sources of information) underpinning these lists of behavioural and physiological cues for pain. It is proposed that this project would form the basis for the development of an education strategy for both aged care workers and undergraduate health professionals.

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Dr Nicky Thomas (NHMRC Peter Doherty Biomedical Research Fellow)

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[Adelaide Biofilm Test Facility](#)

Project 1: “The war against superbugs- improving the efficacy of poorly water-soluble antimicrobials”

Many of the currently available antimicrobials show limited water solubility which restricts their wider application against much needed multi-drug resistant bacteria (superbugs). In this project we will reformulate poorly water-soluble antimicrobials and evaluate the efficacy of the developed formulations against free floating and surface attached pathogens (biofilms).

Project 2: “Antibacterial performance of a novel topical gel”

Novel treatment strategies for chronic infections are urgently needed given the wide-spread resistance of currently available antimicrobial therapies in the community. We have synthesized a novel biocompatible polymer that forms gels with built-in antimicrobial activity. This project aims at the biopharmaceutical characterisation of the gels intended for topical application using advanced infection models (e.g. artificial skin, *C. elegans*).

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Dr Agnes Vitry (Senior Lecturer in Health and Society, Quality Use of Medicines, Issues in Contemporary Pharmacy Practice)

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My research interests primarily revolve around

- medicines policies: regulatory approval, funding, pricing, managed entry agreements, affordability, usage, and pharmaceutical promotion;
- quality use of medicines in people with comorbidities: elderly people, people living with cancer, residents of nursing homes.

I am actively involved in the cancer area, both as a researcher on access and use of cancer medicines and as an active member of a leading cancer consumer organisation, Cancer Voices SA.

Projects that I would like to develop further include the valuation and presentation of the therapeutic benefits of new cancer medicines, stakeholders’ preferences for access to cancer medicines, drug use studies, funding of health consumer organisations by the pharmaceutical industry, international comparisons of usage and prices of medicines. Ultimately, these projects aim to improve pharmaceutical policies for access to and quality use of medicines.

Most projects are primarily office based and require good organisation and computing skills.

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Dr Dorota Zarnowiecki (Child Nutrition)

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Dorota's research investigates how we can improve children's nutrition and health, with a focus on improving outcomes in vulnerable and disadvantaged target groups, including socioeconomically disadvantaged families, pregnant women, Aboriginal people and individuals with mental illness. Her current work also involves the development of a novel, short tool to measure food intake in young children as part of the NHMRC funded Centre for Research Excellence for the Early Prevention of Childhood Obesity (CRE-EPOCH: <http://www.earlychildhoodobesity.com/>).

Proposed research projects include:

Overweight and obesity affect 1 in 5 Australian children by the time they start school, largely due to poor nutrition. Children from socioeconomically disadvantaged families are at even greater risk of obesity and poor nutrition, yet socioeconomically disadvantaged families are less likely to participate in nutrition research. To develop nutrition interventions and health promotion campaigns that are effective at improving nutrition and reducing obesity in those who need it most, socioeconomically disadvantaged families, we need to engage them in the research process. Currently much of the research evidence about the effectiveness of nutrition programs is generated from studies involving predominantly families of middle and higher socioeconomic status. We need to improve understanding of how we to engage socioeconomically disadvantaged families in research to deliver nutrition interventions that are acceptable and effective for disadvantaged families. The following two projects are proposed:

1. Making good food and nutrition accessible for all – how can we engage disadvantaged parents in nutrition research?

Co-supervisors: Dr Rebecca Golley, Mrs Chelsea Mauch

The aims of this Honours project will be to understand the reasons why parents of low socioeconomic status (SES) do not participate in research, and ways in which we could better engage low (SES) parents in research.

2. Making good food and nutrition accessible for all – what do disadvantage parents want as an intervention?

Co-supervisors: Rebecca Golley, Dr Lucy Bell

The aims of this Honours project will be to determine what intervention characteristics (e.g. mode/intensity of delivery, use of technology, format, content) parents of low socioeconomic status feel are needed to enable them to increase their children's intake of core foods and reduce intake of unhealthy foods. This project will be conducted using semi-structured interviews and focus groups, in combination with collecting quantitative data from questionnaires.

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