



University of  
South Australia

# Bachelor of Biomedical Research (Honours)

Research Booklet 2022



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## Why the IHBV Bachelor of Biomedical Research (Honours)?

Thank you for your interest in undertaking the IHBV Bachelor of Biomedical Research (Honours) within 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.

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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

Barberry and Sumac – Potential nutraceuticals for chronic health conditions?\*

*\*This project can be adapted to be offered as either an Honours or Master project*

[Dr Permal Deo](#) and [Dr Evangeline Mantzioris](#)

Barberry and Sumac are berries which grow in the Middle east and are widely used in Middle Eastern cookery. Additionally, they have been used in complementary medicine and used as a supplement for general wellbeing. More recently SR and MA's have reported favourable health benefits of the active ingredients of these berries when for chronic conditions such as overweight and obesity, Type 2 diabetes, hyperlipidemia, non-alcoholic liver disease and poly cystic ovary disease.

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

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.

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[The effect of conventional cooking on phenolics and antioxidant activities of legumes](#)

[Dr Evangeline Mantzioris](#) and [Dr Permal Deo](#)

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

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

[The clinical use of ultra-processed foods in weight management](#)

[Dr Evangeline Mantzioris](#) and A Forsyth (La Trobe University)

Ultra-processed foods (UPF) are defined by the NOVA system as containing five or more ingredients including substances extracted from foods and substances derived from further processing of food components (Monteiro et al., 2016). They may also contain food additives including colours, flavours, non-sugar sweeteners and processing aids found only in UPF. UPF are often attractively packaged and extensively marketed as convenient replacements for less processed foods. Typically high in saturated fat, sugar and salt, and low in micronutrients and fibre, UPF are considered to be energy dense and nutrient poor. They are not recommended in national dietary guidelines, with consumption actively discouraged by some (i.e. Brazil). However, recent evidence has shown high consumption across western countries of up to 60% energy intake, and emerging evidence indicates that UPF consumption is associated with poor mental and physical health including cardiovascular disease, cerebrovascular disease, depression and all-cause mortality (Moubarac et al., 2017; Rauber et al., 2018; Pagliai et al, 2021; Steele et al., 2016).

Given the high caloric values of UPF and their ease of consumption, they are often included by clinical dietitians into high energy diets for weight gain. Given our current understanding that UPF consumption is associated with nutrition-related chronic disease, this raises potential concern for their use as high energy foods. The aims of this study are to:

1. To assess how UPF are recommended and promoted by dietitians for weight gain across all sectors of health.
2. To assess the attitude of dietitians of promoting UPF for weight gain.
3. Review clinical practice guidelines on the use of UPF for weight gain.

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

[A/Prof Karen Murphy](#), [Dr Karma Pearce](#), Dr Diane Hosking (AIHW)

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

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

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

[A/Prof Karen Murphy](#), Prof Catherine Itsiopoulos (La Trobe University)

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

*Ref: Martinez-Gonzalez MA. Public Health Nutr. 2006 Feb;9(1A):127-31.*

## South Australian MedDiet Adherence Study

[A/Prof Karen Murphy](#), [Prof Jon Buckley](#)

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

*Ref: Murphy KJ et al. Nutrients 2013, 5, 4665-4684; doi:10.3390/nu5114665*

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## Fertility– With Repromed

[Dr Karma Pearce](#), Prof K Tremellen

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

conceiving a child this is a growing area of research.

### Effect of nutrients on fertility

#### [Dr Karma Pearce](#)

Previous work has shown that a Western style dietary pattern and in particular dietary fats and sugars reduces testosterone levels in men through impairing gut function and through the production of endotoxins. We now wish to investigate whether specific nutrients can repair gut function. The Aim of this study would be to conduct a clinical trial to evaluate the effect of specific nutrients in reducing endotoxin production and repairing gut function.

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### 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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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.

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

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

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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.

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### Identifying novel genes that play a role in the development of addiction to methamphetamine.

Using an existing pool of tissue samples, we plan to test for statistical association in a number of candidate genes with an increased risk of developing addiction to this stimulant drug. We also hope to better understand the functional consequences of this variation by assessing physiological and psychological differences in response to stimulant drug administration.

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### 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.

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### 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 or 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.

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#### Physical activity and brain atrophy: a large-scale study

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

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

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#### 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.

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#### 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.

