University of South Australia

Bachelor of Biomedical Research (Honours)

Research Booklet 2021

IHBY Bachelor of Biomedical Research (Honours)

Why the IHBY Bachelor of Biomedical Research (Honours)?

Thank you for your interest in undertaking the IHBY Bachelor of Biomedical Research (Honours) within Clinical and Health Sciences at the University of South Australia.

Undertaking an Honours program with UniSA Clinical and Health 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 Unit. 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.

UniSA Clinical and Health Sciences formerly the School of Pharmacy and Medical Sciences 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 Unit, 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.

Program Support Officer:
Ms Hattie Li
Telephone: +61 8 8302 2332
Email: Hattie.Li@unisa.edu.au

IHBY Honours Coordinator:
Dr Kristen Bremmell
Telephone: +61 8 8302 2311
Email: kristen.bremmell@unisa.edu.au

General Enquiries:
CHS-Research@unisa.edu.au

For a general overview of the main research themes across the Unit, please refer to:
https://unisa.edu.au/about-unisa/academic-units/clinical-and-health-sciences/

Acute Leukaemia Laboratory

Acute Myeloid Leukaemia (AML) is the most common form of acute leukaemia in adults, and in children is associated with long-term sequelae, social and emotional issues. 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 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 biological basis for many subtypes is still not well understood, 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 targeting the key biological pathways and transcriptional programs that are essential for AML growth and survival.

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 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 proteomic approaches to identify genes and pathways that contribute to myeloid malignancy. We have identified novel genetic changes associated with childhood AML and new projects in the laboratory will further investigate the role of these, and the potential of these to cooperate with the mutations and gene fusions that characterise childhood AML.

Project 1. The role of the Fanconi Anaemia (FA) DNA repair pathway in AML.

The FA pathway repairs DNA damage caused by endogenous and exogenous aldehydes that lead to inter-strand cross-links in DNA, and is essential in normal blood stem cells to prevent chromosome breaks amd rearrangements and leukaemia development. We hypothesise that rare germline mutations in the FA genes that we have identified in patient samples result in: (i) reduced efficiency of DNA repair, and (ii) an in vivo heterozygous phenotype associated with altered functional properties of blood stem and progenitor cells, and increased susceptibility to AML initiating events. Project work will include using in vitro and in vivo models of FA pathway function, and deficiency, to test the activity of AML mutant proteins.

Project 2: Testing a novel therapy for 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, particularly to treat relapse patients that have dismal outcomes. This project represents a collaborative and cross-disciplinary initiative (with Prof. Thomas Gonda; UniSA) investigating the clinical potential of novel inhibitors of the Myb oncoprotein in AML. Project work will include:

- Testing the activity, sensitivity, selectivity and mechanism of action of novel small molecule MYB inhibitors using AML cell lines, Myb reporter systems, and primary patient samples.
- Use an established xenograft mouse model of MLL-AML to test inhibitors selected based on the assays above.

Project 3: New pathways and targets in AML

The leukaemogenic process is characterised by the accumulation of acquired genetic alterations and epigenetic changes in haematopoietic progenitor/stem cells, which result in the deregulation of cell proliferation, survival and maturation. The use of high-throughput (next-generation) DNA and RNA sequencing in AML patient samples provides a powerful approach to identify the dysregulated pathways that drive AML. We have combined this approach with proteomics allowing an integrated approach for

dissection of AML driver mechanisms and development of new markers for classification and prognosis, and identification of potential therapeutic targets. Project work will include:

- Identification and characterization of changes identified in our AML cohort, including surface proteins and signaling pathways that could be targeted with novel therapeutics.
- Development of bioinformatics approaches to integrate data from multiple "omics" platforms.

Project 4: Understanding the functional significance of GADD45A promoter methylation in AML

GADD45A is a tumour suppressor gene that coordinates cellular stress responses including DNA repair and de-methylation, cell cycle arrest, and pro-apoptotic or pro-survival pathways. Methylation of four discrete CpG (CpG1-4) residues in the distal promoter of GADD45A is a hallmark of many solid tumours and we have shown that this hypermethylation of the promoter of GADD45A is a common event in AML, occurring in 42% of patients. GADD45A hypermethylation is associated with poor survival in AML overall. This project aims to determine the functional significance of GADD45A methylation in AML with a particular focus on the biological mechanism that underlies the poor patient survival.

Project 5: Molecular characterisation of Myeloproliferative Neoplasms (MPN)

MPN are a group of late onset and progressive malignancies characterised by the clonal hyper-proliferation 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 MPN phenotype. Furthermore, treatment with JAK2 inhibitors has shown little evidence of disease-modifying effect so 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 patient outcomes and survival rates. We are investigating the role of altered metabolism in MPN, and AML, with a view to development of approaches that target metabolic vulnerabilities associated with aberrant JAK2 activation and particular initiating mutations in AML. Future work on this project will include:

- Investigation of other the metabolic changes contributing to MPN and AML pathogenesis.
- Testing the effects of metabolic therapies in MPN and AML 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.

For more information on the Acute Leukaemia Laboratory:

Professor Richard D'Andrea (Professor of Leukaemia Biology)
Telephone: +61 8 8302 1230
+61 8 8302 7826
Email: Richard.Dandrea@unisa.edu.au
Debora.Casolari@unisa.edu.au
Saumya.Samaraweera@unisa.edu.au
Sheree.bailey@unisa.edu.au

http://www.centreforcancerbiology.org.au/members/richard-dandrea/
http://www.centreforcancerbiology.org.au/research/laboratories/acute-leukaemia-laboratory/

Australian Centre for Precision Health

Level 8 SAHMRI Building, North Terrace, Adelaide
+ 61 8 830 21153
acpreh@unisa.edu.au

Several projects are offered by researchers at the **Australian Centre for Precision Health** (ACPreH), which is a multi-disciplinary Centre consisting of many world-leading researchers and located at the SAHMRI campus. There is a vibrant and collegial academic atmosphere at ACPreH with a mix of Honours and HDR students, early-to-mid career researchers and senior researchers. The student will have the opportunity to attend the monthly ACPreH seminar, and other networking and professional development events.

Project title
How fatigue impacts upon the ability of military personal to effectively function under stressful operational conditions
Identifying new genes in neurological disorders
Identifying novel genes that play a role in the development of addition to methamphetamine
Improving our understanding of pain and its treatment
Investigating causes of SIDS, Rare childhood diseases and sudden unexplained infant death
Physical activity and brain atrophy: a large-scale study
Population semi-PBPK models for cost-effective drug development
Precision use of biological DMARDs in autoimmune diseases
Quantitative description of the cardiovascular system
Role of pharmacogenomics on multi-morbidity
Safety profile of selenium supplementation: A phenomewide Mendelian randomization study in the UK Biobank
Suicide Prevention and Mental Health Diagnostics and Treatment
The gene for speed and health: phenomewide association study on *ACTN3*
The quality use of medicines
Therapeutic Drug Monitoring (TDM), Target concentration Intervention (TCI) and Bayesian forecasting
Using Drosophila and cell biology to understand the biology of neurological disorders

How fatigue impacts upon the ability of military personnel to effectively function under stressful operational conditions.

This work is 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).

For more information:

Dr Chris Della Vedova Email chris.dellavedova@unisa.edu.au Tel +61 8 830 22267

Identifying new genes in neurological disorders

We have a large number of families and patients affected with various forms of, for example, epilepsy, autism and other neurological conditions 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. We have developed a range of novel bioinformatic tools to investigate genetic variation across families and cohorts and have projects in both molecular genetics as well as bioinformatics and computational biology.

For more information:

Prof Leanne Dibbens Email Leanne.dibbens@unisa.edu.au Tel +61 8 830 21124
Dr Michael Ricos Email Michael.ricos@unisa.edu.au Tel +61 8 830 21525

Identifying novel genes that play a role in the development of addition 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.

For more information:

Dr Chris Della Vedova Email chris.dellavedova@unisa.edu.au Tel +61 8 830 22267

Improving our understanding of pain and its treatment

Pain and its perception is a complex process, with many factors contributing to wide variability between people. Our group has a long history of applying modelling and simulation techniques to better understand the pharmacokinetics and pharmacodynamic (both desirable and undesirable) effects of opioid drugs and their impact on pain. Our work spans modelling using conventional and physiologically-based pharmacokinetic analyses for a range of opioid drugs, and linking these to effects ranging from analgesia to EEG evoked potentials.

For more information:

A/Prof David Foster Email David.foster@unisa.edu.au Tel +61 8 830 22055
Prof Richard Upton Email Richard.upton@unisa.edu.au Tel +61 8 830 22380

Investigating causes of SIDS, Rare Childhood diseases & Sudden Unexplained Infant Death

For many parents the death of a young or newborn child is a tragic loss which is often compounded by the incomplete understanding of the causes of death. This often leaves more questions than answers and being able to understand why this death has occurred is critical for both the family and the treating clinicians. We take on cases of both sudden infant death and severe forms of early onset diseases where there is little hope for cure of treatment. We employ our range of genetic & genomic, bioinformatic, biochemical and metabolic techniques to solve these difficult cases. We work closely with both families, doctors and forensic pathologists to uncover clues and solve these molecular mysteries. We have a range of honors and PhD projects in this area.

For more information:

Prof Leanne Dibbens Email Leanne.dibbens@unisa.edu.au Tel +61 8 830 21124
Dr Michael Ricos Email Michael.ricos@unisa.edu.au Tel +61 8 830 21525

Physical activity and brain atrophy: a large-scale study

Physical activity is important for brain health, and it can help to reduce the risks of cognitive decline and dementia. This study will be based on information from UK Biobank, which is the world's largest population-based study with MRI measures. The aim is to investigate the association between various aspects of physical activity and inactivity with brain neuroimaging abnormalities, including white matter hyperintensities, atrophy in selected regions of the brain and finally, the incidence of dementia and stroke. Information on various aspects of physical activity and disease outcomes is available for the whole cohort (N~502,000) while the imaging study has to date been completed in 40,000 participants. There is an opportunity to provide two projects for students who prefer to work as a team, when the methodologies to be used will be extended to cover genetic approaches and possibly, a systematic review.

This is an exciting opportunity for a high performing student to join the Nutritional and Genetic Epidemiology group based at the SAHMRI campus. The student will need to be research orientated and interested in developing strong skills in statistical analyses and research reporting. The student will be supported through the data analyses, and it is expected that the project will lead to publication of at least one research paper in a rebuttable journal.

For more information:

Professor Elina Hyppönen	Email elina.hypponen@unisa.edu.au	Tel +61 8 830 22518
Dr Terry Boyle	Email terry.boyle@unisa.edu.au	Tel +61 8 830 21143

Population semi-PBPK models for cost-effective drug development

While the oral route remains the preferred mode of administration, it comes at a cost because drug absorption is a highly complex process due to the impact of physiologic variables, such as GI pH and motility, which are highly variable between species and individuals. The application of population semi-PBPK models that incorporate representations of these key factors affecting oral kinetics is pivotal to guiding drug development by predicting what will happen in humans from early pre-clinical data. However, high quality information for standard species (rat, mouse, dogs, human) used in preclinical development is currently lacking in the literature. A range of projects are available in this area to facilitate the implementation of population semi-PBPK models to inform drug development, design future studies, or provide guidance on the clinical use of drugs. Prospective students would require interests in pharmacokinetics and quantitative meta-analysis of literature data.

For more information:

A/Prof David Foster	Email David.foster@unisa.edu.au	Tel +61 8 830 22055
Prof Richard Upton	Email Richard.upton@unisa.edu.au	Tel +61 8 830 22380

Precision use of biological DMARDs in autoimmune diseases

Several biological disease modifying anti-rheumatic drugs (bDMARDs) are approved for use in patients with autoimmune diseases such as rheumatoid arthritis, psoriatic arthritis and Crohn's disease. While effective, bDMARDs are associated with considerable cost, and the therapeutic and toxic responses to these agents can be highly unpredictable. Prognostic tools allow the presentation of personalised likelihoods of response and adverse effects to medicines. Such information allows informed treatment decisions to be made. The data with which the prognostic tools are made are typically "big data". At present we have access to individual participant data from over 20,000 patients treated with various bDMARDs for various autoimmune diseases. A range of analyses and projects are available in these medicines. Prospective students would require an interest in precision medicine and clinical epidemiology.

For more information:

A/Prof David Foster	Email David.foster@unisa.edu.au	Tel +61 8 830 22055
Prof Richard Upton	Email Richard.upton@unisa.edu.au	Tel +61 8 830 22380

Quantitative description of the cardiovascular system

The cardiovascular system is complex, and changes to one part of the system (eg contractility of the heart) affecting the whole system (eg blood pressure) through homeostatic feedback loops. As a result, traditional analyses treating cardiovascular measurements as independent factors can lead to less than optimal conclusions about the impact of treatments, the understanding of how a medicine "works" in and the best way use it. This project aims to further refine a population model of the cardiovascular system we have developed using animal and human data. It will facilitate a deeper understanding of the variability in response to cardiovascular medicines, facilitate future clinical trial design and interpretation of the results, and assist with drug development.

