University of South Australia

# Bachelor of Biomedical Research (Honours)

## Research Booklet 2025

**IHBY Bachelor of Biomedical Research (Honours) contents**

## 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 and School of Nursing and Midwifery 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 Officers:**


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**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/

## Alliance for Research in Exercise, Nutrition and Activity

### Anti-glycation and anti-proinflammatory potential of Australian medicinal and food plants

Dr Permal Deo, 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.

### Impact of *APOE* polymorphism on levels of advanced glycation end products

Dr Permal Deo, Dr Varinderpal S. Dhillon and Prof Michael Fenech

### An optimization of receptor of advanced glycation end-product (RAGE) and pro-inflammatory cytokine expression using ex-vivo models

Dr Permal Deo, A/Prof Maurizio Costabile, Dr Varinderpal, S. Dhillon and Prof Michael Fenech

### Effect of non-nutritive sweeteners and related AGEs on chromosomal DNA damage and telomere dynamics

Dr Permal Deo, Dr Varinderpal S. Dhillon and Prof Michael Fenech

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

Dr Permal Deo, Prof Darren Trott (Uni Adelaide), Dr Sergio Ferro (Ecas4)

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

Dr Alison Hill, Prof Alison Coates and Prof Jon Buckley

Frequent nut consumption is linked with a lower body mass index. The nutrient profile of almonds, which are rich in monounsaturated fats, protein and fibre, may assist with weight management through increased satiety. Currently, data are lacking on the role of almonds in weight control diets to limit weight regain. We have recently completed a large-scale (100+ people) weight loss intervention trial to evaluate the benefits of almonds for weight loss and prevention of weight regain. As part of this study, we have collected data on a range of parameters including dietary intake, physical activity, physical function, pain, and sleep. We have multiple Honours projects available investigating how these parameters change in relation to weight loss, as well as their relationship with each other. We are particularly interested in relationships with pain. Available projects could investigate:

- Medication use, supplements, sleep and pain
- Physical activity (via accelerometry) and pain
- Dietary intake, sleep and pain

Masters projects are also available.

For more information:
Dr Alison Hill Email: alison.hill@unisa.edu.au Tel: +61 8 8302 1817

## Dietary patterns and Mediterranean diet for healthy ageing

A/Prof Karen Murphy, Dr Courtney Davis

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.

We explore the health benefits of dietary patterns such as the DASH diet, the MIND diet as well as other diets like keto and paleo diets, using randomized controlled trials.

We run follow-up studies with volunteers who have previously participated in trials to determine if they have maintained dietary behaviours adopted in trials and sustained health outcomes seen as a result of their participation. We are currently conducting the MedWalk (MedDiet and walking intervention) 1-year follow up trial.

We are currently determining the cost analyses of implementing such dietary patterns and effects on quality adjusted life years. Outcome measures our group explores include: blood pressure, arterial elasticity, body composition, cognition, wellbeing, mood, gut microbiome, inflammation, blood lipids, fatty acids, antioxidants, carotenoids, anthropometry and others.
Students will gain skills in RCTs, including clinical and biochemical measurements, laboratory analyses, working with databases, as well as statistical analyses.

Honours, Masters and PhD Project opportunities available for this research.

*Ref: doi: 10.3390/nu14153098. doi: 10.3390/nu15163645. doi: 10.3390/nu15071692. doi: 10.1007/s11883-018-0732-z. doi: 10.3945/ajcn.116.146803. Epub 2017 Apr 19.*

## Associations between lifetime dietary patterns and cardiovascular health in older Australians: The MedLey Study

A/Prof Karen Murphy, Dr Courtney Davis

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. Honours, Masters and PhD Project opportunities available for this research.

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

## Fad diets, macronutrient and micronutrient composition.

A/Prof Karen Murphy, Dr Courtney Davis

Weight loss diets continue to rise in popularity; however, the associated costs are seldom reported. Certain weight loss diets may be unaffordable and differ from their traditional nutrition composition to include nonconventional premium products. In contrast, healthy eating principles such as the Australian Guide to Healthy Eating (AGHE) and the Mediterranean Diet (MedDiet) place an emphasis on fresh

produce and staple foods but are sometimes thought to be unaffordable, or meet nutritional recommendations. Seven popular dietary patterns were identified: Paleo, keto, Optifast, Intermittent, 8 Weeks to Wow and the Australian Guide to Healthy Eating and the Mediterranean diet. This research explores the nutrients composition, the affordability and whether these diets could lead to nutrient deficiencies if followed long term.

Honours, Masters and PhD Project opportunities available for this research.

*Ref: doi: 10.3390/nu14163414. doi: 10.1017/S0007114521002282. doi: 10.1186/s12889-021-12447-4.*

For more information:
A/Prof Karen Murphy Email: karen.murphy@unisa.edu.au Tel: +61 8 8302 1033

### Long-term effects of illicit drug use on movement

A/Prof Gabrielle Todd

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:
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## Australian Centre for Precision Health

Prof Elina Hyppönen


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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.

## Exploring the health impact of Ozempic (GLP-1 Receptor Agonists): Insights from Mendelian Randomization

Ozempic (Semaglutide) is a drug prescribed for managing Type 2 diabetes. Due to its significant weight reduction effects, it has become one of the most widely used off-label medications for managing obesity worldwide. Recent clinical trial evidence highlights its potential to reduce the risk of kidney failure and death in people with Type 2 diabetes and chronic kidney disease. Another study has also demonstrated its benefits in alleviating symptoms of heart failure and reducing the risk of heart attacks and strokes, showcasing the drug's advantages beyond weight loss.

Ozempic targets the Glucagon-like Peptide-1 (GLP-1) receptor and mimics the activity of GLP-1. In recognition of the groundbreaking impact of GLP-1 receptor agonists, particularly their unprecedented efficacy in weight reduction and broader health benefits, Science journal named this class of drugs the "Breakthrough of the Year" in 2023. However, the comprehensive benefits and potential adverse effects of this drug have not yet been fully explored.