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Population semi-PBPK models for cost-effective drug development

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

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Quantitative description of the cardiovascular system

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Suicide Prevention and Mental Health Diagnostics and Treatment

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

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Using Drosophila and cell biology to understand the biology of neurological disorders

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## **Bone Growth and Repair**

**Prof Cory Xian**

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

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

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

- Growth plate cartilage injury responses, repair mechanisms, and growth factor and/or stem cell-based approaches for regeneration
- Pathobiology for and prevention of cancer chemotherapy-induced bone defects

Roles of matrix proteins glypicans in regulating skeletal cell formation, bone growth and repair  
Roles of neurotrophic factors in regulating skeletal cell formation, bone remodelling and bone healing

Mechanisms for injury-induced growth plate cartilage degeneration and bone growth defects  
Development of growth factor/hydrogel composites for growth plate cartilage regeneration  
Pro-inflammatory cytokine – NF- $\kappa$ B signaling in osteoclast formation and bone loss after cancer chemotherapy

Roles of Wnt/ $\beta$ -catenin signaling in cancer chemotherapy-induced bone loss and marrow adiposity

Roles of oxidative stress in bone loss following cytotoxic chemotherapy

Skeletal cell apoptosis and molecular signals for osteoclastic bone resorption following cancer chemotherapy

Prevention of bone loss caused by cancer chemotherapy

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

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## **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

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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)

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

[damon.tumes@unisa.edu.au](mailto: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

[yeesim.khew-goodall@unisa.edu.au](mailto:yeesim.khew-goodall@unisa.edu.au)

#### Identifying targets to overcome chemoresistance in breast cancer

Our laboratory has identified signalling pathways controlled by reversible phosphorylation that regulate how secreted growth factors, cytokines and cell surface receptor tyrosine kinases (RTKs) are trafficked. These signalling pathways play a critical role in controlling the sensitivity of triple negative breast cancers (TNBCs) to chemotherapy, which is the first line of therapy for TNBCs. However, about 20-25% of TNBCs are/become chemoresistant and for whom there are few other treatment options, making this a critical unmet need. We have projects to elucidate the mechanisms underpinning how these signalling pathways

control chemoresistance in TNBC as well as projects to elucidate how these signalling pathways regulate RTK trafficking to impact on the aggressiveness of cancers. We utilise a range of platforms for our research, including molecular biological, biochemical and cell biological (including advanced microscopy).

#### Cellular Stress and Immune Response Laboratory led by Dr Nirmal Robinson

([nirmal.robinson@unisa.edu.au](mailto:nirmal.robinson@unisa.edu.au))

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

#### Cytokine Receptor Laboratory led by Prof Angel Lopez

([angel.lopez@sa.gov.au](mailto:angel.lopez@sa.gov.au))

Cytokine receptors transmit signals between the extracellular environment and the cell's internal machinery and cause cells to respond in a variety of ways such as maintenance of viability or proliferation. Abnormalities including enhanced cell viability or survival, and increased cell proliferation are hallmarks of cancer.

Our laboratory seeks to understand the mechanism of cytokine receptor activation, in particular GM-CSF, IL-3 and IL-5 receptors, in health and disease. This will reveal universal biological rules and allow the development of new drugs for diseases such as leukaemia, asthma and arthritis.

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

#### Gene Regulation in Cancer Group led by A/Prof Philip Gregory

([philip.gregory@unisa.edu.au](mailto:philip.gregory@unisa.edu.au))

With a particular focus on breast and prostate cancers (the two most common cancers in women and men) we seek to understand how cancer cells gain aggressive features that ultimately lead to therapy resistant and metastatic disease. During cancer progression, cancer cells undergo significant changes in their cell structure and invasive ability. These cellular changes are caused by alterations in both coding and non-coding RNAs.

Our goal is to identify key molecular mechanisms driving the development of aggressive breast and prostate cancer. We use a range of advanced molecular techniques including microRNA profiling, transcriptomics, and CRISPR based genome editing to identify important genes causing cancer aggressiveness.