For more information

A/Prof David Foster	Email David.foster@unisa.edu.au	Tel +61 8 830 22055
Prof Richard Upton	Email Richard.upton@unisa.edu.au	Tel +61 8 830 22380

Role of pharmacogenomics on multi-morbidity

Medications used in the treatment of many conditions do not always work for every patient. One of the factors that determine this variability in treatment outcomes, such as response and adverse effects, is the patient's genetic make-up. This effect is then multiplied once multiple medications are added to the mix. This project aims to elucidate the role of pharmacogenomics in patients who take multiple medications for the treatment of multiple conditions.

For more information:

Dr Vijay Suppiah	Email vijay.suppiah@unisa.edu.au	Tel +61 8 830 21130

Safety profile of selenium supplementation: A phenomewide Mendelian randomization study in the UK Biobank

Selenium is a trace element nutritionally essential for humans. Despite its antioxidant properties and protective effects on DNA repair, apoptosis, and the endocrine and immune systems reported in animal models, health effects of selenium supplementation in human studies is still inconclusive. This project will use large-scale epidemiological data to establish the safety profile of selenium supplementation.

You will be using the state-of-the-art technique, 'Mendelian Randomisation' (MR), which is also called nature's randomised controlled trial (RCT), to examine the health effects of selenium supplementation. One of attractive features with this approach is that rather than directly exposing participants to selenium supplements, MR uses genetic variants influencing plasma concentration of selenium as a proxy for exposure to selenium supplements, avoiding safety issues with traditional RCTs. Therefore, health effects of selenium supplementation is inferred by examining the association of 'selenium variants' with the disease outcome of interest. By coupling a MR study with phenome-wide outcome data constructed using health records from hospital and death registry, you will be able to examine the health effects of selenium supplementation across a broad spectrum of phenotypes, building more comprehensive safety profiles related to selenium supplements intake.

This project is well suited for a high performing student who enjoys writing and who is considering post-graduate studies. The student will learn skills in genetic epidemiology, and data analyses. She/he will receive extensive guidance and support through the project, data analyses and reporting with a view of producing at least one high quality scientific publication.

For more information:

Professor Elina Hyppönen	Email elina.hypponen@unisa.edu.au	Tel +61 8 830 22518
Dr Ang Zhou	Email ang.zhou@unisa.edu.au	Tel +61 8 830 20286

Suicide Prevention and Mental Health Diagnostics and Treatment

Until now the task of identifying people who are at risk from developing certain mental illnesses has been a difficult one that could only be done after people experienced severe symptoms of mental illness. Our team has developed a novel modelling methodology to identify diagnostic tools that could give clues as to who is at risk of mental illness before they experience symptoms. We employ genetic, genomic, metabolic, biochemical and behavioural modeling parameters to develop our diagnostic and prognostic tools. We have projects in collaboration with Clinical Psychiatrists and Mental Health Nursing and Suicide Prevention experts to develop and evaluate these tools. Mental health is an ever more important area of research and healthcare that will grow in the future.

For more information:

Prof Leanne Dibbens	Email Leanne.dibbens@unisa.edu.au	Tel +61 8 830 21124
Dr Michael Ricos	Email Michael.ricos@unisa.edu.au	Tel +61 8 830 21525

The gene for speed and health: phenomewide association study on ACTN3

One of the most promising candidate genes for sport performance is ACTN3 which is also called as the 'gene for speed'. This variant is often found in top athletes and there is evidence to suggest that a common variant in ACTN3 is associated with improvements in muscle strength, and that it helps to protect from sports injuries and training-induced muscle damage. This study aims to look at whether this common variant in ACTN3 is associated with differences in objectively measured physical activity levels at middle- to older age adults, and further, whether this variant has any broader effects on their future health outcomes, based on information on hospitalisations and mortality registrations.

To address the second part of the aim, the successful candidate will be conducting a phenome-wide association study (PheWAS), in which health effects of *ACTN3* will be evaluated by examining the association of the variant with outcomes across the 'Phenome', constructed using health records from hospital and death registry. The PheWAS approach represents the most comprehensive way of evaluating health effects of an exposure of interest, and therefore this project will offer you an exciting opportunity to build a complete picture of health benefits and consequences associated with the *ACTN3* variant.

This project is well suited for a high performing student who enjoys writing and who is considering post-graduate studies. The student will learn skills in genetic epidemiology, and data analyses. She/he will receive extensive guidance and support through the project, data analyses and reporting with a view of producing at least one high quality scientific publication.

For more information:

Professor Elina Hyppönen	Email elina.hypponen@unisa.edu.au	Tel +61 8 830 22518
Dr Ang Zhou	Email ang.zhou@unisa.edu.au	Tel +61 8 830 20286
Dr Terry Boyle	Email terry.boyle@unisa.edu.au	Tel +61 8 830 21143

The quality use of medicines

A number of projects to be developed covering such topics as:

- 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.

For more information:

Dr Agnes Vitry	Email agnes.vitry@unisa.edu.au	Tel +61 8 830 22389

Therapeutic Drug Monitoring (TDM), Target concentration Intervention (TCI) and Bayesian forecasting

Therapeutic drug monitoring (TDM) uses measured drug concentrations with clinical interpretation to adjust dosing regimens. However, for some drugs the complex relationship between pharmacokinetics and individual patient factors, interpreting and deciding upon the appropriate regimen is often not straightforward. Bayesian forecasting provides a mathematical method for selecting a dose regimen by considering previous experience ("the prior") and observations ("the new data"), where the prior is structured in the form of a population pharmacokinetic and/or pharmacodynamic model, thus removing much of the "guess work".

For more information:

A/Prof David Foster	Email David.foster@unisa.edu.au	Tel +61 8 830 22055
Prof Richard Upton	Email Richard.upton@unisa.edu.au	Tel +61 8 830 22380

Using Drosophila and cell biology 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. We also have PhD track projects for highly advanced and skilled students to learn electrophysiology to dissect the effects of ion channels and gene mutations in cells, isolated Drosophila neurons and whole organisms.

For more information:

Prof Leanne Dibbens	Email Leanne.dibbens@unisa.edu.au	Tel +61 8 830 21124
Dr Michael Ricos	Email Michael.ricos@unisa.edu.au	Tel +61 8 830 21525

Bioengineering Research Group

The Bioengineering group is led by Prof Benjamin Thierry. It is a node of the ARC Centre of Excellence for Convergent Bio-Nano Science and Technology and funded by the NHMRC, ARC and the Bill and Melinda Gates research Foundation. Our research is highly interdisciplinary and integrate cutting-edge technologies towards addressing significant biomedical problems, including: 1. Cancer diagnostic and image-guided surgery/therapy; 2. Precision cancer radiotherapy; 3. CAR T cell manufacturing; 4. Prenatal diagnostic and care; 5. Point-of-care biodiagnostics.

The translational focus of the group is illustrated by the establishment of Ferronova Ltd, a spin-off company aimed at improving the staging of solid tumours (Oral cancer, prostate cancer and colorectal cancer) through improved imaging. Ferronova has received over $3.5 million in investment and is currently conducting/planning several clinical trials in Australia and the US. Several other technologies developed within the group are at various stage of translation, including our cell-based non-invasive prenatal testing with comprehensive genomic coverage (NIPDx), our Point-of-Care blood biomarker platform (supported by the Medical Device Partnering Program), and our CAR T cells manufacturing technology (collaboration with Carina Biotech).

Scholarships are available for high performing students interested in an Honours research project in bioengineering. Projects available for Hons includes (but are not limited to – come and talk to us!):
Development of a blood micro sampling/processing cartridge for point of care diagnostic of pregnancy complications. We have recently developed a prototype of a point of care preeclampsia diagnostic technology (read more in the Herald Sun). This is significant as the condition is the direct cause of death for over 500,000 infants and 76,000 pregnant women, mostly in low resource countries. Despite its

significance and global prevalence, effective diagnosis of preeclampsia remains a challenge and our technology based on solid-state sensing nanotechnology can measure blood biomarkers with very high sensitivity. An integral part of decentralized testing for diagnostic biomarkers is the ability to accurately sample and process finger-prick blood without using any of external equipment. The Honours project will aim to develop a blood collection/processing device using for example 3D printing and to validate its performance with clinical samples. **Contact**: Dr Duy Tran.

Improved manufacturing of CAR T cells using "Sleeping beauty" Transposons. Inspired by outstanding response rates in acute lymphoblastic leukemia, T-cells genetically modified with Chimeric Antigen Receptors (CARs) are actively being developed for treating solid cancers. However, viral manufacturing of CART- cells is well recognized as a major bottleneck limiting their wide scale implementation. Cutting-edge non-viral methods, such as the piggyBac transposon system offer simpler and more cost-effective alternatives to viral vectors but still require electroporation for efficient gene delivery. However, electroporated cells typically suffer from decreased viability and/or functionality. Better manufacturing protocols towards clinical trialling of CART-cells are therefore needed. To this end, this Hons project will develop a novel concept of microfluidic transfection with the "sleeping beauty" transposon system towards enabling high throughput manufacturing of CART-cell therapies for blood cancer and head and neck cancer. **Contact**: Dr Michelle Maritz (or Prof Benjamin Thierry until February 2021).

Nano-formulation of kinase inhibitors. Kinase inhibitors target specific intracellular pathways and are actively being investigated towards better cancer therapy. However, kinase inhibitor therapy is associated with serious and dose-limiting side effects. The formulation of kinase inhibitors within nanomedicine is a promising approach towards improving their therapeutic index. The student will work closely with PhD students to optimize the formulation of various kinase inhibitors within nanoparticles targeted to cancer tissues. He/she will be exposed to advanced formulation principles (microfluidic technologies, hydrophobic ion pairing etc) as well as biological evaluation within patient derived tumour organoids. **Contact**: Dr Nicole Dmochowska.

Towards molecular imaging-guided cancer treatment. There is an urgent need to develop better targeted cancer treatment, including for surgery and radiotherapy. The implementation of cutting-edge molecular imaging approaches into treatment algorithms has strong potential to both improve their overall efficacy and decrease morbidity and long-term side-effects. In collaboration with Ferronova and researchers at the University of Queensland, we are developing molecular contrast agents able to guide surgery/radiotherapy using Magnetic Resonance Imaging. The specific focus of the Hons project will be on prostate cancer. The student will join an interdisciplinary research team and focus on the biological evaluation of the molecular contrast agents, including in preclinical models. **Contact**: Dr Nicole Dmochowska.

Advanced bioengineered models of the placenta and its dysfunction during preeclampsia. Preeclampsia affects 5-8% of pregnancies and is associated with placental and endothelial dysfunction. The precise mechanisms that trigger and lead to these dysfunctions vary widely and are not well understood. Bioengineered *in vitro* culture models ("Placenta-on-a-chip") provide a dynamic and more physiologically relevant environment for cells, compared to conventional 2D cell culture. In this project bioengineered models of the maternal-fetal interface will be developed and used to study the function and dysfunction that occurs in normal pregnancy and preeclampsia, respectively. **Contact**: Dr Marnie Winter.

Non-invasive insight into pregnancy health and disease through placental extracellular vesicles. Secreted by many cell types under both physiological and pathological conditions, extracellular vesicles (EVs) are small membrane-bound cargos capable of carrying signalling molecules which play important roles in intercellular communication. During pregnancy the placenta secretes EVs which can be found in low numbers in the mother's blood stream. These placental EVs help maintain the communication

between the fetus and mother as well as regulate many immunological mechanisms in pregnancy by interacting with immune and endothelial cells and an abnormal profile may indicate problematic development. Isolation of specific placental EVs remains a challenge with standard approaches. However, the combination of cutting-edge EV isolation techniques with transcriptomics and proteomics has strong potential to provide significant new insights into pregnancy health and disease. In this project, a state-of-the-art EV isolation approach will be combined with transcriptomics to investigate RNA profiles from placental EVs throughout pregnancy. **Contact**: Dr Marnie Winter.

For more information on projects available, please contact:
Professor Benjamin Thierry / Tel: 83023689 / Benjamin.thierry@unisa.edu.au

Bioinorganic Synthesis and Imaging Group

The Bioinorganic Synthesis and Imaging group is focused on advancing knowledge in biology and improving health. The group is focused on developing new fluorescent and luminescent molecules for diagnosis, understanding the roles of lipids in cancer progression and advancing technologies for the delivery of clean water. This is a multi-disciplinary research group with a wide variety of collaborators ranging from postdoctoral fellows to industry partners.

Associate Professor Sally Plush (Fluorescent probes, sensors and water purification)
http://people.unisa.edu.au/Sally.Plush
Associate Professor Plush is a bioinorganic chemist with strong interdisciplinary interests in synthetic organic and inorganic chemistry, lipid biology and cancer. I have spent many years developing new fluorescent and luminescent molecules whose interactions (lipid binding) or function (anticancer, antimicrobial activity) within the cell is characterised using a variety of advanced imaging techniques. I also leverage my expertise in chemistry and the understanding of small molecular interactions to deliver innovative solutions to water remediation that eliminate the presence of cancer-causing chemicals in water.