This project will leverage a genetic methodology called Mendelian Randomization, which uses genetic variants as instruments to investigate drug targets. Students will analyse extensive observational data, encompassing information on over a thousand diseases as well as proteomic and metabolic profiles, to explore the positive and negative effects of GLP-1 receptor agonists like Ozempic. This research will provide valuable insights into the broader implications of this widely prescribed drug.

Given that the methods and data have been extensively utilized in our prior research, this project is achievable within the student's timeframe, provided there is active engagement with the supervisory team.

For more information:
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## 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

## 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:

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|---|---|---|
| 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 |

## Post-GWAS: elucidating the role of genetic variants in psychiatric disease risk

Genetic discovery efforts (e.g., genome-wide association studies) have collectively identified several hundred independent risk loci for psychiatric disease, though the precise biological mechanisms underlying most of them are not well understood. Projects are available across all areas of psychiatry and related traits (including drug treatment response), can be tailored according to interests, and will be dry lab based. Some examples of general themes include (with associated PubMed IDs or DOIs):

- Focused analyses of single genetic risk variants of interest to formulate testable hypotheses (e.g., PMIDs: 35264566; 38735581).
- Integration of publicly available molecular (e.g., proteins, metabolites) data with genetic discovery data using methods including Mendelian randomisation and statistical colocalization (e.g., PMIDs: 38401803; 37563310).
- Prioritisation of novel drug target candidates and identification of drug repurposing opportunities (e.g,DOIs:https://doi.org/10.1101/2024.06.27.24309406; https://doi.org/10.1101/2024.02.18.24303002).
- Biological network-based approaches (e.g., PMIDs: 30185780; 37563310).

For more information:

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| Dr David Stacey | Email: David.stacey@unisa.edu.au | Tel +61 8 830 28339 |

## 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:

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| 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:

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|---|---|---|
| Prof Elina Hyppönen | Email elina.hypponen@unisa.edu.au | Tel +61 8 830 22518 |

## Population semi-PBPK models for cost-effective drug development

For more information:

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| Prof Richard Upton | Email Richard.upton@unisa.edu.au | Tel +61 8 830 22380 |

## Precision use of biological disease modifying anti-rheumatic drugs (bDMARDs) in autoimmune diseases

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## Quantitative description of the cardiovascular system

For more information

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## Suicide Prevention and Mental Health Diagnostics and Treatment

For more information:

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

For more information:

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| 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

For more information:

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| Dr Michael Ricos | Email Michael.ricos@unisa.edu.au | Tel +61 8 830 21525 |

## Centre for Cancer Biology

Prof Natasha Harvey

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 Bradley 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.

### Acute Leukaemia Laboratory led by Prof Richard D'Andrea and A/Prof David Ross

Richard.Dandrea@unisa.edu.au

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.

#### 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 and 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.

#### 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.

#### New pathways and targets in AML

## Understanding the functional significance of GADD45A promoter methylation in AML

## Molecular characterisation of Myeloproliferative Neoplasms (MPN)

Cancer Pharmacogenomics Laboratory led by A/Prof Pascal Duijf
pascal.duijf@unisa.edu.au

Project 1: 'Wet' laboratory project:

### New drugs to treat cancer

Cancer is a leading cause of death in Australia and globally. Many patients are treated with targeted therapies. These are drugs that 'target' small genetic defects in the cancer cell's DNA, such as mutations, and thereby kill the cancer cells. However, these therapies are often ineffective and can only be used for some patients. Thus, we need better therapies.
We have identified candidate drugs that target large genetic defects, i.e., chromosomal gains and losses, which frequently occur in cancers. This new type of cancer therapy may be more effective that current targeted therapies.
This project aims to create such large genetic defects in cells and test how effectively our candidate drugs can eradicate them. If successful in 2-dimensional cell culture, we will test the drugs in 3-dimensional cell models, which better mimic cancer development in patients.
Thus, this project may ultimately lead to the development of new therapies for cancer patients.

Project 2: Bioinformatics/computational biology project:

### Identify new opportunities to treat cancer

Unlike normal cells, cancer cells can divide indefinitely. They often acquire this property through mutations, deletions or amplifications in their DNA. Indeed, the genomes of cancer cells are typically very abnormal. While these genomic abnormalities can drive cancer development, therapy resistance and the spread of cancer cells through the body, they also offer opportunities to target cancer cells with drugs.
This bioinformatics project aims to identify genetic abnormalities in cancer cells that can be targeted with drugs. For this, we will explore large genomic (DNA level), transcriptomic (mRNA level), proteomic (protein level) and drug screen datasets from cancer cell lines and patient samples.
This 'dry-lab' project requires bioinformatics skills in R programming language. We will test if DNA-level abnormalities in cancers result in abnormal levels of mRNAs and proteins that can be targeted with drugs. This may ultimately enable development of new therapies for cancer patients.

Allergy and Cancer Immunology Laboratory led by Dr Damon Tumes (Laboratory Head) and A/Prof Harshita Pant (Clinical Lead)
damon.tumes@unisa.edu.au

### 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.

### 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.

### 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.

## Cell Signalling Laboratory led by Prof Yeesim Khew-Goodall

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### 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

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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 Prof Angel Lopez

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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

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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

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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 Prof Susan Branford

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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 Prof 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:

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.

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 Prof 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 Prof 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 Prof 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/Prof 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 Prof 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/Prof 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 Prof 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 devices to 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.

A/Prof Maurizio Costabile

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:

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| A/Prof Maurizio Costabile | Email: Maurizio.Costabile@unisa.edu.au | Tel: +61 8 8302 2176 |

For more information on the Centre for Cancer Biology:

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

## Centre for Pharmaceutical Innovation

Prof Sanjay Garg and Prof Clive Prestidge

### Bioinorganic Synthesis and Imaging

A/Prof Sally Plush

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.