#### Gene Regulation Networks Group led by Dr Cameron Bracken

([cameron.bracken@unisa.edu.au](mailto:cameron.bracken@unisa.edu.au))

Dr Bracken's laboratory focuses on the mechanisms through which networks of genes are regulated in breast cancer. His laboratory is especially interested in the role of microRNAs and the "rules" by which they choose the genes that they target. There are also ongoing projects in less well characterized aspects of microRNA biology such as microRNA co-operatively, what role they play in the nucleus and what is the effect of naturally occurring microRNA sequence variants. Many of these projects are performed within

the context of Epithelial-Mesenchymal Transition (EMT), a reversible phenotypic switch that is essential throughout development and for various processes in the adult, but which also drives human pathologies such as metastasis where its inappropriate activation promotes cancer motility. These projects typically blend wet bench experimentation and bioinformatic analysis to provide a systems-level view of gene expression and the roles played by microRNAs in gene regulation.

**Leukaemia Unit, Molecular and Genetic Pathology Laboratory** led by Prof Susan Branford ([susan.brandford@sa.gov.au](mailto:susan.brandford@sa.gov.au))

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

We are investigating the response to therapy by examining the genetic abnormality that causes chronic myeloid leukaemia: the BCR-ABL1 gene. Specific therapy targets and kills the leukaemic cells containing BCR-ABL1. We monitor the kinetics of drug response by using molecular techniques to measure the levels of BCR-ABL1 mRNA. A rapid reduction of BCR-ABL1 is associated with the best long-term outcome, although this occurs in a minority of patients. We are investigating whether the heterogeneity of drug response is associated with variation in genes that initiate leukaemic cell death.

A major interest of ours is the sensitive detection of mutations within the BCR-ABL1 gene and genome-wide deep sequencing for the detection of mutated genes that lead to disease progression. We are currently developing techniques for the detection of an ultra-rare leukaemic signature using deep sequencing with single molecule barcodes. The aim is to determine if there is a level of leukaemia below which patients can safely cease drug therapy without rapid relapse.

Current research projects include characterising the rate of leukaemic cell death and the heterogeneity of response to tyrosine kinase inhibitor therapy; and defining the role of additional genomic mutations discovered in BCR-ABL1-expressing cells.

**Lymphatic Development Laboratory** led by Prof Natasha Harvey ([natasha.harvey@unisa.edu.au](mailto: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](mailto: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](mailto: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](mailto: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](mailto: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](mailto: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](mailto: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](mailto: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](mailto: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](mailto: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](mailto: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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## 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.

#### [Fingerprinting lipids](#)

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

#### [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.

#### [Clean water](#)

Develop enhanced filtration device This project will investigate different chemical modification/treatments of activated carbon filters that will improve the capture of both dissolved organic matter and water borne pathogens from water. The key aim of this research is to deliver a more efficient carbon filter for dissolved organic matter whose manufacture and chemical treatment can be easily upscaled from in-house to full production in South Australia by Puratap. *Students who choose to undertake a project focused on delivering clean water can expect to become proficient in key skills related to sensor development, carbon block preparation and analytical chemistry (spectroscopy, GC, HPLC).*

#### [Development of water-soluble luminescent cation sensors](#)

For more information on the Bioinorganic Synthesis and Imaging Group:

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#### [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 be taken either with or within food; this introduces extreme compliance challenges. This project is focused on developing novel solid dosage forms based on lipid encapsulated in porous excipients; these drug carriers optimise the pharmaceutical food effect and facilitate oral medicines without a food effect and hence will potentially increase compliance for patients with psychotic disorders.

#### [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:

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#### [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](#)

In addition, I am 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):

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[Dr Franklin Afinjuomo](#) (Formulation Scientist)

Dr. Franklin Afinjuomo interest and area of research focus on the development of novel drug delivery systems and the use of different carriers such as hydrogels, solid dispersions, microparticles, and films for the delivery of drugs. I also have a strong interest in formulation, solubility improvement, rational drug design, synthesis, characterization, and the biomedical application of polysaccharides conjugates. Projects in drug delivery may be available for students interested in formulation and drug delivery. (please kindly email or talk to Dr. Afinjuomo for more information). Available projects: Oral disintegrating film (ODF) for delivery of melatonin and Vitamin D; Novel Inulin hydrogel for the delivery of nutrients/prebiotics.

[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.