Dr Shane Hickey (Synthetic medicinal chemistry)
https://people.unisa.edu.au/Shane.Hickey
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 strong interests in developing new potent antimicrobial agents, fluorescent biosensing devices and theranostic compounds which are capable of both diagnosing and treating diseases.

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.

Cancer diagnosis
Cancer is one of the leading causes of death in Australia. Altered lipid distribution and metabolism are hallmarks of cancer pathogenesis and oxidative stress can mediate cancer initiation and drive cancer

progression.

In situ diagnosis of altered metabolism: This project will develop a compact fibre optic sensor that allows in vivo and real-time measurements of the markers of altered metabolism: REDOX, pH and ROS in cancer tissue. The collection of this information will be used to build a 'fingerprint' of cancer activity, which we will relate to different stages of cancer growth, allowing for rapid diagnosis.

Fingerprinting lipids: This project will work in collaboration with Professor Hoffman's team will develop lipid profiles of a range of tissues and relate this knowledge back to disease progression. In this study we also propose to use lipid specific fluorescent probes (sourced from ReZolve Scientific) to develop a fluorescent fingerprint as a green, lower-cost, high throughput accurate method for understanding metabolic networks.

Students who choose to undertake a cancer diagnosis project can expect to become proficient in key skills related to a variety of areas including analytical chemistry (mass spectrometry), imaging (confocal and fluorescence) and physics (fibre optic preparation and use).

Medicinal Chemistry

Medicinal chemistry is the cornerstone of the pharmaceutical industry. A synthetic medicinal chemist has a wide range of organic chemistry and analytical skills which can be applied to tackle any disease of interest. Our research group has specific focuses in the cancer and antibiotic arenas where there is a constant need to develop new drugs for effective treatment.

New Classes of antimicrobials Antibacterial resistance continues to remain an imminent threat and by 2050 is predicted to be the direct cause of 10 million deaths annually; *more than cancer*. This research aims to develop new types of antibacterial compounds which act against bacteria in ways which are difficult for the bacteria to develop resistance against.

Theranostic agents The emerging field of theranostics offer medical science new systems where diseases can be *detected* and *treated* simultaneously. Our research group looks at applying these types of systems to diagnose and treat cancer and reactive oxygen species (ROS)-related diseases.

Students who choose to undertake a medicinal chemistry project 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.

Clean water

Develop enhanced filtration device 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.

Detection and remediation of water contaminated with perfluorinated substances This project will introduce cost-effective technologies for sensing and removal of perfluorinated alkyl substances (PFAS) from water. Defense forces commonly use firefighting measures that release PFAS into the environment, so cost-effective technologies are needed to remove it from water. This project works closely with Flinders University and field work is expected to be part of this project.

Development of water-soluble luminescent cation sensors The presence of harmful impurities in drinking water has been attributed to an array of serious human health diseases and is particularly evident in under-developed countries. Included in this group of toxic substances are cationic metal ions, which when present in high concentrations, can have devasting effects of human and animal health. Graphene quantum dots (GQDs) are a relatively new class of water-soluble luminescent material which can be used for a variety of chemo-sensing applications. This project aims to append known cationic trapping groups to the GQD framework as a means to detect and report the presence of harmful cations

in water systems.

Students who choose to undertake a project focused on delivering clean water can expect to become proficient in key skills related to sensor development, carbon block preparation and analytical chemistry (spectroscopy, GC, HPLC).

For more information on the Bioinorganic Synthesis and Imaging Group:
Associate Professor Sally Plush (Research Group Leader)
Telephone: +61 8 8302 2586
Email: Sally.Plush@unisa.edu.au

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, bone growth and repair;
2. Roles of neurotrophic factors in regulating skeletal cell formation, bone remodelling and bone healing;
3. Mechanisms for injury-induced growth plate cartilage degeneration and bone growth defects;
4. Development of growth factor/hydrogel composites for growth plate cartilage regeneration;
5. Pro-inflammatory cytokine – NF-κB signaling in osteoclast formation and bone loss after cancer chemotherapy;
6. Roles of Wnt/β-catenin signaling in cancer chemotherapy-induced bone loss and marrow adiposity;

7. Roles of oxidative stress in bone loss following cytotoxic chemotherapy;
8. Skeletal cell apoptosis and molecular signals for osteoclastic bone resorption following cancer chemotherapy;
9. Prevention of bone loss caused by cancer chemotherapy;

For more information on the Bone Growth and Repair Research Group:
Professor Cory Xian (Research Group Leader)
Telephone: +61 8 8302 1944
Email: cory.xian@unisa.edu.au
http://people.unisa.edu.au/Cory.Xian
http://www.unisa.edu.au/Research/Health-Research/Research/Bone-Growth-and-Repair-Research-Group/

Centre for Cancer Biology

http://www.centreforcancerbiology.org.au/students/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, largely situated in the UniSA Cancer Research Institute Building.

CCB laboratories carry out research across a broad spectrum of solid and blood cancers, focusing on the specialised areas of gene regulation, cell 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.

CCB Research Laboratories

Each CCB laboratory offers exciting opportunities for Honours students. Some of these are listed below. For full laboratory details and more project details visit our website: http://www.centreforcancerbiology.org.au/research/laboratories-overview/ or contact the relevant CCB laboratory leaders or CCB Operations Manager, Tim Murphy (tim.murphy@unisa.edu.au).

Acute Leukaemia Laboratory led by Professor Richard D'Andrea and Associate Professor David Ross Studies the genetic and epigenetic mechanisms involved in normal blood cell development and the changes associated with acute myeloid leukaemia, myeloproliferative neoplasms, and other haematological malignancies.

Allergy and Cancer Immunology Laboratory led by Dr Damon Tumes (Laboratory Head) and A/Professor Harshita Pant (Clinical Lead)

Projects:

1) **Epigenetic regulation of lymphocyte differentiation and function.** We are using modern technology including chromatin immunoprecipitation/next generation sequencing (ChIP-Seq) and CRISPR gene targeting to define novel regulatory mechanisms controlling inflammation.

2) **Understanding the molecular basis of allergic disease.** We are defining novel pathways causing eosinophil accumulation and tissue destruction that may explain the spectrum of disease severity in allergic asthma, atopic dermatitis and nasal polyposis. Techniques include single cell RNA-Sequencing, spatial transcriptomics and flow cytometry.

3) **Harnessing the pro-inflammatory power of allergic-causing cells to treat cancer.** This project aims to define the role of T cells and eosinophils in head and neck squamous cell carcinoma to support the development of new therapies. Techniques include single cell RNA-Sequencing and flow cytometry.

For more information please contact Damon Tumes
Telephone: 83029016
Email: damon.tumes@unisa.edu.au
https://people.unisa.edu.au/Damon.Tumes
https://www.centreforcancerbiology.org.au/research/laboratories/allergy-and-cancer-immunology-laboratory/

Cell Signalling Laboratory led by A/Professor Yeesim Khew-Goodall
(yeesim.khew-goodall@unisa.edu.au)
Identifying targets to overcome chemoresistance in breast cancer.
Our laboratory has identified signalling pathways controlled by reversible phosphorylation that regulate how secreted growth factors, cytokines and cell surface receptor tyrosine kinases (RTKs) are trafficked. These signalling pathways play a critical role in controlling the sensitivity of triple negative breast cancers (TNBCs) to chemotherapy, which is the first line of therapy for TNBCs. However, about 20-25% of TNBCs are/become chemoresistant and for whom there are few other treatment options, making this a critical unmet need. We have projects to elucidate the mechanisms underpinning how these signalling pathways control chemoresistance in TNBC as well as projects to elucidate how these signalling pathways regulate RTK trafficking to impact on the aggressiveness of cancers. We utilise a range of platforms for our research, including molecular biological, biochemical and cell biological (including advanced microscopy).

Cellular Stress and Immune Response Laboratory led by Dr Nirmal Robinson
(nirmal.robinson@unisa.edu.au)
A successful survival of an organism depends on how well it adapts to different stress. Cells survive insults by mounting specific repair mechanisms such as oxidative stress response, unfolded protein response (UPR), and DNA damage response (DDR) which aid in regaining normal physiology. When they fail to restore homeostasis, they undergo cell death or they survive in a maladaptive phase resulting in pathologies such as malignancies, neurodegenerative, cardiovascular and metabolic disorders. In our lab we investigate the function of these stress responses in innate immune defences, in the context of pathologies such as cancer and infection which will help in understanding disease pathogenesis and present novel targets for therapeutic treatments.

Cytokine Receptor Laboratory led by Professor Angel Lopez
(angel.lopez@sa.gov.au)
Cytokine receptors transmit signals between the extracellular environment and the cell's internal machinery and cause cells to respond in a variety of ways such as maintenance of viability or proliferation. Abnormalities including enhanced cell viability or survival, and increased cell proliferation are hallmarks of cancer.
Our laboratory seeks to understand the mechanism of cytokine receptor activation, in particular GM-CSF, IL-3 and IL-5 receptors, in health and disease. This will reveal universal biological rules and allow the development of new drugs for diseases such as leukaemia, asthma and arthritis.

Our research program includes structural biology approaches to elucidate the structure and function of these receptors; and functional and proteomics approaches to elucidate the signalling mechanisms and functional consequences of cytokine receptor engagement. Current projects include; Establishing the biological significance of increased IL-3 receptor expression in leukaemia; Dynamic assembly of the human GM-CSF receptor and role in signalling initiation; The human GM-CSF and IL-3 receptor signalling complexes; and Characterising downstream effectors of sphingosine and determining their role in cancer biology.

Gene Regulation in Cancer Group led by A/Prof Philip Gregory
(philip.gregory@unisa.edu.au)
With a particular focus on breast and prostate cancers (the two most common cancers in women and men) we seek to understand how cancer cells gain aggressive features that ultimately lead to therapy resistant and metastatic disease. During cancer progression, cancer cells undergo significant changes in their cell structure and invasive ability. These cellular changes are caused by alterations in both coding and non-coding RNAs.
Our goal is to identify key molecular mechanisms driving the development of aggressive breast and prostate cancer. We use a range of advanced molecular techniques including microRNA profiling, transcriptomics, and CRISPR based genome editing to identify important genes causing cancer aggressiveness.

Gene Regulation Networks Group led by Dr Cameron Bracken
(cameron.bracken@unisa.edu.au)
Dr Bracken's laboratory focuses on the mechanisms through which networks of genes are regulated in breast cancer. His laboratory is especially interested in the role of microRNAs and the "rules" by which they choose the genes that they target. There are also ongoing projects in less well characterized aspects of microRNA biology such as microRNA co-operatively, what role they play in the nucleus and what is the effect of naturally occurring microRNA sequence variants. Many of these projects are performed within the context of Epithelial-Mesenchymal Transition (EMT), a reversible phenotypic switch that is essential throughout development and for various processes in the adult, but which also drives human pathologies such as metastasis where its inappropriate activation promotes cancer motility. These projects typically blend wet bench experimentation and bioinformatic analysis to provide a systems-level view of gene expression and the roles played by microRNAs in gene regulation.

Leukaemia Unit, Molecular and Genetic Pathology Laboratory led by Professor Susan Branford
(susan.brandford@sa.gov.au)
Investigating the molecular response to therapy of patients with chronic myeloid leukaemia and the mechanisms of drug resistance.
We are investigating the response to therapy by examining the genetic abnormality that causes chronic myeloid leukaemia: the BCR-ABL1 gene. Specific therapy targets and kills the leukaemic cells containing BCR-ABL1. We monitor the kinetics of drug response by using molecular techniques to measure the levels of BCR-ABL1 mRNA. A rapid reduction of BCR-ABL1 is associated with the best long-term outcome, although this occurs in a minority of patients. We are investigating whether the heterogeneity of drug response is associated with variation in genes that initiate leukaemic cell death.
A major interest of ours is the sensitive detection of mutations within the BCR-ABL1 gene and genome-wide deep sequencing for the detection of mutated genes that lead to disease progression. We are currently developing techniques for the detection of an ultra-rare leukaemic signature using deep sequencing with single molecule barcodes. The aim is to determine if there is a level of leukaemia below which patients can safely cease drug therapy without rapid relapse.
Current research projects include characterising the rate of leukaemic cell death and the heterogeneity of response to tyrosine kinase inhibitor therapy; and defining the role of additional genomic mutations discovered in BCR-ABL1expressing cells.