### 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.

### 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.

For more information on the Bioinorganic Synthesis and Imaging Group:
A/Prof Sally Plush Email: Sally.Plush@unisa.edu.au Tel: +61 8 8302 2586

## Biomaterials, Biotechnology and 3D-bioprinting

A/Prof 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

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

### Frontier Biotechnologies: Biocompatible and orthogonal coupling chemistries

### Frontier Biotechnologies: Revolutionizing peptide synthesis and peptide therapeutics

### Environmental Sciences: Saving native wildlife from predators with protective implants

### Environmental Sciences: Developing a cloak of invisibility for native animals

### Environmental Sciences: Biosurfactants from waste streams

For more information on the Biomaterials, Biotechnology and 3D-bioprinting group:
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## Nanostructure and Drug Delivery

Prof 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.

### 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.

### 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.

### Improving the Oral Delivery of Anti-Psychotic Drugs – Advanced Pharmaceutical Formulation Approaches

Many of the currently available and new pharmaceutical agents used in the treatment of psychotic conditions (e.g. schizophrenia and depression) are poorly soluble and poorly absorbed upon oral administration. One negative outcome of these drug properties is that the associated medicines are required to 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.

### Novel Antibiotics – Formulation and Mechanistic Understanding

### Hybrid Particle Carriers for Antibiotics - Eradication of Bacterial Biofilms

### Improving the efficacy of poorly water-soluble antimicrobials

For more information on the Nanostructure and Drug Delivery Group:
Prof Clive Prestidge Email: Clive.Prestidge@unisa.edu.au Tel: +61 8302 2438

## Pharmaceutical Innovation and Development

Prof Sanjay Garg

Through the Pharmaceutical Innovation and Development Group (PIDG), 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.

### 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

I am also happy to tailor a project, matching your interests and dreams. 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 Pharmaceutical Innovation and Development Group (PIDG):
Prof Sanjay Garg Email: sanjay.garg@unisa.edu.au Tel: +61 8 8302 1575

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

These projects are suitable for a student with: an interest in pharmaceutical science; Laboratory based practical work.

### Using bacteriophages to control bacterial infections: A formulation challenge

Dr Timothy Barnes, Dr James Munro (Uni Adelaide), Emeritus Professor 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.

### Multiple emulsions for vaccine delivery

Dr Tim Barnes, 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.

## Use of liquid crystal lipid for the delivery of poorly soluble drugs

Dr Tim Barnes, 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.

For more information:
Dr Tim Barnes Email: tim.barnes@unisa.edu.au Tel: +61 8 8302 2334

Dr Kristen Bremmell (Senior Lecturer, Pharmaceutical Science)
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.

## Lipid Hybrid Nanoparticle delivery of RNA – how particle properties drive cellular interaction and translation

RNA therapy has potential in medicine to illicit an immune response and treat diseases such as cancer and genetic disorders. Lipid nanoparticles (LNPs) have emerged as a revolutionary platform for the delivery of RNA therapeutics, including mRNA and siRNA. These nanocarriers enhance the stability and bioavailability of RNA molecules, facilitating their uptake by cells. Through modification of lipid composition, incorporation of other polymers and control of surface properties, LNPs can be tailored for specific tissues or cell types. This research will explore nanoparticle composition and structure to drive cellular interaction, uptake and endosome escape. Students will participate across all areas of pharmaceutical formulation, characterisation, cellular and in vivo delivery to achieve an effective bio-therapeutic product.

For more information:
Dr Kristen Bremmell Email: kristen.bremmell@unisa.edu.au Tel: +61 8 8302 2311

Dr May Song (Research fellow)
Dr Song has broad research interests in the development of pharmaceutical preparations:

- Novel drug delivery system development
- Formulation improvement & development
- Analytical methods development and validation
- *In-vitro & in vivo* studies
- Applications of the above in the pharmaceutical industry

## A long-acting intramuscular injection development and in-vitro release profile evaluation

A daily injection can be a troublesome problem for a patient to stay on schedule for long-term treatment. Consequently, a long-acting intramuscular injection can significantly improve the patient's quality of life. The objective of this project is to optimize a long-acting intramuscular injection formulation. The analytical method development and validation for the drug using HPLC will be carried out. The challenge of this project is to simulate the in-vivo environment for the drug release assessment, therefore the conditions of an evaluation model for its in-vitro release profile need to be established.

## A novel drug delivery system for taste masking of bitter drugs

The medicine taste is a big issue for pediatrics that leads to a lack of medication adherence. Many drugs are very bitter and aversive to children. Flavors (e.g. sweet, sour, or salty) cannot successfully mask their bitterness. As for the oral dosage form, the best formulation for children is an oral suspension since it is difficult for children to swallow a tablet. A novel taste-masking technique will be developed in this project to overcome the above obstacle and achieve patient acceptability and compliance. The objective of this project is to develop a "child-friendly" oral suspension with a novel taste-masking delivery system for a bitter drug.