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### [Dr Kristen Bremmell](#) (Senior Lecturer, Pharmaceutical Science)

Dr Kristen Bremmell undertakes research in the areas of formulation science, drug delivery and biopharmaceutical purification. We use advanced formulation strategies such as porous particles, lipid-based systems and nano vesicles to improve the oral delivery of drugs. Improvement in drug solubility, absorption and bioavailability can be achieved. Interesting cell models that mimic the gut wall are used and further developed to investigate how the formulation drives oral drug absorption. We have a number of projects in this area where a student could select a project according to their interest. An example of a current research project follows.

### Silica-lipid hybrid microparticles for protein delivery

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

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### [Paris Fouladian](#)

The overall goal of 3D printing projects at PIDG is to develop patient-centric customised and innovative formulations platform to minimise drug-related problems (DRPs), thus improving the quality use of medicines. Formulation issues that increase the risk of DRPs include frequent medication administration, unpleasant taste, size, stability, dose inaccuracies, and release kinetics associated with conventional dosage forms. The findings from these projects will serve as a basis for the move towards introducing 3D printing technologies into on-demand production to improve the quality use of medicines.

### [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.

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### [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 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.

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### [Dr Des Williams](#) (Adjunct Senior Research Fellow)

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

Dissolution of drugs from sustained release dosage forms

[Dr Des Williams, A/Prof David Foster](#)

Environmental fate and potential effects of organic contaminants, such as pharmaceuticals

[Dr Des Williams, Mike Williams \(CSIRO\)](#)

Formulation, stability and *in vitro* efficacy of cyclodextrin inclusion complexes with selected suitable antibiotics for 24-hour infusion in the ambulatory care setting

[Dr Des Williams, Prof Sanjay Garg](#), CPIE Pharmacy Services (Andrew Sluggett)

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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 earned them the 2001 Nobel Prize in Physiology & Medicine. CDKs catalyze the phosphorylation of substrate proteins by transferring phosphate from ATP via their serine or threonine residues. Tumour-associated cell-cycle defects are mediated by alterations in CDK activity. Although many CDK inhibitors have been identified, little progress has been made in the discovery of mono-specific inhibitors of CDK4, a kinase that is dysregulated in several cancers. High specificity will reduce off-target activities of the



inhibitors and allow them to be minimally toxic. The aim of this project is to design, synthesise and evaluate a novel class of drug-like molecules that specifically targeting CDK4, and are cytotoxic to cancer cells.

#### [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:

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#### [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.

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#### [Dr Matt Sykes \(Program Director: Pharmaceutical Science\)](#)

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](#)

[Dr Matt Sykes](#), Prof John Miners (Flinders University)

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

This project will look at the role that OATP and other enzymes (such as P450s) play in this important clinical interaction. Computational work will also be undertaken in order to understand the theoretical

basis for the drug-drug interaction. Experimental work for this project would be conducted in the Department of Clinical Pharmacology at Flinders University.

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

[Dr 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. The outcomes of this project will significantly advance the current understanding of the structure and mechanism underpinning kinase activity. The ligands will be invaluable chemical biology tools to study the role of kinases in protein translation leading to pharmacological target validation. We are interested in a number of different kinases; students will have the opportunity to work on the most current kinase of interest.

*Various other projects in the area of drug design and discovery may be available (please talk to Dr. Sykes for more information)* Please note: Students working with Dr. Sykes will be offered the opportunity to be involved in chemistry laboratory teaching.

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### 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:

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## [Future Industries Institute](#)

### Bioengineering

The Bioengineering group is led by [Prof Benjamin Thierry](#). It is a node of the ARC Centre of Excellence for [Convergent Bio-Nano Science and Technology](#) and funded by the NHMRC, ARC and the Bill and Melinda Gates research Foundation. Our research is highly interdisciplinary and integrate cutting-edge technologies towards addressing significant biomedical problems, including: 1. Cancer diagnostic and

image-guided surgery/therapy; 2. Precision cancer radiotherapy; 3. CAR T cell manufacturing; 4. Prenatal diagnostic and care; 5. Point-of-care biodiagnostics.

#### Development of a blood micro sampling/processing cartridge for point of care diagnostic of pregnancy complications

We have recently developed a prototype of a point of care preeclampsia diagnostic technology (read more in the [Herald Sun](#)). This is significant as the condition is the direct cause of death for over 500,000 infants and 76,000 pregnant women, mostly in low resource countries. Despite its significance and global prevalence, effective diagnosis of preeclampsia remains a challenge and our technology based on solid-state sensing nanotechnology can measure blood biomarkers with very high sensitivity. An integral part of decentralized testing for diagnostic biomarkers is the ability to accurately sample and process finger-prick blood without using any of external equipment. The Honours project will aim to develop a blood collection/processing device using for example 3D printing and to validate its performance with clinical samples. Contact: [Dr Duy Tran](#).