Lymphatic Development Laboratory led by Professor Natasha Harvey
(natasha.harvey@unisa.edu.au)
Lymphatic vessels are a crucial component of our cardiovascular system. These specialised vessels control fluid homeostasis, lipid metabolism and immune cell trafficking throughout our bodies. My research goal is to understand how lymphatic vessels are built during development and how this process goes wrong in human diseases including vascular malformations, lymphoedema and cancer. Current projects:

1. Understanding the genetics of human lymphatic vascular disease. We have identified mutations in several novel genes that cause foetal death due to profound lymphatic vessel defects. This project will define the role of these genes in lymphatic vascular development and investigate the mechanisms by which mutations cause disease.
2. Defining gene function in valve development. Lymphatic valves, like venous and cardiac valves, are crucial for lymphatic vessel function. This project will define the roles of novel genes we have identified during valve development.

Molecular Pathology Research Laboratory led by Professor Hamish Scott
(hamish.scott@sa.gov.au).
We are interested in how and why genetic mutations occur, how these changes cause diseases or disease predisposition such as cancer and autoimmunity, and ways of better treating and monitoring these diseases. Our model diseases are typically, blood cell diseases, such as leukaemias, lymphomas and autoimmunity (such as arthritis). We also work on rare or orphan diseases with unmet clinical needs, such as genetic diagnoses for family planning.
Our laboratories are co-located with the ACRF Cancer Genomics Facility, which provides access to powerful cutting edge genetic/genomic technologies including bioinformatics, next-generation sequencing (NGS) and sample preparation robotics. We perform both basic and translational research, which includes implementing these new technologies into its diagnostic tests for personalized medicine. Current projects include Genetics and pathologic mechanisms of haematological malignancy (HM = leukaemia and lymphoma) predisposition and progression; Diagnostic implementation of NGS for personalised medicine; and Genetic autopsy of perinatal death: diagnosis and discovery by whole genome sequencing.

Molecular Regulation Laboratory led by Professor Sharad Kumar
(sharad.kumar@unisa.edu.au)
Focusing on the cellular and molecular mechanisms underlying cancer and other diseases. We study how cell death and ubiquitination control cell homeostasis during development and in disease. We use multiple model systems to study chromosomal instability and aneuploidy, protein trafficking and extracellular vesicles, salt homeostasis and kidney disease, and the mechanisms and regulation of autophagy and cell death.

Molecular Signalling Laboratory led by Professor Stuart Pitson
(stuart.pitson@unisa.edu.au)
Examining the molecular mechanisms driving the formation, growth and therapeutic resistance of brain tumours and acute myeloid leukaemia, and how this can be targeted for therapeutic benefit. We study these cancers using the most advanced models, capitalizing on our access to patient tumour material and cutting-edge approaches to growth these tumour cells in the laboratory and in mice.

Neurovascular Research Laboratory led by A/Professor Quenten Schwarz
(quenten.schwarz@unisa.edu.au)
Advancing the understanding of cellular interactions that control tissue morphogenesis during embryonic and postnatal development. We particularly focus on defining the molecular pathways through which the neuronal and vascular systems coordinate formation of the brain, craniofacial skeleton, heart, skin

and peripheral nervous system. Our work impacts on understanding the origins and treatment of common congenital birth defects and childhood cancers.

Tissue Architecture and Organ Function Laboratory led by Dr Guillermo Gomez (guillermo.gomez@unisa.edu.au)
Physical forces are a key determinant of tissue architecture controlling cellular behaviours that range from the differentiation of stem cells to cell transformation and cancer invasion. We have made significant progress in understanding the mechanisms involved in capacity of the cells to generate forces and the regulation of epithelial organization. We now are using this knowledge to understand how dysregulation of tissue mechanics contributes to the loss of tissue architecture and organ function. Research projects include: Epithelial architecture and the establishment of cell polarity; Role of the metabolic microenvironment in the loss of epithelial architecture and cancer progression; and Tissue regeneration in response to epithelial injury.

Translational Oncology Laboratory led by Professor Michael Brown (michaelp.brown@sa.gov.au)
In a bench to bedside effort, researchers in the Translational Oncology Laboratory are applying advances in immunotherapeutic technologies to the treatment of melanoma, myeloid leukaemias, brain and lung cancers, which affect millions around the world. The two major technologies of interest are chimeric antigen receptors (CARs) for re-directing lymphocytes toward cancers and antibody drug conjugates (ADCs) for targeting potent cytotoxins to cancers.
We are developing pre-clinical and clinical approaches for the treatment of these cancers to aid in diagnosis, therapy monitoring and treatment. Much of our research is collaborative, working in association with the RAH Cancer Clinical Trials Unit and partnering with other laboratories within the Centre for Cancer Biology.
Current research areas include: Chimeric Antigen Receptor (CAR) Technology (Pre-clinical studies of CAR T cells in animal models of leukaemia and brain cancer); Antibody Drug Conjugate Technology (Preclinical development of an imaging agent for detection of cancer cell death); and Translational Oncology (Cancer Genomics Initiative).

Tumour Microenvironment Laboratory led by A/Professor Michael Samuel (michael.samuel@unisa.edu.au)
Our laboratory works to understand the molecular toolkit that cancers use to exploit and modify the capabilities of other cells and tissues around them (the microenvironment). This altered microenvironment can promote disease progression and metastasis. We have shown that cancer cells engage a key stress pathway to alter the types of proteins that they secrete. These new secreted proteins are then able to initiate signalling pathways within normal cells of the microenvironment to hijack their functions and help cancer cells to proliferate, migrate and spread. These novel mechanisms provide us with tantalising ways to design new therapies against difficult cancers. We are studying invasive breast cancers, squamous cell carcinoma of the skin and colorectal cancers to identify such potentially useful new mechanisms. You will use state of the art microscopy techniques such as super-resolution microscopy, coupled with gene-targeted models of cancer to investigate cancer-microenvironment interactions.

Vascular Biology and Cell Trafficking Laboratory led by Professor Claudine Bonder (claudine.bonder@unisa.edu.au)
Our laboratory investigates how blood vessels form and contribute to disease progression. A better understanding of the blood vasculature promises to provide (i) new treatment opportunities for the difficult to treat cancers such as melanoma, pancreatic cancer and breast cancer, (ii) improved islet transplantation to cure diabetes and (iii) provide 'bioinvisible' vascular devicesto combat heart disease. We use leading imaging technology alongside cell culture, surface antigen expression by flow cytometry,

protein detection by Western blot, in vitro blood vessel forming assays, gene expression by real time PCR, immunohistochemistry of tissue samples and when required, animal models of disease.

ACRF Cancer Genomics Facility led by A/Prof Andreas Schreiber
(andreas.schreiber@adelaide.edu.au)
The Australian Cancer Research Foundation (ACRF) Cancer Genomics Facility offers the research community the full benefit of the expertise and technology available at the Centre for Cancer Biology. We provide a full range of state-of-the-art genomics and applied bioinformatics of high throughput experiments, ranging from analysis of transcriptomic microarray or RNASeq data, gene regulation studies using ChIP and CLIPSeq, to the search for disease-associated point and structural mutations of the human genome.
The Facility is equipped with the latest instrumentation for next-gen sequencing, including: Sanger sequencing; Next generation sequencing from Illumina, Ion Torrent and Roche; Sequenom MassArrays; Microarrays from Affymetrix and Illumina; Fluidigm equipment for the study of single cells; and a number of other validation methods and sample preparation robotics. We have the capability to analyse and interpret the vast amounts of data generated by these new technologies. This includes not only 'super'-computer infrastructure, but also people skilled in analysing and interpreting this data. Honours projects associated with data analysis, pipeline development, software development can be discussed on a case-by-case basis.

CCB Flow Cytometry Facility managed by Dr Bradley Chereda
(bradley.chereda@unisa.edu.au)
A number of projects are available to develop pilot experiments that establish new flow cytometry tools for users of the facility.
Flow cytometry is a powerful platform that collects fluorescence data from thousands of individual cells per second! When a tube of cells is loaded into a flow cytometer, the cells travel in a fluidic stream through a flow cell. As a cell passes through the flow cell, lasers excite any fluorophores in the cell. Scientists can make a cell fluoresce by fluorescently staining cellular proteins or structures. The machine records the fluorescence profile of each cell, which provides an in depth overview of the cell populations within the loaded sample.
Students can choose from some of the following projects

- **3D-printing accessories** to enhance functionality of the cytometers.
- **Establishing a small particle analysis procedure** (particles 0.2-2.0 microns in size) - the size-range of viruses, exosomes and bacteria.
- **Water quality**. Create a method to analyse water samples for bacteria, viruses and even microplastics using flow cytometry. From site-collection to flow analysis. Such as, the River Torrens, rain-water-tanks and tap water.
- **Cell telemetry.** By fluorescently tagging genes involved with specific cell activities (growth, death, export, energy use), scientists can monitor cellular response to drugs or other challenges. Tagging genes will be accomplished using crispR. Then cell telemetry monitored by flow and/or microscopy.
- **Colour competition.** Engineer knockdown and over expression plasmids with a specific fluorescent protein. Then create individual cell populations with a unique gene change. Mix them together and track the colour by flow to monitor cell enrichment or depletion of the gene change.
- **FRET-Flow** (FRET = fluorescence resonance energy transfer). FRET allows for the detection of closely interacting molecules. Traditionally performed on a microscope, using flow cytometry will allow for high-throughput screening of molecular interactions in genetic, drug or library screening.

For more information on the Centre for Cancer Biology:
info@centreforcancerbiology.org.au or

Professor Richard D'Andrea	Telephone: +61 8 8302 1230	Email: richard.dandrea@unisa.edu.au
Professor Natasha Harvey	Telephone: +61 8 8302 7835	Email: natasha.harvey@unisa.edu.au
A/Professor Quenten Schwarz	Telephone: +61 8 8302 7834	Email: quenten.schwarz@unisa.edu.au
Dr Tim Murphy	Telephone: +61 8 8302 9000	Email: tim.murphy@unisa.edu.au

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 earnt 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 RNApolymerase 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.

For more information on the Centre for Drug Discovery and Development:
Professor Shudong Wang (Professor in Medicinal Chemistry)
Telephone: +61 8 8302 2372
Email: shudong.wang@unisa.edu.au
http://people.unisa.edu.au/Shudong.Wang
http://www.unisa.edu.au/Research/Sansom-Institute-for-Health-Research/Research/drugdiscovery/

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):
Professor Sanjay Garg (Director, CPID)
Telephone: +61 8 8302 1575
Email: sanjay.garg@unisa.edu.au
http://people.unisa.ed.au/Sanjay.Garg
http://www.unisa.edu.au/Research/Sansom-Institute-for-Health-Research/Research/Centre-for-Pharmaceutical-Innovation-and-Development/

Early Origins of Adult Health Research Group (EOAHRG)

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.
EOAHRG is led by Professor Janna Morrison, whom has been funded as a fellow by the Heart Foundation and NHMRC and is currently an ARC Future Fellow. Her current research focuses 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.
Dr Jack Darby is a postdoctoral fellow in EOAHRG whom has a particular interest in understanding the molecular mechanisms by which sub optimal *in utero* conditions such as fetal hypoxaemia and hypoglycaemia influence cardiac development and program adult onset cardiovascular disease. More recently he has been focused on combining clinically translatable MRI measures with molecular techniques to test the effectiveness of intervention strategies.

EOAHRG has supervised 10 PhD students to completion and they all continue to perform research as postdoctoral fellows and group leaders in Australia and the UK. Janna has supervised over 40 Honours students, many of whom have gone on to complete PhDs, medical or veterinary school.

Current Projects

Does the preterm male fetus have greater cardiovascular vulnerability due to delayed cardiomyocyte maturation?
Prof Janna Morrison, Dr Jack Darby and Dr Max Berry
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 and Dr Jack Darby

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.

Impact of maternal undernutrition on fetal cardiac development

Human studies show that babies whom are born small as a result of intrauterine growth restriction (IUGR) 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 and therefore we are limited in our capacity to implement effective intervention strategies. One factor that may cause IUGR and the programmed risk of cardiovascular disease is maternal undernutrition. Here, the developing fetus does not receive enough nutrients from the mother. This project will use both a well-established sheep model as well as a one of a kind non-human primate model of maternal undernutrition to determine the molecular links between poor growth *in utero* and the predisposition toward poor heart health in later life. To address this, this project will use techniques as qRT-PCR to measure the gene expression and Western Blot to measure the protein abundance of signaling molecules involved in cardiac growth and development.

Improving lung development through increased pulmonary oxygen delivery

Prof Janna Morrison, Dr Jack Darby and Prof Sandra Orgieg

Intrauterine growth restriction (IUGR), where a baby weighs below the 10th percentile for their gestational age, occurs in 6.5 % of live births. These IUGR babies have an increased risk of preterm birth with impaired maturation of the lung. This increases their risk of respiratory distress syndrome (RDS). One way of preventing IUGR and thus the risk of preterm birth and RDS, would be to increase fetal substrate (oxygen and nutrients) supply. Resveratrol, a polyphenol found in the skins of red grapes, increases uterine artery blood flow. We hypothesize, that increased uterine artery blood flow will accelerate lung maturation via increased oxygen delivery to the fetal lung. This study will determine the impact of maternal resveratrol supplementation on the expression surfactant proteins (qRT-PCR and immunohistochemistry) in the fetal lung and align this expression with pulmonary oxygen delivery (fetal MRI data) in the late gestation fetus.