For more information:
Dr May Song Email: May.Song@unisa.edu.au Tel: +61 8 830 22429

A/Prof Michael Wiese (A/Prof in Pharmacotherapeutics)

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:
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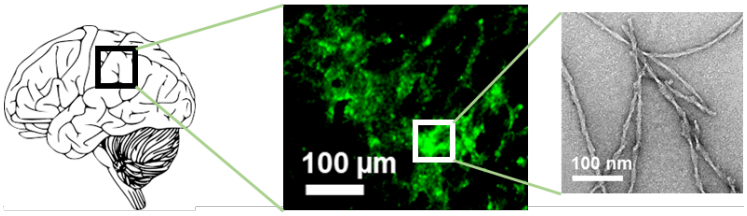
## Gut-Brain axis: Neurodegeneration, aging and future medicine

Dr Ibrahim Javed (Enterprise Fellow)

### Development of novel biomedicines against Alzheimer's disease.

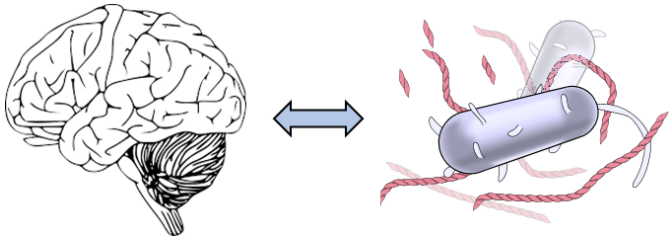
Alzheimer's disease (AD) is the most severe form of neurological disorder, characterized by the presence of extracellular amyloid-β (Aβ) plaques and intracellular tau tangles. Despite AD is becoming more prevalent with aging population, yet the mechanisms that lead to synapse destabilization and neuron death remain elusive. Deposition of fibrillar plaques in the brain correlates with neurodegeneration and cognitive disfunctions in AD. The development of biomedicine has become a new frontier in the detection, treatment and prevention of human amyloid diseases. Our team has investigated the interaction between Aβ and various classes of biomolecules and pharmaceutical formulations for controlling Aβ aggregation. This project aims to develop novel smart biocompatible biomedicines to inhibit pathogenic amyloid plaque formation in AD using *in vitro* and *in vivo* disease models.




Pathological aggregation of protein happens in the brain during AD. These aggregates look like protein fibrils, and it can be prevented by medicine.

### Gut-Brain Axis: Understanding the effect of gut-bacteria and their biofilms on neurodegeneration and aging

Neurodegeneration and brain aging have a major socioeconomic impact on aging citizens and touch every other household in Australia. Gut-bacteria has recently been demonstrated as a silent driver in various diseases, including aging and neurodegeneration. However, exact molecular triggers from gut-bacteria, that drives pathology of diseases or accelerate the physiology of aging, are unknown. In this project, we are specifically identifying the biomolecules produced by gut-bacteria that can be responsible for these paradigms and preventing them from accessing other organs can help in designing future medicine. We will be studying how these biomolecules access brain and what are the mechanisms involved when they interact with regular biological processes and how brain and gut-bacteria talk to each other in a bidirectional communication.

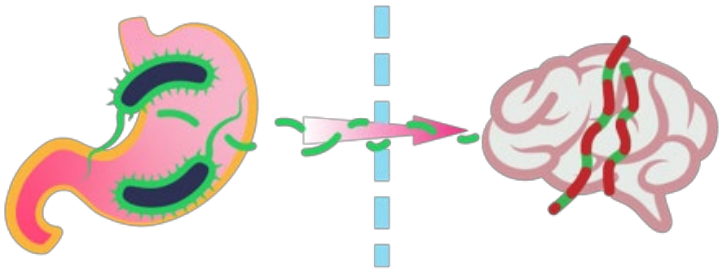


### Translocation of bacterial biofilm components from gut to the brain and its implications in brain disease.

Deposition of fibrillar tangles and amyloid plaques in the brain derived from the aberrant aggregation of tau- and amyloid-β (Aβ) peptides correlates with neurodegeneration and cognitive disfunctions in Alzheimer's Disease (AD). Notably, gut bacteria produce similar amyloid structures to support their biofilms. The interaction between bacterial amyloid fibrils and Aβ has been hypothesized to accelerate

Bidirectional communication between gut-bacteria and brain can mediate health and disease conditions and help in healthy aging.

AD symptoms. Certain bacterial proteins have potential to induce gaps in gastric epithelial cells. This can result in leak and transportation of gut-bacterial products into the blood or lymphoid tissues, and then to the brain. This project aims to study the mutual collaboration of gut-bacteria to produce these biofilm amyloids and their translocation from gut to the brain using in vitro and in vivo models.



Gut-bacteria collaborate with each other to produce joint biofilms that are more toxic to the human host. These joint biofilms can access brain to trigger or accelerate brain pathologies.

For more information:
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## Drug Discovery and Development

Prof Shudong Wang

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 Bradley Building (City West 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 Prof 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 (A/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:

### 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.

### 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.

### Targeting CDK9 for the treatment of prostate cancer

### Targeting CDK8 for the treatment of colorectal cancer

### Discovery of novel inhibitors of CDK5 for treating cancer

### Developing novel inhibitors of FLT3 for treating leukemia

### Repurposing existing drugs for cancer treatment

For more information on the Centre for Drug Discovery and Development:
Prof Shudong Wang Email: shudong.wang@unisa.edu.au Tel: +61 8 8302 2372

### Dr Hugo Albrecht (Senior Lecturer in Pharmaceutical Science)

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:
Dr Hugo Albrecht Email: Hugo.Albrecht@unisa.edu.au Tel: +61 8 8302 1093

A/Prof 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:

### Investigation of the reported interaction between fusidic acid and statins

A/Prof Matt Sykes, 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. 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.

### Identification of kinase inhibitors using structure-based approaches

A/Prof Matt Sykes, Prof Shudong Wang

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 Prof 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. 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.

Various 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:
A/Prof Matt Sykes Email: Matt.Sykes@unisa.edu.au Tel: +61 8 8302 2598

## Experimental Therapeutics

Prof John Hayball

Our laboratory aims to develop novel prophylactic vaccines and immunotherapeutics to aid in the global prevention of infectious diseases and to improve chronic and acute health outcomes with a focus on allergy and cancer. We undertake fundamental, translational and clinical research and using our broad range of experience and expertise we exploit the power and specificity of the immune system to develop cutting edge approaches to prophylactics and therapeutics.

With close industry engagement and targeted national and international collaborations we have developed vaccines, including a 'second generation' COVID-19 vaccine, a combination Zika-Chikungunya vaccine, a therapeutic vaccine for peanut allergy, with other vaccines in development as well as manufacturing process development to enable commercialisation.