#### Improved manufacturing of CAR T cells using “Sleeping beauty” Transposons

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

Nano-formulation of kinase inhibitors. Contact: Dr [Nicole Dmochowska](#).

Towards molecular imaging-guided cancer treatment. Contact: Dr [Nicole Dmochowska](#).

Advanced bioengineered models of the placenta and its dysfunction during preeclampsia. Contact: [Dr Marnie Winter](#).

Non-invasive insight into pregnancy health and disease through placental extracellular vesicles. Contact: [Dr Marnie Winter](#).

For more information on projects available, please contact

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#### 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.

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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 Cowin](#) and [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 and NHMRC and is currently an ARC Future Fellow. Her current research focuses on how the fetal cardiovascular system responds to changes in nutrient supply before conception and during pregnancy. Initial work focused on understanding how the small baby maintains its blood pressure *in utero* and if these mechanisms might lead to an increased risk of hypertension in adult life. Dr Jack Darby is a postdoctoral fellow in EOAHRG whom has a particular interest in understanding the molecular mechanisms by which sub optimal *in utero* conditions such as fetal hypoxaemia and hypoglycaemia influence cardiac development and program adult-onset cardiovascular disease. More recently he has been focused on combining clinically translatable MRI measures with molecular techniques to test the effectiveness of intervention strategies.

[Does the preterm male fetus have greater cardiovascular vulnerability due to delayed cardiomyocyte maturation?](#)

[Prof Janna Morrison](#) and [Dr Jack Darby](#)

In Australia, 7% of babies are born preterm. Males are more vulnerable during the transition to living

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

#### [The role of microRNA in cardiac proliferation](#)

[Prof Janna Morrison](#) and [Dr Jack Darby](#)

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

#### [Impact of maternal undernutrition on fetal cardiac development](#)

[Improving lung development through increased pulmonary oxygen delivery](#)

[Prof Janna Morrison](#), [Dr Jack Darby](#) and [Prof Sandra Orgeig](#)

[Does resveratrol influence placental development?](#)

[Prof Janna Morrison](#), [Ash Meakin](#), [Dr Jack Darby](#) and [A/Prof Michael Wiese](#)

[Does maternal supplementation with resveratrol in late gestation alter insulin signalling in the mother or the fetus?](#)

[Prof Janna Morrison](#), [Dr Jack Darby](#) and [A/Prof Michael Wiese](#)

[Epigenetic basis of left ventricular hypertrophy in the small baby](#)

[Prof Janna Morrison](#), [Dr Jack Darby](#) and [A/Prof Michael Wiese](#)

[Fetal and maternal drug metabolism in complicated pregnancies](#)

[Prof Janna Morrison](#), [Ash Meakin](#), [Dr Jack Darby](#) and [A/Prof Michael Wiese](#)

[Impact of cortisol on drug exposure in the fetus](#)

[Prof Janna Morrison](#), [Ash Meakin](#), [Dr Jack Darby](#) and [A/Prof Michael Wiese](#)

[Investigating changes in fetal lipid profiles in response to changes in maternal nutrient supply](#)

[Prof Janna Morrison](#) and [A/Prof Sally Plush](#)

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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 to 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 of bacterial cell division. Other cell division proteins can then be recruited and a septum forms that allows a single cell to divide into two daughter cells. FtsZ is an attractive target to develop new antibacterial agents with selective toxicity to bacteria because it is essential to bacterial cell division, it is highly conserved in different bacterial species and it is not present in higher eukaryotes. This project aims to identify and develop new inhibitors targeting the FtsZ protein of antibiotic resistant bacteria.

### **Antimicrobial Resistance in Residential Aged Care Facilities**

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

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

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#### Musculoskeletal 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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#### [Neuro-Regeneration](#)

[A/Prof Larisa Bobrovskaya](#)

[Prof Xin-Fu Zhou \(Adjunct Prof\)](#)

Dr Frances Corrigan (Uni Adelaide)

Dr Mohammed Al-Hawwas (Flinders Uni)

Our group's research focuses on the three main areas:

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

### 3. Cell therapy for treatment of diabetes, liver failure and Parkinson's disease

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

#### [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](#)

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 and 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.