Does resveratrol influence placental development?

Prof Janna Morrison, Dr Jack Darby and A/Prof Michael Wiese

Impaired fetal substrate supply as a result of either placental insufficiency, preeclampsia or maternal undernutrition causes intrauterine growth restriction (IUGR). These IUGR babies are not only at an increased risk of longer stays in the NICU and increased perinatal morbidity but may also be at an increased risk of epigenetic programming and the development of chronic disease in adult life. In an effort to reduce the risk of these poor outcomes, the development of interventions to improve fetal substrate delivery is at the forefront of perinatal research. The pregnant sheep model is often used to study fetal development in the setting of *in utero* substrate restriction and has led to medical advances such as the use of antenatal steroids in pregnancies at risk of preterm birth. Using this animal model, we

have shown resveratrol to increase uterine artery blood flow and fetal oxygenation. However, unlike the human placenta; the sheep placenta does not appear to allow resveratrol to cross from the maternal to the fetal circulation. This project will use techniques such as qRT-PCR to measure placental gene expression and immunohistochemistry to determine protein abundance and distribution of signaling molecules known to be both involved in placental development and responsive to resveratrol and MRI data. We hypothesize that resveratrol will activate signaling molecules on the maternal but not the fetal side of the sheep placenta.

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

Prof Janna Morrison, Dr Jack Darby, and A/Prof Michael Wiese

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, Dr Jack Darby and A/Prof Michael Wiese

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 and therefore we are limited in our capacity to 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.

Fetal and maternal drug metabolism in complicated pregnancies

Prof Janna Morrison, Dr Jack Darby and A/Prof Michael Wiese

To obtain the best outcomes for both mum and fetus during pregnancy, drugs are often required to treat illness. However, there is limited information available on the short and long term adverse fetal effects of a large proportion of drugs used during pregnancy. Animal studies can provide preliminary data regarding the safety of a drug during pregnancy. There is a large amount of human and animal evidence showing hormonal and metabolic changes that occur in both the mother and the fetus because of reduced or accelerated fetal growth. These changes could affect maternal, placental and fetal expression of drug metabolising enzymes and drug transporters and hence alter fetal drug exposure. This project will isolate microsomes from maternal and fetal livers in animal models of high and low substrate supply. Using in vitro protocols, we will assess the activity of cryptochrome P450 enzymes to determine if pregnancy complications impair drug metabolism.

Impact of cortisol on drug exposure in the fetus
Prof Janna Morrison, Dr Jack Darby, 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.

Investigating changes in fetal lipid profiles in response to changes in maternal nutrient supply
Prof Janna Morrison and Dr Sally Plush
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.

For more information on EOAHRG:
Professor Janna Morrison (Physiology)
Telephone: +61 8 8302 2166
Email: janna.morrison@unisa.edu.au
http://people.unisa.edu.au/Janna.Morrison
https://www.unisa.edu.au/research/Health-Research/Research/Early-Origins-of-Adult-Health-Research-Group/

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)
http://people.unisa.edu.au/Kerrilyn.Diener
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)
http://people.unisa.edu.au/Tamara.Cooper
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)
http://people.unisa.edu.au/Liang.Liu
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)
http://people.unisa.edu.au/Preethi.Eldi
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)
http://people.unisa.edu.au/Pablo.GarciaValtanen
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.

For more Information on the Experimental Therapeutics Laboratory:
Telephone: +61 8 8302 1202
Email: john.hayball@unisa.edu.au
http://www.unisa.edu.au/Research/Sansom-Institute-for-Health-Research/Research/Experimental-Therapeutics/

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 (EPIs) 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 to 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.

For more information on IDMRG:
Telephone: +61 8 8302 2933
Email: Rietie.Venter@unisa.edu.au
http://www.unisa.edu.au/Research/Sansom-Institute-for-Health-Research/Research/Infectious-Diseases-and-Microbiology/

Mass Spectrometry and Proteomics group

Professor Peter Hoffmann
https://people.unisa.edu.au/peter.hoffmann

The Mass Spectrometry and Proteomics group 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 Peter Hoffmann is Strand Leader and Lloyd Sansom Chair in Biomaterials Engineering & Nanomedicine at FII, President of the Australasian Proteomics Society, and Conference Chair for the National Meeting of the Australasian Proteomics Society. He has a keen interest in comparative proteome analysis and finding tailored solutions for industry partners. He is leader in the field of Mass Spectrometry Imaging and has experience transforming research into industry-relevant outcomes.

Honours projects available:

Project 1: Mapping α2,3- and α2,6-linked sialic acid in gynaecological cancer tissues

Dr Mark Condina, Dr Matthew Briggs and Prof Peter Hoffmann (FII, UniSA)

Project overview: Matrix-assisted laser desorption/ionisation mass spectrometry imaging (MALDI-MSI) is an analytical technique used to spatially map analytes, such as *N*-glycans (i.e. complex sugars attached to asparagine residues on proteins), across tissue sections. Our group has successfully implemented *N*-glycan MALDI-MSI on formalin-fixed paraffin-embedded (FFPE) tissue sections that are heterogenous, including ovarian cancer, endometrial cancer and osteoarthritis. However, there currently are several challenges with regards to the analysis of sialylated *N*-glycans (i.e. *N*-glycans containing sialic acid) in positive ion mode; (1) multiple salt adducts form resulting in peak splitting and lower sensitivity, (2) their labile character leads to in-source or post-source decay, and (3) isomeric information (i.e. α2,3- and α2,6) is lost. It has been previously reported that ovarian cancer cells lines have higher levels of α2,6-linked sialic acid relative to α2,3-linked. This project aims to develop an optimised sample preparation workflow that stabilises sialylated *N*-glycans while differentiating between α2,3- and α2,6-linked sialic acids on FFPE gynaecological cancer tissues (ovarian, endometrial, cervical and vulvar) to better understand the isomeric differences between each cancer for the first time. With this workflow optimised, a potential biomarker or therapeutic target for gynaecological cancers may be discovered leading to future clinical applications. The student will participate in collection and interpretation of results, and development and optimisation of MS analytical methods to characterise *N*-glycans from tissue.

Methods and Techniques: mass spectrometry imaging, quantitative mass spectrometry, cancer tissue sample preparation, bioinformatics

Project 2: Pushing the boundaries of high throughput quantification by mass spectrometry

Prof Peter Hoffmann and Dr Manuela Klingler-Hoffmann and Dr Mark Condina (FII, UniSA)

Project overview: Analytical measurements of any kind should be sensitive, fast, accurate and reproducible. To achieve the most sensitive measurement, lengthy sample preparation and complex analysis might be necessary. Both are not compatible with high throughput applications. Although Matrix assisted laser desorption/ionization (MALDI) MS can acquire data as fast as 10 ms/sample, it is currently underperforming as a high throughput technology. To develop this enabling technology, innovative sample preparation protocols using different matrixes will be developed, which will together

with advanced data analysis disrupt the current status quo. This project will have a transformative impact on multiple research areas, such as monitoring of biologicals for the pharmaceutical industry, mapping and quantifying environmental exposures to humans, plants and animals and quantifying molecules on tissue.

Methods and Techniques: quantitative MALDI imaging mass spectrometry, imprinting, tissues, method development

Project 3: Predicting chemoresponse in ovarian cancer
Prof Peter Hoffmann and Dr Manuela Klingler-Hoffmann (FII, UniSA)

Project overview: For women in Australia, ovarian cancer is the 6th most common cause of cancer death, despite being 10th in frequency. After diagnosis, patients have less than 50% chance of surviving for five years. Between 60-80% of patients respond to standard first-line chemotherapy, but a large proportion relapse and need treatment with a different drug. No test currently exists to predict which drug will work best for each patient. However this vital information could contribute to the overall aim to getting each patient the right therapy, the first time every time. Through working closely with a gynaecological oncologist (Prof Martin Oehler) and a collaborative team of multidisciplinary researchers we have developed a test pre-screening test to predict response before treatment stars. Our mission is to substantially shift the survival statistics for women with ovarian cancer. While performing the testing, additional essential data such a proteomics data will be collected.
Methods and Techniques: quantitative mass spectrometry, drug response testing, tissue culture, spheroids,

Opportunities exist for the projects to be continued and developed into PhD studies.

Project 4: Mapping signaling pathways activated in ovarian cancer with PARP inhibitors
Dr Clifford Young, Dr Mark Condina, and Prof Peter Hoffmann (FII, UniSA)

Project overview: Poly(ADP-ribose) polymerase-1 (PARP1) inhibitors are a promising class of cancer drugs, and a typical initial treatment for patients diagnosed with ovarian cancer. Previous studies have shown the therapy applicable with patients shown to have mutations in the BRCA1 and BRCA2 genes, yet a subset of patients without these mutations can still have improved prognosis with PARP inhibition treatment. At present, the differences between these patients compared with non-responding patients that also don't have the BRCA mutations is not clear. Through working closely with a gynaecological oncologist (Prof Martin Oehler), we have representative and primary cell lines with and without the BRCA mutations, and cells that respond well to treatment with PARP without such mutations. Using the latest mass spectrometry-based approaches coupled with phosphoproteomics, the research will aim to elucidate variances between the signalling pathways activated upon exposure with PARP inhibitors over time. The project will adopt various strategies for enrichment of phosphorylated proteins and couple this with high resolution mass spectrometry and data analytics. The developed approach will be applicable for monitoring signalling cascades in a range of complex samples and to better understand mechanism of action for current and future therapeutics.

Methods and Techniques: phosphoproteomics, quantitative mass spectrometry, cell culture, bioinformatics

For more information on the Mass Spectrometry and Proteomics group, please contact **Prof Peter Hoffmann** (Strand Leader and Lloyd Sansom Chair in Biomaterials Engineering & Nanomedicine)
Telephone: 0434 079 108
Email peter.hoffmann@unisa.edu.au

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, protein biochemists, physiologists, histopathologists 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 Doug 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' 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 benefits patients and the wider community.

Professor Sandra Orgeig (Professor in Pulmonary Biology)
http://people.unisa.edu.au/Sandra.Orgeig
Professor Orgeig is a research leader in pulmonary biology, with over 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.

Research Projects are available in the following areas:

1. **Cancer Cell Biology**

a. Defining altered endosome-lysosome biogenesis in cancer; companion diagnostics and therapeutics
Prof. Doug Brooks (UniSA), Dr Rob Brooks (UniSA), Dr Jessica Logan (UniSA), Dr Alexandra Sorvina (UniSA), Dr Carmela Martino (UniSA), Dr Ian Johnson (UniSA), Dr Stavros Selemidis (RMIT), Dr Emma Parkinson-Lawrence (UniSA), Prof. Sandra Orgeig (UniSA), Dr Joanna Lazniewska (UniSA), Ms Chelsea Thomas (UniSA), Dr Brian Dale (UniSA), Prof. Paul Reynolds (SA PATH), Prof. Adrian Esterman (UniSA), Prof. Ian Olver (Uni of Adelaide), Assoc. Prof. Lisa Butler(Uni of Adelaide) and Prof. John O'Leary (Dublin).

Due to the high incidence of prostate, ovarian and pancreatic 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 prostate, ovarian and pancreatic 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 prostate, ovarian and pancreatic 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, histology, imaging, protein chemistry, immunochemistry, gene expression and mechanisms of vesicular traffic.

b. Developing biomarkers and therapeutics for primary and metastatic lung cancer

Prof. Doug Brooks (UniSA)**,** Prof. Sandra Orgeig (UniSA), Dr Brian Dale (UniSA), Dr Ian Johnson (UniSA), Dr Emma Parkinson-Lawrence (UniSA), Prof. John O'Leary (Dublin), Dr Stavros Selemidis (RMIT), Dr Rob Brooks (UniSA), Dr Jessica Logan (UniSA), Dr Alexandra Sorvina (UniSA), Dr Carmela Martino (UniSA), Prof. Ian Olver (Uni of Adelaide), Prof. Paul Reynolds (Uni of Adelaide), Dr Joanna Lazniewska (UniSA), Dr David Ross (Flinders Uni).

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. We have identified a critical cell biological pathway that is 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, histology, imaging and immunochemistry.

c. The role of the lung microbiome in lung cancer

Prof. Sandra Orgeig (UniSA), Dr Emma Parkinson-Lawrence (UniSA), Prof. Paul Reynolds (Uni of Adelaide), Dr Andrea Stringer (UniSA) & Prof. Doug Brooks (UniSA).

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. 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

d. Developing precision medicine tools using "big data"

Dr Jessica Logan (UniSA), Dr Ashley Hopkins (Flinders Uni), Dr Carmela Martino (UniSA), Prof. Andrew

Rowland (Flinders Uni), Prof. Doug Brooks (UniSA) and Prof. Michael Sorich (Flinders Uni).