Prof John Hayball
Prof 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. Prof 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.

A/Prof Kerrilyn Diener
A/Prof Diener's interests lie in understanding the early innate immune mechanisms behind antigen recognition and presentation, particularly those relating to viral infection and pregnancy. A/Prof 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 Tamara Cooper (Senior Research Fellow)
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 Preethi Eldi (Research Fellow)
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.

## 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.

### Peanut Allergy (allergic disease)

### Sepsis

### T cells and Vaccine responses

For more information on the Experimental Therapeutics Laboratory:
Prof John Hayball Email: john.hayball@unisa.edu.au Tel: +61 8 8302 1202

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## Future Industries Institute

### Bioengineering

The Bioengineering group is led by Prof Benjamin Thierry. It's research is funded by the NHMRC, MRFF, ARC, CRC, Heart Foundation, and Tour de Cure and the Bill and Melinda Gates Research Foundation. The research is highly interdisciplinary and integrate cutting-edge technologies towards addressing significant biomedical problems, including: 1. Targeted mRNA Therapeutic; 2. Image-guided cancer surgery/therapy; 3. Prenatal diagnostic and care; 4. Organoids, organotypic culture and organs-on-chips.

### A Trojan-horse approach to mRNA Therapeutics

In the context of COVID-19 vaccines, mRNA is delivered to lymph nodes near the injection site. In this project, we are leveraging this technology and investigating the feasibility of delivering therapeutic mRNAs to far more challenging targets, pancreatic and brain tumours as well as damaged heart tissues. Our approach relies on decorating lipid nanoparticles (LNPs) with ligands to specifically target the cells responsible in these pathologies for the omnipresent fibrotic tissues. Turning foes into allies, these cells will be hijacked to produce the protein encoded by the mRNA, paving the way to the development of new therapeutic approaches for these devastating conditions. The project provides excellent opportunities to be trained in nanomedicine, advanced formulation science and preclinical research, including via our collaborators at the Garvan Institute (Pancreatic cancer), QIMR (Brain cancer) and Barker Institute (Heart Failure). The project is also very timely as massive investment is being made worldwide, providing significant employment opportunities beyond academia.

### Molecular imaging-guided cancer surgery.

There is a critical need for practice-redefining treatments that increase survival of brain and pancreatic cancer patients, and/or improve the quality of life of survivors. Image-guided tumour surgery with fluorescent molecules such as ICG partially addresses this need but remains limited by the poor tumour specificity of the agents currently available. In this cross-disciplinary research project, our team is developing a novel highly fluorescent molecular imaging nanoformulation designed to specifically accumulate within tumour tissues. You will primarily work within the Future Industries Institute's bioengineering lab, which is fully equipped for the preparation of nanoformulation, including molecular imaging agents. You will also engage with the Sid Faithfull Brain Cancer Laboratory at the QIMR Berghofer in Queensland and Garvan Institute in Sydney, where cutting-edge tumour models have been developed.

Through the collaboration with our industry partners Diagnostic Green and Ferronova's R&D team, you will also gain knowledge in the GMP manufacturing of pharmaceutical products. There is a shortage of these critical skills so you will be positioned for exciting career opportunities post-graduation. Contact: Dr Nicole Dmochowska.

### Non-invasive insight into pregnancy health and disease through placental extracellular vesicles.

Since non-invasive prenatal testing (NIPT) was globally introduced in 2011, it has revolutionised prenatal testing and drastically reduced the number of invasive procedures. NIPT utilises fragments of placentally derived cell-free DNA (cfDNA) that is released into maternal blood during gestation. However, cfDNA NIPT currently only serves as a screening, not diagnostic, tool due to false positives and negatives. Our team is investigating a next-generation NIPT based on placental Extracellular vesicles (pEVs). During pregnancy, placental cells release EVs which contain DNA (which is generally identical to the fetus). This research aims to answer some fundamental questions on the biogenesis of cfDNA and pEVs, and to exploit this knowledge to develop more reliable and comprehensive NIPT based on sequencing technology. Contact: Dr Marnie Winter.

### Organoids, organotypic culture and Organs on Chips

Preclinical tools that reflect cancer patients' individual physiology and response to treatment are critical to the development of better therapy. Patient-derived organoids and organotypic tissue slices have emerged as excellent tools for testing personalised cancer therapy due to their ability to conserve the cellular and molecular heterogeneity of patients' tumours. These advanced cultures closely mimic the characteristics of the original tumour or parenchyma, allowing researchers to study biology and response to treatments in a more representative and controlled environment. Conversely, microphysiological "organ-on-a-chip" models significantly improve the preservation of the Tumour Microenvironment in explants, organoids and tissue slices. The objective of this cross-disciplinary research project is to develop an organ-on-chip platform that enables long-term culture of glioblastoma patient-derived tissue slices and cerebral organoid slices. The project is supported by the Hospital Research Foundation and in collaboration with SAHMRI. Contact: Dr Chih-Tsung Yang

For more information on projects and top-up scholarships available, please contact
Prof Benjamin Thierry Benjamin.thierry@unisa.edu.au Tel: 8302 3689

## Biophysics

### A/Prof Ivan Kempson

A/Prof (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:
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## Regenerative Medicine and Wound Healing

Prof Allison Cowin

Impaired wound healing is a spiraling epidemic that is affecting millions of people world-wide and costing the healthcare system billions of dollars each year. These wounds include burns that lead to hypertrophic scarring, chronic non-healing venous leg ulcers, arterial ulcers, diabetic wounds, pressure injuries and skin tears. Our research is primarily focused on understanding the mechanisms involved in wound healing and developing new therapeutic approaches, dressings and technologies to make wounds heal better.

### Role of inflammation in diabetic wound healing

Prof Allison Cowin and Dr Stuart Mills

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.

### Novel delivery system to facilitate oral drug administration for ulcerative colitis

Prof Allison Cowin and Dr Christopher Turner

The oral route is by far the most common route for drug administration in the gastrointestinal tract (GI tract) and can be used for both systemic drug delivery and for treating gastrointestinal disease. However, numerous hurdles limit effective drug delivery, including penetration of the mucosal layer and traffic through the hostile environment of the stomach. We have adapted porous silicon nanoparticle (pSi NP) technology to facilitate efficient drug delivery to the GI tract. Emerging data suggests nanoparticles better penetrate mucosa and improve drug retention compared to the delivery of drugs alone. Critically, pSi NPs are pH sensitive and shelter the payload from the highly acidic conditions of the stomach, with further evidence of protection from stomach proteases. Additional advantages of pSi NPs include biocompatibility, the capacity to be loaded with clinically relevant doses of RNA, proteins and monoclonal antibodies (mAb), and can be tuned to facilitate slow release. We hypothesize pSi NPs will efficiently deliver therapeutic payloads to the GI tract of those affected by ulcerative colitis (UC), a common

inflammatory bowel disease. We aim to deliver clinically relevant doses of Flightless I neutralizing antibody, a mAb being developed to treat UC. Although oral drug delivery is a significant area of research, few have translated to the clinical phase. The development of improved treatment approaches would provide enormous benefit to those with UC and other gastrointestinal diseases.

### New approaches for the treatment of wound infections

Prof Allison Cowin and Dr Zlatko Kopecki

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.

### Role of autophagy in wound healing

Prof Allison Cowinand Dr Xanthe Strudwick

### Understanding the role of Flightless protein in pressure wound injuries

Prof Allison Cowin and Dr Zlatko Kopecki

For more information on the Regenerative Medicine and Wound Healing Laboratory
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## Health and Biomedical Innovation

Prof Janna Morrison

### Early Origins of Adult Health

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 Prof Janna Morrison, whom has been funded as a fellow by the Heart Foundation, NHMRC and ARC. 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. She has collaborated internationally to bring new methods to fetal physiology including MRI to measure placental function and fetal cardiac function and hemodynamics. Her longstanding interest in the effects of maternal drugs on fetal development has expanded to testing interventions to improve outcomes in complicated pregnancies. Dr Jack Darby is a postdoctoral fellow in EOAHRG whom has a particular interest in using MRI to study fetal development. His research focuses on reducing the incidence of stillbirth, neonatal mortality and long-term morbidity following fetal growth restriction (FGR) as well as developing novel interventions to ensure successful cardiorespiratory transitions in these babies following preterm birth. Dr Ashley Meakin is a postdoctoral fellow in EOAHRG whom has an interested in the role of sex hormones in fetal and placental development and function. He has developed several LC-MS/MS methods for measuring enzyme activity to understand how drugs are metabolised in the

maternal-placenta-fetal unit and the role of sex hormones. Dr Mitchell Lock is a postdoctoral fellow in EOAHRG whom focusses on the molecular regulation of cardiorespiratory development in the fetus.

EOAHRG collaborates widely within SA and internationally. Students have the opportunity to participate in these collaborations and, if appropriate, visit international labs. While working in EOAHRG students will be exposed to a wide range of methods and techniques including real-time PCR, Western blots and immunohistochemistry to analyse gene expression as well as protein expression and distribution in samples collected from heart, lung, brain, placenta, etc. Students will also participate in fetal surgery, MRI, post-op care, and sample collection.

Potential projects include:

### Does maternal hyperoxygenation rescue the growth restricted fetus?

Babies that are born too small (fetal growth restriction) are at increased risk of poor outcomes at birth and chronic disease in adulthood. Currently there are no treatments to improve growth in these fetuses but we know that they have less oxygen and glucose than normally grown babies. In this project, oxygen and glucose are normalised in the fetus in an attempt to rescue the growth restricted fetus with the aim of normalising the development of the cardiorespiratory system to reduce the risk of cardiac and respiratory disease.

### Understanding the role of male sex hormones in the placenta and regulation of fetal growth

Rates of early pregnancy loss and stillbirth are higher for male than female fetuses. A major contributor to miscarriage and stillbirth is reduced fetal growth that is often the result of poor placental function. Placental-specific androgen signalling axis may be regulators of male fetal growth outcomes. In this project we will test the hypothesis that: Increased activity of the androgen signalling axis in gestation maximises male birthweight and therefore survival; however, if reduced oxygen and/or glucose in gestation, this androgen driven adaptation will be dysregulated in males that have reduced growth.

### Nutritional supplement to break the cycle of poor maternal and fetal cardiovascular health in hyperandrogenic pregnancies

Polycystic ovary syndrome (PCOS) affects 20% of women of reproductive age. During pregnancy with PCOS, excess androgens result in serious complications for both mothers and their babies. There are currently no effective therapies. Our project therefore aims to test whether a simple, cost-effective nutritional supplement restores normal blood vessel function and development in a clinically relevant PCOS-like sheep model during pregnancy. We investigate the efficacy of this supplement compared to standard treatment with metformin to improve cardiometabolic outcomes in mothers and their offspring, refining the clinical management of PCOS during pregnancy.

### Predicting the impact of drugs taken by the mother on the fetus

Medications are taken in 99% of pregnancies. However, pregnancies complicated by fetal growth restriction are more likely to involve medications, often aimed at treating the causes of FGR. This project will determine the pharmacokinetics of these drugs when given to either the mother or the fetus. We also have physiological data from these fetuses, which will allow us to perform pharmacodynamic analysis of these samples. This information will inform the development of new medications to treat fetal growth restriction to improve outcomes in these vulnerable babies.