This project aims to develop prognostic tools for advanced cancer treatments using clinical epidemiology and pharmacometric techniques. Prognostic tools allow the presentation of personalised likelihoods of response and adverse effects to medicines, thus allowing informed decisions to be made. This is particularly important in advanced cancers where there are significant consequences to the high variability in the likelihood and severity of adverse effects, as well as response to the various treatments.

The data with which the prognostic tools are made are typically "big data", sourced from clinical trials conducted by pharmaceutical companies, or from data registries. The data include large amounts of demographic, laboratory and tumour data which may be predictive of efficacy or toxicity to cancer medicines. We have access to individual participant data from >100,000 advanced breast, lung, prostate or colorectal cancer patients treated with immunotherapies, targeted therapies and chemotherapies. The project will be focused depending on your areas of interest. Prospective students require an interest in clinical epidemiology, pharmacology and improving the use of cancer medicines. Students will develop skills in data management, R programming, biostatistics and epidemiological analyses.

2. Medicinal Chemistry

e. Hypoxia-activated Prodrug Chemotherapeutics for Advanced Cancer

Dr Shane Hickey (UniSA), Dr Trent Ashton (Walter and Eliza Institute of Medical Research), Dr Martin Sweetman (UniSA) and Prof. Doug Brooks (UniSA).

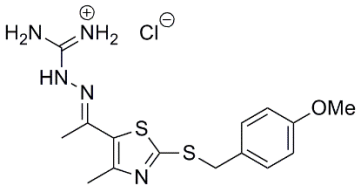
Cancer was responsible for approximately 9.6 million deaths globally in 2018, making it a major cause of mortality and a significant healthcare concern worldwide. Current chemotherapeutics are plagued by off-target effects and consequently novel systems which effectively and selectively kill cancer cells are desperately needed. This project aims to take advantage of the tumour hypoxic microenvironment—an attractive target for drug design—where drugs are equipped with a protective mask which is removed upon being exposed to the hypoxic conditions indicative of advanced tumours.

Students who choose to undertake medicinal chemistry projects (e and f) 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.

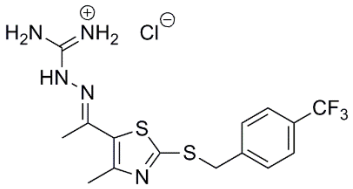
f. The Synthesis of Novel Drugs to Target a Global Issue: Bacterial and Parasitic Resistance

Dr Shane Hickey (UniSA), Dr Trent Ashton (Walter and Eliza Institute of Medical Research), Assoc. Prof. Sally Plush (UniSA) and Prof. 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.



MRSA MIC = 1.0 µg/mL
P. falciparum 3D7 EC_{50} = 0.64 µM



P. falciparum 3D7 EC_{50} = 0.33 µM

3. Cell Biology of Paediatric Metabolic Disease

g. 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; the major degradative compartment in cells. 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. Specifically, we aim to identify the causes and mechanisms of respiratory dysfunction and the role of the pulmonary surfactant system in LSD. The surfactant system is a complex mixture of lipids and proteins that forms a film at the air-liquid interface of the lung where it performs critical functions enabling the lung to inflate and deflate and in protecting the lung from foreign organisms and particles.

We have access to two mouse models of the mucopolysaccharidoses (MPS), namely MPS I (Hurler/Scheie Disease) and MPS IIIA (Sanfilippo Syndrome). These MPS diseases are characterized by the primary lysosomal storage of polysaccharides including heparan sulphate (HS) or dermatan sulphate (DS) and secondary storage of lipids. In the MPS IIIA mouse we have recently shown an accumulation of HS in both lung tissue and bronchoalveolar lavage fluid (BALF). This is also accompanied by a decrease in pulmonary surfactant phospholipids and reduced surfactant and lung function. We now wish to follow up these studies in the MPS I mouse (and ultimately in MPS IIIA patients), to determine whether the changes in surfactant amount and function are a common pathology.

h. Lung pathology in the lysosomal storage disorder, Mucopolysaccharidosis I

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

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 characterise the accumulation of HS and DS in lung tissue and in the alveolar compartment, lung structure, surfactant composition and function and lung function in the lungs of MPS I mice, that we have recently acquired through collaborations with colleagues at SA Pathology.

i. Innate immune function of alveolar macrophages and lung inflammation in MPS IIIA mice

Prof. Sandra Orgeig (UniSA) & Dr Emma Parkinson-Lawrence (UniSA); Assoc. Prof. Greg Hodge (Uni of Adelaide); Doug Brooks (UniSA).

In this project we will assess murine BALF for macrophage function i.e. activity of the innate immune system. We hypothesise that the reduction in the activity of surfactant in the MPS IIIA mouse is as a result of surfactant inactivation via the addition of extra-pulmonary factors, which may include increased alveolar HS or an increase in inflammatory cells and soluble mediators (e.g. cytokines). We will determine the number and function of alveolar macrophages and measure the levels of inflammatory mediators. Specifically, we propose that the presence of HS in the alveolar compartment will stimulate alveolar macrophages to phagocytose these foreign particles and produce inflammatory mediators. In turn the phagocytic activity of these macrophages may become impaired, thereby compromising the lung's ability to fight pulmonary infections. In addition, we will determine 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.

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

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

Pulmonary surfactant is synthesized in alveolar epithelial type II cells and stored in lysosomal-derived organelles known as lamellar bodies. 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 use both immunohistochemical and immunocytochemical approaches to characterise the relative expression and distribution of key proteins in MPS IIIA relative to control mice in fixed lung tissue and isolated alveolar type II cells, respectively. Specifically, we will use antibodies against surfactant proteins (SP-A, -B, -C, -D) and key proteins involved in the metabolic pathway for the production and recycling of pulmonary surfactant which involves early endosomes (Rab5), late endosomes (Rab7), lysosomes (LAMP-1) and lamellar bodies (LAMP-3). Finally, we will investigate key proteins involved in the transport, and attachment of lamellar bodies, to the plasma membrane of the cell, ready for secretion into the lung (syntaxin-2, SNAP-23 and VAMP-2). Students will gain experiences in tissue processing, immunohistochemistry, primary cell culture and live cell imaging.

For more information on the Mechanisms in Cell Biology and Disease Research Group:
Telephone: +61 8 8302 1229
Email: doug.brooks@unisa.edu.au
http://www.unisa.edu.au/Research/Sansom-Institute-for-Health-Research/Research/Mechanisms-in-Cell-Biology-and-Diseases-Research-Group/

Telephone: +61 8 8302 2649
Email: sandra.orgeig@unisa.edu.au
http://www.unisa.edu.au/Research/Sansom-Institute-for-Health-Research/Research/Molecular-and-Evolutionary-Physiology-of-the-Lung/

Postdoctoral researchers in the group:
Dr Christie Byrne - https://people.unisa.edu.au/Christie.Bader
Dr Robert Brooks - https://people.unisa.edu.au/Robert.Brooks
Dr Shane Hickey - https://people.unisa.edu.au/Shane.Hickey
Dr Ian Johnson - https://people.unisa.edu.au/Ian.Johnson
Dr Joanna Lazniewska - https://people.unisa.edu.au/Joanna.Lazniewska
Dr Jessica Logan - https://people.unisa.edu.au/Jessica.Logan
Dr Carmela Martino - https://people.unisa.edu.au/Carmela.Martino
Dr Isabel Morrow - https://people.unisa.edu.au/Isabel.Morrow
Dr Emma Parkinson-Lawrence - https://people.unisa.edu.au/Emma.Parkinson-Lawrence
Dr Alexandra Sorvina - https://people.unisa.edu.au/Alexandra.Sorvina
Dr Martin Sweetman - https://people.unisa.edu.au/Martin.Sweetman
Dr Ben Ung - https://people.unisa.edu.au/Ben.Ung

Musculoskeletal Biology Research Laboratory

Researchers within Musculoskeletal Biology Research Laboratories (MBRL) develop therapies to prevent bone pathologies, such as rickets, fractures, infections and cancer that can occur due to several different genetic, environmental and surgical reasons. All research questions use a range of different studies which range from using cells to clinical studies and state-of-the-art facilities and techniques.

Drug Discovery for treating Bone and Mineral Disorders

Associate Professor Paul Anderson and Professor Gerald Atkins

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, and Intestinal Function

Dr Andrea Stringer and Associate Professor Paul Anderson

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.

Therapeutics for Rare Genetic Bone and Mineral Disoders

Associate Professor Paul Anderson and Professor Rene St-Arnaud

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.

Novel Antimicrobial Implants for Orthopaedic Devices

Associate Professor Paul Anderson and Professor Krasimir Vasilev

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. This research is set to transform the orthopaedic industry and help solve a major world-wide health problem.

Discovering Novel targets to treat and prevent Osteoarthritis

Associate Professor Paul Anderson and Professor Peter Hoffmann

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.

For more information on Musculoskeletal Biology Research Laboratory:
Telephone: (08) 8302 7387
Email: paul.anderson@unisa.edu.au
Home Page: http://people.unisa.edu.au/paul.anderson

Neurophysiology and Human Movement Laboratory

Associate Professor Gabrielle Todd
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.

For More information on the Neurophysiology and Human Movement Laboratory:
Telephone: +61 8 8302 1979
Email: gabrielle.todd@unisa.edu.au

Neuro-Regeneration Group

Professor Xin-Fu Zhou (Research Chair in Neuroscience)
http://people.unisa.edu.au/Xin-Fu.Zhou
Telephone +61 8 8302 2329
Email: Xin-Fu.Zhou@unisa.edu.au

Dr Larisa Bobrovskaya (Associate Professor)
http://people.unisa.edu.au/larisa.bobrovskaya
Telephone +61 8 8302 1218
Email: larisa.bobrovskaya@unisa.edu.au

Dr Frances Corrigan (Senior Lecturer)
http://people.unisa.edu.au/Frances.Corrigan
Telephone : + 61 8 8302 1289
Email: frances.corrigan@unisa.edu.au

Dr Mohammed Al-Hawwas (Research Associate)
http://people.unisa.edu.au/Mohammed.Al-Hawwas
Telephone +61 8 8302 2173
Mobile 0432537698
Email: Mohammed.Al-Hawwas@unisa.edu.au

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 neurotorphins 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 (Group Leader)
http://people.unisa.edu.au/cobus.gerber

Prof. Jason White
https://people.unisa.edu.au/Jason.White

Dr. Richard Bade
https://people.unisa.edu.au/richard.bade

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 group has ongoing local, national and international collaborations and are renowned for our qualitative and quantitative methods for the analysis of licit and illicit drugs in wastewater. 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. Current projects include the development of methods to detect:

- Licit and illicit benzodiazepines
- Pseudoephedrine and methcathinone and examine the relationship between these compounds
- GHB and examine whether temporal trends can show illicit use

Students who join these projects will become proficient in aspects of analytical chemistry including sample preparation, sample treatment, method validation and will gain experience in liquid chromatography – mass spectrometry. The expertise required in our field can be diverse, relating to analytical chemistry, drug metabolism (pharmacokinetics), pharmacology and statistics, to name a few and projects can be catered to the student's interests.

For more information:
Telephone: +61 8 8302 2568
Email: Cobus.Gerber@unisa.edu.au

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

Prof Libby Roughead	Pharmacoepidemiology, Post market surveillance of medicines, Medicines policy, Health care program evaluation
Dr Nicole Pratt	Pharmacoepidemiology, Statistical methods
Dr Nagham Ailabouni	Deprescribing, Medicines associated dementia
Dr Andre Andrade	Digital health
Dr Gerel Dorj	Pharmacy practice, Antibiotics use and stewardship
Dr Svetla Gadzhanova	Pharmacoepidemiology, Data mining, Evaluation of change management in primary health care
Dr Marianne Gillam	Health services research, medical device epidemiology, quality use of pathology
Dr Jodie Hillen	Quality Use of medicines, Pharmacoepidemiology, Medicines use in the Aged Care population, Post marketing surveillance of medicines.
Dr Lisa Kalisch Ellett	Medicines that cause or worsen dementia and cognitive impairment, Quality use of medicines, Post market surveillance of medicines, Pharmacoepidemiology
Dr Gizat Kassie	Medicines associated with dementia and cognitive impairment
Dr Lan Kelly	
Dr Renly Lim	Quality use of medicines, Medicines utilisation
Dr Tuan Nguyen	Medicine associated dementia and cognitive impairment, Access to medicines Quality use of Medicines
Dr Emily Reeve	Deprescribing in the elderly, Polypharmacy, Medicines associated dementia
Dr Stephanie Reuter Lange	Pharmacology, Medication issues associated with the sub-optimal use
Dr Kham Tran	Dementia research
Dr Susan Semple	Australian Medicinal Plants, Antimicrobials, Complementary and Alternative Medicines
Dr Ty Stanford	Health data analytics, Bioinformatics

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 compete 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: 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) Co-designing a consumer driven tool to detect side effects due to medicines
Supervisors: Renly Lim, Lisa Kalisch Ellett, Libby Roughead

This project aims to develop a patient self-reported tool which can be used to detect side effects due to medicines. Students will have the opportunity to be involved in the co-design workshops with consumers, learn how vocabulary and language use can impact of patient symptom reporting, assist with data collection in the community setting, and learn how to analyse the data collected and interpretation of the results.

8) An overview of systematic reviews of medicines 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.

9) An overview of systematic reviews of medicines 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.

10) Strengthening responses to dementia: Building an evidence platform for the development of Vietnam's National Dementia Plan

Supervisors: Tuan Nguyen, Thu Ha Dang, Kham Tran, Libby Roughead

Dementia is a costly condition in its social, economic, and health dimensions that has a significant impact on individuals, their carers and society. Low- and middle-income countries (LMICs) including Vietnam will be the home of two-third of global dementia cases by 2050. However, health and social care systems in LMICs are not well-developed or well-funded, resulting in lack of diagnosis and poor quality of treatment and care, which is unresponsive to the needs of people with dementia, their carers and families. Urgent action is necessary for the development of national dementia plans in LMICs to ensure that adequate care and services are provided to people with dementia and their carers now and in the future. In this project, research capacity in dementia will be built using policy, epidemiological and qualitative analyses, and local stakeholders will be engaged to develop an understanding of the impact of dementia, population needs and existing resources in Vietnam with the aim of formulating sound recommendations for an effective Vietnam's national dementia plan.

Different studies are available under this project including:

- Scoping review of international dementia policy framework and plans;
- Systematic review of dementia research among Vietnamese and Vietnamese diaspora;
- Interview dyads of people with dementia and carers to map common pathways of care and identify their high priority concerns
- Public and physician surveys about knowledge, attitudes, beliefs and practices toward dementia

11) Physician perspective on their current prescribing practice for people with dementia in Australia, China and Vietnam

Supervisors: Tuan Nguyen, Thu Ha Dang, Kham Tran, Libby Roughead

Use medicines in people with dementia (PWD) is challenging because of several factors such as their progressive cognitive decline, high sensitivity to the effect of medication on cognition and increased likelihood of comorbidities. Potential inappropriate medication (PIM) used in PWD is therefore common, ranging from 10% to 70% depending on the setting and criteria used to measure. High prevalence PIM used in PWD was observed in Australia, China and Vietnam. Focusing on PIM that can further impair cognition (PIMcog) in PWD, our recent studies showed that 56% and 41% of patients with dementia in China and Vietnam respectively used at least one PIMcog during the two-year study period, while the prevalence of PIMcog was 21.4% of patient with dementia in Australia. About 44%, 39% and 31% patients

with dementia in Australia, Vietnam and China used acetylcholinesterase inhibitors concurrently with anticholinergic agent despite their potential to antagonise each other. The use of antipsychotic medicines seemed suboptimal from the selection of antipsychotic products to the initiation dosing to the treatment duration.

This project aims to explore factors underlying the current prescribing practice for PWD in Australia, China and Vietnam and document the information needed to design effective intervention packages to improve medicine use in PWD in these countries. For this project, students will be trained to conduct in-depth interview/focus group discussion with geriatricians in Australian study site (Adelaide) and to analyse qualitative data.

12) Identifying reasons for non-adherence of clinical guidelines for mental conditions
Supervisors: Andre Andrade

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 stablished 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.

13) Optimising deprescribing in practice
Supervisor: Emily Reeve
Deprescribing is the process of supervised withdrawal of inappropriate medications (ones where the potential harms outweigh the potential benefits). While deprescribing is a part of good prescribing, it doesn't happen in practice as often as it should.

Several different projects are available under this topic with flexibility available depending on student interest. Projects include conducting a systematic review of the literature about adverse drug withdrawal reactions (ADWRs) or optimal tapering regimens as well as analysing data about ADWRs from a cluster randomised deprescribing intervention. Other projects could consider how communication about medications, culture and treatment guidelines influence deprescribing in practice and could include quantitative and qualitative data collection and/or analysis.

These projects are suitable for students with an interest in:
- Medicine utilization and data analysis
- Population health
- Regulatory pharmacoepidemiology
- Quality use of medicines

14) Quality use of pathology
Supervisors: Marianne Gillam, Libby Roughead
This is a health services research project with the overall aim to identify areas for improvement in the use of pathology tests. The consequences of inappropriate pathology testing are substantial, however the prevalence of inappropriate testing in Australia is not known. There are several potential projects

available including examination of utilisation of pathology tests in in GP and specialist practices in South Australia, examination of inappropriate use of tests, therapeutic drug monitoring, and follow up of abnormal test results. Students will have the opportunity to work with stakeholders, perform data management and data analysis, conduct literature review and write papers for publication.

15) *Innovative post-marketing surveillance: identification and preparation of medicine information to use in a universal PE database with a common data model.*

Supervisors: Nicole Pratt, Ty Stanford and Jodie Hillen.

This project will initially involve searching scientific literature, regulatory and sponsor websites to develop an international list of all registered medicines to treat:

- Multiple Sclerosis
- Psoriasis
- Inflammatory bowel diseases

Using these findings, you will use multiple databases to assign global concept criteria for each medication to enable use in a universal-language pharmacoepidemiologic database with a common data model. Lastly, linking identified medications to utilization criteria for each medication to enable our international partners to run independent analyses using the common data model.

You will gain skills in: searching of drug regulatory databases; the language used and built environment of a common data model used in post marketing surveillance; post marketing study designs and data extraction criteria relevant to individual countries and impact of safety information on clinical practice.

For more information on the Quality Use of Medicines and Pharmacy Research Centre (QUMPRC):
Telephone: +61 8 8302 1234
Email: annette.paschke@unisa.edu.au
http://www.unisa.edu.au/Research/Sansom-Institute-for-Health-Research/Research/Quality-Use-of-Medicines-and-Pharmacy-Research-Centre/

Regenerative Medicine Laboratory

Professor Allison Cowin
http://people.unisa.edu.au/Allison.Cowin

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
Prof Allison Cowin (Research Group Leader, NHMRC Senior Research Fellow)
Telephone: +61 8 8302 5018
Email: Allison.Cowin@unisa.edu.au

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 2020 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.
- 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:
Dr Lorraine Mackenzie
Centre Manager
Telephone: +61 449 754 589
Email: lorraine.mackenzie@unisa.edu.au

Dr Amy Holmes (Post-doctoral researcher in biomedical engineering)
http://people.unisa.edu.au/Amy.Holmes

Dr Holmes' area of research is advancing the dermatological sciences and wound healing. Experimental work includes human skin preparation, cell culture, state-of-the-art imaging, microbiology and formulation design.

Available Projects-
Development of novel prevention and treatment strategies for postpartum vaginal and perineal infections that occur during childbirth
More than 85% of women who have a vaginal birth will suffer from a vaginal/perineal tear. Subsequent infections cause 11% of maternal deaths globally yet there are limited options for management with sitz baths the first line of defense. This project will investigate the use of novel antiseptic and probiotic creams to reduce infections and promote wound healing after child birth. This project is laboratory based and the student will develop skills in a number of key areas that include tissue preparation, state-of-the-art microscopy, cell culture and formulation design. This project is a collaborative effort between Dr Holmes, Professor Roberts, Dr Mahdi, Professor C. Roberts (Uni Adelaide) and senior clinicians.

Honours scholarships available
Previous Honours students studying with Dr Amy Holmes have won awards from the Australian Society of Medical Research and have been successful in securing a scholarships and travel grants from a range of sources, some of which are specific to the project. Dr Holmes previous students have published as a

result of their project and have secured PhD scholarships. Scholarship sources include NHMRC Translational Australian Clinical Toxicology network, The Hospital Research Foundation and Medical Advances without Animals Trust.

For more information:
Telephone: +61 8 8133 4006
Email: amy.holmes@unisa.edu.au

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

For more information:
Telephone: +61 8 8302 2334
Email: tim.barnes@unisa.edu.au

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.

We use advanced formulation strategies such as porous particles, lipid based systems and nano vesicles to improve the oral delivery of drugs. Improvement in drug solubility, absorption and bioavailability can

be achieved. Interesting cell models that mimic the gut wall are used and further developed to investigate how the formulation drives oral drug absorption. We have a number of projects in this area where a student could select a project according to their interest. 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.

For more information:
Telephone: +61 8 8302 2311
Email: kristen.bremmell@unisa.edu.au

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 hypercholestrolaemia 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.*

For more information:
Telephone: +61 8 8302 2598
Email: Matt.Sykes@unisa.edu.au

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.

For more information:
Telephone: +61 8 8302 2429
Email: May.Song@unisa.edu.au

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 is 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.

For more information:
Telephone: +61 8 8302 2312
Email: Michael.Wiese@unisa.edu.au

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

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.

For more information:
Telephone: +61 8 8302 1093
Email: Hugo.Albrecht@unisa.edu.au

Emeritus Professor Mary Barton

http://www.unisanet.unisa.edu.au/staff/Homepage.asp?Name=Mary.Barton

Use of bacteriophage to control *Rhodococcus equi* infection in foals
Professor Mary Barton[1], Ms Carla Giles[1], Dr Gary Muscatello[2]
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.

For more information:
Telephone: +61 8 8302 2933
Email: Mary.Barton@unisa.edu.au

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.

For more information:
Telephone: +61 8 8302 2493
Email: anton.blencowe@unisa.edu.au
Website: Blencowe Laboratories

Dr Maurizio Costabile (Senior Lecturer; Project Leader)
http://people.unisa.edu.au/Maurizio.Costabile

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.

For more information:
Telephone: +61 8 8302 2176
Email: Maurizio.Costabile@unisa.edu.au

Dr Giordana Cross (Dietetics)

http://people.unisa.edu.au/Giordana.Cross

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.

For more information:
Telephone: +61 8 8302 2843
Email: giordana.cross@unisa.edu.au

Dr Brian Dale (Senior Lecturer in Haematology)

http://www.unisanet.unisa.edu.au/staff/homepage.asp?name=brian.dale

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; the role of platelet mitochondria in myeloproliferative neoplasms; 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; evaluation of the haemostatic effects of new treatments for haemophilia.

For more information
Telephone: +61 8 8302 1062
Email: brian.dale@unisa.edu.au

Dr Permal Deo (Lecturer)

http://people.unisa.edu.au/Permal.Deo

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-κB 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 biological and food samples. Current studies focus 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.
Co-supervisors: Dr Bradley Simpson and Dr Susan Semple

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: Impact of *APOE* polymorphism on levels of advanced glycation end products
Co-supervisors: Dr Varinderpal S. Dhillon and Prof Michael Fenech, UniSA Clinical and Health Sciences

After the discovery of the APOE gene and knowledge of its genetic variants, several studies have demonstrated the association between the *APOE* polymorphisms and chronic conditions, such as Alzheimer's disease, age-related cognitive decline, osteoporosis, breast cancer, end-stage renal disease, atherosclerosis, diabetes, coronary disease and longevity.

The *APOE* gene, located on chromosome 19, is composed by three alleles (ε2, ε3 and ε4) that give rise to six different genotypes (ε2/2, ε2/3, ε2/4, ε3/3, ε3/4, and ε4/4). The ε3 allele differs from the ε2 allele by

an amino acid substitution of arginine for cysteine at codon 158, while the ε4 differs from ε3 by a substitution of additional arginine for cysteine at residue 112.

APOE is highly susceptible to glycation, with ε4 showing a three-fold greater AGE binding activity than ε3. This suggests that glycation of ε4 may be an early step in the Alzheimer's cascade and that an increased affinity of ε4 and AGEs may be a significant contributor to increased risk of AD. We have previously shown ε4 carriers have greater propensity to glycation in South Australian populations. In this study, we will investigate the impact of APOE alleles in the formation of arginine related advanced glycation end-products using invitro models. The study will further explore by analyzing related dicarbonyls and arginine related advanced glycation end-products in plasma collected from a previous study.

Project 3: An optimization of receptor of advanced glycation end-product (RAGE) and pro-inflammatory cytokine expression using ex-vivo models
Co-supervisors: Dr Maurzio Costabile, Dr Varinderpal S. Dhillon and Prof Michael Fenech, UniSA Clinical and Health Sciences

Chronic hyperglycemia plays a significant role in disease complications such as atherosclerosis, coronary disease and end-stage renal disease. It has been postulated that advanced glycation end products (AGEs) and it's certain receptor (RAGE) pathway is one of the major pathways involved in diabetic complications. We have previously shown, AGEs activate cellular signaling pathways in order to be linked with enhanced production of free radicals and inflammatory processes, through RAGE interactions in cell lines, The RAGE signaling pathway results in inducing nuclear factor-κβ (NF-κB) translocation that increased transcription of endothelial dysfunction biomarkers. This study aims to optimize the AGE-RAGE axis and the downstream activation pathway using ex-vivo models.