### Predicting fetal growth early in pregnancy with non-invasive MRI: Validation in a preclinical model with a focus on the lung

Nearly 50% of all pregnancies complicated by fetal growth restriction (FGR) go undetected until after birth, despite improvements in obstetric imaging and management. A major risk in these babies is respiratory distress syndrome. This project will use Magnetic Resonance Imaging (MRI) of the fetal lung to comprehensively model and measure markers of placental maturation, growth and function in FGR. We hypothesise that MRI in early gestation used to measure fetal growth and oxygenation will correlate with gene and protein expression of molecular markers of the regulation of lung development in late gestation.

### How low can you go?: Impact of weight loss drugs on fetal development

Over half the population is overweight or obese. However, with the recent introduction of effective weight loss drugs, the prevalence of obesity is not increasing. Recommendations are to stop use of these drugs at least 2 months prior to conception; however, this may not happen. Thus, it is important to understand the impact of a mother taking weight loss drugs during pregnancy on the development of the fetus and cardiometabolic health of the offspring.

### Impact of microRNA 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. MicroRNA play a role in cardiac development and their expression can be manipulated pharmacologically, which may be a strategy to improve cardiac development in IUGR.

### Does increasing uterine artery blood flow improve placental and fetal development?

Fetal growth restriction (FGR), where a baby weighs below the 10th percentile for their gestational age, occurs in 6.5 % of live births. These FGR 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 FGR may be to increase fetal substrate (oxygen and nutrients) supply. Resveratrol, a nutritional supplement, increases uterine artery blood flow. We hypothesize that increased uterine artery blood flow will normalise placental function and accelerate lung.

For more information on EOAHRG:
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## Infectious Diseases and Microbiology

A/Prof Rietie Venter

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. 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 focus 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.

### 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.

### 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**

### 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:
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## Musculoskelet Biology

A/Prof Paul Anderson

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

A/Prof Paul Anderson and Prof 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.

### Therapeutics for Rare Genetic Bone and Mineral Disorders

A/Prof Paul Anderson and Prof 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

A/Prof Paul Anderson and Prof 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

A/Prof Paul Anderson and Prof 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:
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## Neuroscience

A/Prof Larisa Bobrovskaya and Prof Xin-Fu Zhou (Adjunct Prof)

We conduct research within the field Parkinson's disease, stress, depression, diet and gut-brain connections. We use animal models and human samples to investigate cellular and biochemical mechanisms of diseases, identifying novel biomarkers and testing novel treatments.

A specific project can be developed depending on student's interest.

### 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.

### 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.

### Pro-BDNF and its receptors as biomarkers and therapeutic targets for major depression

Treatment of liver failure with human-urine derived induced hepatocyte-like cells
A role of p75 and its toxic ligands in the type II diabetes, energy metabolism and insulin resistance
Roles of p75 and its degenerative ligands in the development of diabetic microvascular complications
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)
Can the proBDNF/p75 signal pathway be targeted for the brain cancer therapy?

For more information on the Neuro-Regeneration Group:
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## Population Health Chemistry

A/Prof Cobus Gerber, Emeritus Professor Jason White and Dr 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:
A/Prof Cobus Gerber Email: Cobus.Gerber@unisa.edu.au Tel: +61 8 8302 2568

Dr Layla Mahdi (Senior lecturer in Clinical Microbiology)
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 includes 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:
Dr Layla Mahdi Email: layla.mahdi@unisa.edu.au Tel: +61 8 8302 2383

A/Prof 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.

### The role of vitamin D in the development of chemotherapy-induced mucositis

A/Prof Andrea Stringer, A/Prof Paul Anderson, Bronwen Mayo

### The effect of vitamin D on the intestinal microbial ecosystem

For more information:
Dr Andrea Stringer Email: Andrea.Stringer@unisa.edu.au Tel: +61 8 8302 1760

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## Mass Spectrometry and Proteomics

Prof Peter Hoffmann
The Mass Spectrometry and Proteomics group houses more than $5 M worth of equipment. We are the National Collaborative Research Infrastructure Strategy (NCRIS) node for tissue mass spectrometry imaging and provide service to industries and national and international researchers. Specific applications of mass spectrometry in our lab include, food safety and quality control, PFA analysis, monitoring of yeast health during the brewing process, glycan monitoring in osteoarthritis, protein identification and quantification of cancer samples, and patient derived sample testing.

Prof Peter Hoffmann is Lloyd Sansom Chair in Clinical & Health Sciences, President of the Australasian Proteomics Society, and Conference Chair for the National Meeting of the Australasian Proteomics Society and Treasurer of the International Human Proteome Organisation (HUPO). 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. He collaborates with Coopers brewery and CSL on multiple industry relevant projects.

## Mapping signaling pathways activated in ovarian cancer with PARP inhibitors

Prof Peter Hoffmann and Dr Clifford Young

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.

## Pushing the boundaries of high throughput quantification by mass spectrometry

Prof Peter Hoffmann and Dr Manuela Klingler-Hoffmann

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.

## Predicting chemoresponse in ovarian cancer

Prof Peter Hoffmann and Dr Manuela Klingler-Hoffmann

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 starts. 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 to reveal the affected protein pathways associated with different drug treatments. There will be ample opportunity to improve aspects of the methodology from sample preparation through to the analytical performance of our mass spectrometry platform to help resolve and understand the different chemoresponses.

## Mapping α2,3- and α2,6-linked sialic acid in gynaecological cancer tissues

Prof Peter Hoffmann, Dr Matthew Briggs and Dr Clifford Young

## Go with the flow: enabling deeper proteomic analysis with improved chromatography

Prof Peter Hoffmann and Dr Clifford Young

## Mechanisms in Cell Biology and Disease

Prof Doug Brooks

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 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 Prof 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.

Prof Doug Brooks

Prof 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. Prof 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.

Prof Sandra Orgeig

Prof 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.

### Cancer Cell Biology

Defining altered endosome-lysosome biogenesis in cancer; companion diagnostics and therapeutics

Prof Doug Brooks, Dr Rob Brooks, Dr Jessica Logan, Dr Alexandra Sorvina, Dr Carmela Martino, Dr Ian Johnson, Dr Stavros Selemidis (RMIT), Dr Emma Parkinson-Lawrence, Prof Sandra Orgeig, Dr Joanna Lazniewska, Chelsea Thomas, Dr Brian Dale, Prof Paul Reynolds (SA PATH), Prof Adrian Esterman, Prof Ian Olver (Uni Adelaide), Prof Lisa Butler (Uni 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.

### Developing biomarkers and therapeutics for primary and metastatic lung cancer

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

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.

### The role of the lung microbiome in lung cancer

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

### Developing precision medicine tools using "big data"

Dr Jessica Logan, Dr Ashley Hopkins (Flinders Uni), Dr Carmela Martino, Prof Andrew Rowland (Flinders Uni), Prof Doug Brooks and Prof Michael Sorich (Flinders Uni)

## Medicinal Chemistry

### Synthesis of novel therapeutics to treat late-stage prostate cancer

Dr Shane Hickey, Dr Trent Ashton (WEHI), Prof Lisa Butler (UoA) and Prof Doug Brooks

This medicinal chemistry project will develop small molecule inhibitors of critical enzymes which control the progression of prostate cancer from an early treatable stage to a late stage known as castration-resistant prostate cancer. The student will develop skills in synthetic chemistry (such as performing chemical reactions and product isolation), analytical chemistry (such as nuclear magnetic resonance, and high resolution mass spectrometry), and will be exposed to biological assays and *in silico* drug design.

### Synthesis of fluorescent biological tools to better understand disease

Dr Shane Hickey, Dr Ian Johnson, Dr Trent Ashton (WEHI), and Prof Doug Brooks

This synthetic chemistry project will develop small fluorescent molecules which target specific cellular organelles and provide capacity to visualize critical cellular events in real-time using fluorescence

microscopy. The student will develop skills in synthetic chemistry (such as performing chemical reactions and product isolation), analytical chemistry (such as nuclear magnetic resonance, and high resolution mass spectrometry), photophysical chemistry (such as UV-Vis and fluorimetry), and will be exposed to cell biology and confocal microscopy.

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

Dr Shane Hickey and A/Prof Sally Plush

### Cell Biology of Paediatric Metabolic Disease

### Lung pathology in lysosomal storage disorders

### Lung pathology in the lysosomal storage disorder, Mucopolysaccharidosis I

Prof Sandra Orgeig and Dr Emma Parkinson-Lawrence

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

Prof Sandra Orgeig, Dr Emma Parkinson-Lawrence, A/Prof Greg Hodge (Uni Adelaide), Prof Doug Brooks

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

Prof Sandra Orgeig, Dr Emma Parkinson-Lawrence, Prof Doug Brooks and Dr David Ketteridge (WCHs)

For more information on the Mechanisms in Cell Biology and Disease Research Group:
Prof Doug Brooks Email: doug.brooks@unisa.edu.au Tel: +61 8 8302 1229

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## Quality Use of Medicines and Pharmacy Research Centre

Prof Libby Roughead

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

Medicines use is rapidly increasingly and impacts on both the health care system and individual consumers' quality of life. Whilst medicines play a critical role in curing disease and preventing poor health outcomes, problems with medicines use such as overuse, inappropriate use, and side-effects adversely affect millions of Australian lives each year and add to the burden on our health care system through avoidable primary care visits and hospital admissions.

If you have an interest in the following research fields:

- Health data and analytics
- Education for health care professionals
- Safety of medicines, medical devices, and digital health tools
- Medicines use in the community and aged care
- Optimising the use of medicines
- Bioactivities and/or chemistry of specific Australian bush foods and medicines
- Pharmacy practice and practice change
- Digital health

Please contact one of our researchers below to discuss available projects.

Research staff available to supervise Honours Students:

| | |
|---|---|
| Prof Nicole Pratt | Pharmacoepidemiology, Statistical methods |
| A/Prof Andre Andrade | Digital health |
| 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 |
| A/Prof Lisa Kalisch Ellett | Medicines that cause or worsen dementia and cognitive impairment, Quality use of medicines, Medicines safety |
| Dr Gizat Kassie | Medicines associated with dementia and cognitive impairment |
| Dr Lan Kelly | Pharmacoepidemiology, Statistical methods |
| Dr Renly Lim | Quality use of medicines, Medicines utilization, Aged Care |
| A/Prof Stephanie Reuter Lange | Clinical Pharmacology, Dose Optimisation |
| Dr Susan Semple | Australian medicinal plants, Antimicrobials, Complementary and Alternative Medicines |
| Dr Imaina Widagdo | Quality use of medicines, Pharmacoepidemiology, Frailty, Linked data analysis, Health services use and health outcomes. |

### Complexity and number of changes in medicines post admission in aged-care facilities.

Svetla Gadzhanova and 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.

### Risk management plans for newly marketed medicines

Nicole Pratt and 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.

### Product Information and the influence on prescribing

Nicole Pratt, Emmae Ramsay and Lisa Kalisch Ellett

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.

Development of a medicine complexity index using administrative health claims data
Lisa Kalisch Ellett

Can Pharmaceutical Benefits Scheme (PBS) data be used to assess chemotherapy dosing?
Libby Roughead and Nicole Pratt

Medicines and frailty
Renly Lim, Libby Roughead, Lisa Kalisch Ellett and Nicole Pratt

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

Identifying reasons for non-adherence of clinical guidelines for mental conditions
Andre Andrade

Quality use of pathology
Marianne Gillam and Libby Roughead

Innovative post-marketing surveillance: identification and preparation of medicine information to use in a universal PE database with a common data model.
Nicole Pratt, Ty Stanford and Jodie Hillen

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## Therapeutics and Pharmaceutical Science Centre

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.

For more information on TPSRG:
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