Project 4: Effect of non-nutritive sweeteners and related AGEs on chromosomal DNA damage and telomere dynamics.
Co-supervisors: Dr Varinderpal S. Dhillon and Prof. Michael Fenech, UniSA Clinical and Health Sciences

Non-nutritive sweeteners are used regularly as a replacement for sugar due to their low-energy content, however emerging research suggests that the breakdown products of some sweeteners are associated with health implications. Previous studies including systematic reviews and meta-analyses suggest that artificial sweeteners are metabolically inert and are not associated with increased risk of obesity and metabolic diseases such as type 2 diabetes mellitus, cardiovascular disease, and hypertension. However, emerging research suggests that the breakdown products of some artificial sweeteners are associated with diabetogenic, mutagenesis, glycation and formation of advanced glycation end-products (AGEs), and hence have important health implications.

In our previous study, we have shown that sugar alcohols ie., xylitol and sorbitol, showed formation of protein-bound fluorescent advanced glycation endproducts (AGEs), N^{ε}-carboxymethyllysine (CML), and N^{ε}-carboxyethyllysine (CEL) levels in AGE-BSA model and food models. Additionally, we have also shown that dietary sugars and related AGEs have genotoxic effect and causes telomere attrition. In this study we aim to investigate the effect of non-nutritive sweeteners and related AGEs on DNA damage and telomere dynamics.

Project 5: Barberry and Sumac – Potential nutraceuticals for chronic health conditions?
Co-supervisor: Dr Evangeline Mantzioris., UniSA Clinical and Health Sciences

Barberry and Sumac are berries which grow in the Middle east and are widely used in Middle Eastern cookery. Additionally, they have been used in complementary medicine and used as a supplement for general wellbeing. More recently SR and MA's have reported favourable health benefits of the active

ingredients of these berries when for chronic conditions such as overweight and obesity, Type 2 diabetes, hyperlipidemia, non-alcoholic liver disease and poly cystic ovary disease.

This project will entail two components. The first will be to evaluate the inhibitory of barberry and sumac extracts against protein glycation, pro-inflammation and key enzymes relevant to hyperglycemia. These tests will be done using in-vitro and cell model systems in understanding the possible mode of action. The second part will be to research the evidence base and prepare an review from the literature, capturing all the evidence of use of the barberry and sumac for different health conditions. It is expected most of this would be from pre-existing meta-analyses and systematic reviews. This project will form an important of the evidence base for the recommendation of barberry and sumac as a nutraceutical.

Project 6: Induction into viable but non-culturable (VBNC) status of foodborne pathogens
Co-supervisors: Prof. Darren Trott, Uni Adelaide, Dr Sergio Ferro, Ecas 4

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.

For more information:
Telephone: +61 8 8302 1189
Email: permal.deo@unisa.edu.au

Dr Alison Hill (Senior Lecturer in Nutrition)

http://www.unisanet.unisa.edu.au/staff/homepage.asp?name=alison.hill

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 loss [3-6]. The

nutrient profile of almonds, which are rich in monounsaturated fats, protein and fibre, may assist with weight management through increased satiety [9]. 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.

For more information:
Telephone: +61 8 8302 1817
Email: alison.hill@unisa.edu.au

Associate Professor Ivan Kempson (Biophysics)

http://people.unisa.edu.au/ivan.kempson

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.

For more information:
Telephone: +61 8 8302 3677
Email: Ivan.Kempson@unisa.edu.au

Associate Professor Jennifer Keogh (Nutrition)

http://people.unisa.edu.au/Jennifer.Keogh

Jennifer's research is on the prevention and management of chronic disease using dietary change to achieve health benefits in heart disease, diabetes and obesity. Her recent research and publications focus on the use of intermittent fasting as a strategy for weight loss. Her projects would suit students who have an interest in nutrition.

There are several projects available including:

1. Effect of non-nutritive sweeteners (NNS) on blood sugar control in type 2 diabetics?

Many people consume artificial or non-nutritive sweeteners (NNS) often to reduce sugar intake or lose weight. Common food sources include diet soft drinks and diet foods such as diet yoghurt. Given the popularity of diet drinks and foods it is important to understand if NNS have any harmful effects. The aim of this study is to investigate in a 12 week study the effects of NNS (acelfameK and aspartame) on blood sugar control in people with type 2 diabetes. We will recruit men and women with type 2 diabetes for a parallel study with three arms. Participants will be asked to consume their allocated test drinks for12 weeks. During two-week periods at the beginning and end of the study participants will wear a continuous glucose monitor on the upper arm. A finger-prick blood test will also be taken. Students will be involved in all aspects of the study.

Collaborators Professor Peter Clifton and Ms Deepti Sharma

For more information:
Telephone: +61 8 8302 2579
Email: jennifer.keogh@unisa.edu.au

2. The effect of nuts on glucose profile, cardiovascular disease risk markers and the microbiome
Associate Professor Jennifer Keogh (Nutrition) and Dr Andrea Stringer

People with type 1 and type 2 diabetes suffer from heart and blood vessel disease at two to three times the rate of the general population. Easy ways of reducing the burden of heart disease are needed to help people with diabetes and eating nuts may be one way to do this. Eating nuts improves diet quality and improves blood sugar control both of which are associated with reducing heart disease. Nut consumption appears to exert a protective effect on cardiometabolic disease, which is likely be through improved concentrations of fasting glucose, blood lipids and changes in the microbiome that in turn have a beneficial effect on host glycaemic control.

Specific Aims:
The aim of this study is to demonstrate that a snack sized portion of nuts each day compared with a carbohydrate-rich snack will reduce the overall daily glucose concentrations as assessed by continuous glucose monitoring in a sample representative of the general population.

We will recruit participants for a randomized study comparing 30g/day of mixed nuts to a carbohydrate rich snack. Measurements of glycaemic control and the microbiome will be undertaken in the project.

For more information:
Email: andrea.stringer@unisa.edu.au or jennifer.keogh@unisa.edu.au

Dr Layla Mahdi (Senior lecturer in Clinical Microbiology)

https://people.unisa.edu.au/Layla.Mahdi

Dr Layla Mahdi has research interests in the area of Molecular Microbiology, which focuses on studying the molecular basis of physiological mechanisms that occur in microorganisms. This include gene expression and regulation, pathogenicity and virulence, host immune responses during progression of infection, metabolism, and synthesis of macromolecules, cloning, and sequencing. Her research objectives are focused on the characterisation of novel pneumococcal virulence proteins, elucidating their specific roles in pathogenesis, and evaluating their vaccine potential, in alignment with global efforts geared towards the development of affordable and effective pneumococcal common protein vaccines.

For more information:
Telephone: +61 8 8302 2383
Email: layla.mahdi@unisa.edu.au

Dr Evangeline Mantzioris (Nutrition, Dietetics, Sports Nutrition, Mediterranean diet)

http://people.unisa.edu.au/Evangeline.Mantzioris

Current projects:

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.

Barberry and Sumac – Potential nutraceuticals for chronic health conditions?*
**This project can be adapted to be offered as either an Honours or Master project*
Supervisors: Dr Permal Deo, Dr Evangeline Mantzioris. Clinical and Health Sciences, University of South Australia.

Barberry and Sumac are berries which grow in the Middle east and are widely used in Middle Eastern cookery. Additionally, they have been used in complementary medicine and used as a supplement for

general wellbeing. More recently SR and MA's have reported favourable health benefits of the active ingredients of these berries when for chronic conditions such as overweight and obesity, Type 2 diabetes, hyperlipidemia, non-alcoholic liver disease and poly cystic ovary disease.

This project will entail two components. The first will be to evaluate the inhibitory of barberry and sumac extracts against protein glycation, pro-inflammation and key enzymes relevant to hyperglycemia. These tests will be done using in-vitro and cell model systems in understanding the possible mode of action. The second part will be to research the evidence base and prepare a review of berberine and sumac from the literature, which would include capturing all the evidence for different health conditions. It is expected most of this would be from pre-existing meta-analyses and systematic reviews. This project will form an important of the evidence base for the recommendation of barberry and sumac as a nutraceutical.

For more information:
Telephone: +61 8 8302 2574
Email: Evangeline.Mantzioris@unisa.edu.au

Dr Karen Murphy (Nutrition, Dietetics, Chronic Disease)

http://people.unisa.edu.au/Karen.Murphy
http://www.unisa.edu.au/Research/Health-Research/Research/ARENA/

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: 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: LUiSA (La Trobe University & Uni of South Australia Cohort study)
Co-Supervisor: Prof Catherine Itsiopoulous (La Trobe University)
Project overview: The LUiSA 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 LUiSA 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 (UniSA Allied Health & Human Performance)
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

For more information
Telephone: +61 8 8302 1033
Email: karen.murphy@unisa.edu.au

Dr Karma Pearce (Senior Lecturer in Nutrition)
http://people.unisa.edu.au/Karma.Pearce

Current project:

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: Effect of nutrients on fertility
Previous work has shown that a Western style dietary pattern and in particular dietary fats and sugars reduces testosterone levels in men through impairing gut function and through the production of endotoxins. We now wish to investigate whether specific nutrients can repair gut function. The Aim of

this study would be to conduct a clinical trial to evaluate the effect of specific nutrients in reducing endotoxin production and repairing gut function.

For more information:
Telephone: +61 8 8302 1133
Email: karma.pearce@unisa.edu.au

Dr Nenad Petrovic (Pharmacology)

http://people.unisa.edu.au/Nenad.Petrovic

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.

For more information:
Telephone: +61 8 8302 1127
Email: Nenad.Petrovic@unisa.edu.au

Mr Cameron Phillips (Adjunct Lecturer)

http://people.unisa.edu.au/Cameron.Phillips

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 you work is published.

For more information:
Telephone: +61 8204 6939
Email: Cameron.Phillips@unisa.edu.au

Professor Clive Prestidge (Pharmaceutical Science)

http://people.unisa.edu.au/Clive.Prestidge

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 depession) are poorly soluble and poorly absorbed upon oral administration. One negative outcome of these drug properties is that the associated medicines are required to me 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.

For More information:
Telephone: +61 8302 2438
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.

For more information:

Telephone: +61 8 8302 1872
Email: Stephanie.ReuterLange@unisa.edu.au

Associate Professor Mark Stevens

https://people.unisa.edu.au/Mark.Stevens

Bee venom allergy

There is a lot of research about venom allergy in bee keepers but much less in the children of bee keepers. There is anecdotal evidence, from beekeepers, that their children have higher rates of bee venom allergy and often have severe reactions. A possible project could be;

1. literature review
2. Survey of bee keepers and offspring with matching to a "non-beekeeper group" to determine if rates and severity are higher in children
3. Venom sampling in the homes of bee keepers. We have anecdotal reports of children reacting to clothing worn by bee keepers and plausible given number of stings to clothing. Many published studies in sampling house dust mite proteins and peanut proteins from houses. This would be very novel I suspect, and fits in with latest theories of developing food allergies via skin exposure to the allergen rather than ingestion.

This project would be supervised by Prof. John Hayball (john.hayball@unisa.edu.au) and Assoc. Prof. Mark Stevens (mark.stevens@unisa.edu.au) with Prof Michael Gold (michael.gold@adelaide.edu.au)

For more information:

Telephone: +61 8307 7685
Email: mark.stevens@unisa.edu.au
Mark.Stevens@samuseum.sa.gov.au

Dr Andrea Stringer

http://people.unisa.edu.au/Andrea.Stringer

Dr Andrea Stringer leads research in the field of gut health and disease, exploring primarily the digestive system, and its role in healthy and diseased or inflammatory states. Diseases states currently under investigation are the toxic effects of cancer treatments on the digestive system, inflammatory bowel disease, and colorectal cancer. In particular, we are looking at the role of vitamin D on tissue structure and function in the digestive system, with regards to its anti-inflammatory properties, effects on apoptosis, and effects on cell development and maturation.

We can currently develop projects around the following topics:

- *The role of vitamin D in the development of chemotherapy-induced mucositis (with Assoc Prof Paul Anderson, Ms Bronwen Mayo)*
- *The effect of vitamin D on the intestinal microbial ecosystem*

For more information:

Telephone: +61 8302 1760
Email: Andrea.Stringer@unisa.edu.au

Dr Nicky Thomas (Senior Research Fellow; Head Adelaide Biofilm Test Facility)

http://people.unisa.edu.au/nicky.thomas
Adelaide Biofilm Test Facility

The battle against multidrug resistant pathogens

Project: **"Improving the efficacy of poorly water-soluble antimicrobials"**
Many of the currently available antimicrobials show limited water solubility with restricts their wider application against much needed multi-drug resistant bacteria (superbugs) and fungi. In this project we will re-formulate poorly water-soluble antimicrobials and evaluate the efficacy of the developed formulations against free floating and surface attached pathogens (biofilms). Formulations include polymeric nanoparticles, liposomes, and other biocompatible materials.

For more information:

Telephone: +61 8302 21025
Email: nicky.thomas@unisa.edu.au