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[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.

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[Dr 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

[Dr Andrea Stringer](#), [A/Prof Paul Anderson](#), [Bronwen Mayo](#)

The effect of vitamin D on the intestinal microbial ecosystem

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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  $\alpha$ 2,3- and  $\alpha$ 2,6-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](#)

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## **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 particular cancers. The Mechanisms in Cell Biology and Diseases Research Group is a collective of highly innovative research scientists who work cohesively to answer the bigger questions and develop an understanding of cell biology and diseases states, which is coordinated by a world leader in cell biology 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

Hypoxia-activated Prodrug Chemotherapeutics for Advanced Cancer

[Dr Shane Hickey](#), Dr Trent Ashton (WEHI), Dr Martin Sweetman and [Prof Doug Brooks](#)

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

[Dr Shane Hickey](#), Dr Trent Ashton (WEHI), [A/Prof Sally Plush](#) and [Prof Doug Brooks](#)

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)

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

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

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

- Developing novel methods to enable early detection of adverse events associated with medicines and medical devices.
- Investigating innovative ways of using pharmaceutical and medical data to improve patient safety
- Pioneering better ways to work with consumers and industry partners to provide solutions to medicines issues.
- Working across the healthcare spectrum with expertise ranging from pharmacy and medicines safety to statistics, mathematical modelling, database management, health informatics, indigenous medicines, chemistry and health promotion.
- Collaborating internationally to achieve greater understanding and impact.
- Translating research into real world resources to help doctors, pharmacists and consumers better manage health care.

Research staff available to supervise Honours Students

<a href="#">Prof Libby Roughead</a>	Pharmacoepidemiology, Post market surveillance of medicines, Medicines policy, Health care program evaluation
<a href="#">Prof Nicole Pratt</a>	Pharmacoepidemiology, Statistical methods
<a href="#">Dr Nagham Ailabouni</a>	Deprescribing, Medicines associated dementia
<a href="#">Dr Andre Andrade</a>	Digital health
<a href="#">Dr Svetla Gadzhanova</a>	Pharmacoepidemiology, Data mining, Evaluation of change management in primary health care
<a href="#">Dr Marianne Gillam</a>	Health services research, medical device epidemiology, quality use of pathology
<a href="#">Dr Jodie Hillen</a>	Quality Use of medicines, Pharmacoepidemiology, Medicines use in the Aged Care population, Post marketing surveillance of medicines.
<a href="#">A/Prof Lisa Kalisch Ellett</a>	Medicines that cause or worsen dementia and cognitive impairment, Quality use of medicines, Post market surveillance of medicines, Pharmacoepidemiology
<a href="#">Dr Gizat Kassie</a>	Medicines associated with dementia and cognitive impairment

<a href="#">Dr Lan Kelly</a>	Improving safety of implantable medical devices
<a href="#">Dr Renly Lim</a>	Quality use of medicines, Medicines utilisation
<a href="#">A/Prof Stephanie Reuter Lange</a>	Pharmacology, Medication issues associated with the sub-optimal use
<a href="#">Dr Kham Tran</a>	Dementia research
<a href="#">Dr Susan Semple</a>	Australian Medicinal Plants, Antimicrobials, Complementary and Alternative Medicines
<a href="#">Dr Ty Stanford</a>	Health data analytics, Bioinformatics

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

Svetla Gadzhanova, Libby Roughead

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

### Risk management plans for newly marketed medicines

Nicole Pratt, Emmae Ramsay

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

### Product Information and the influence on prescribing

Nicole Pratt, Emmae Ramsay, 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, Nicole Pratt

#### Medicines and frailty

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

#### Co-designing a consumer driven tool to detect side effects due to medicines

Renly Lim, Lisa Kalisch Ellett, Libby Roughead

#### An overview of systematic reviews of medicines inducing cognitive impairment

Tuan Nguyen, Thu Ha Dang, Libby Roughead

#### An overview of systematic reviews of medicines worsening cognitive impairment

Tuan Nguyen, Thu Ha Dang, Libby Roughead

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

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

#### Physician perspective on their current prescribing practice for people with dementia in Australia,



China and Vietnam

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

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

Andre Andrade

Optimising deprescribing in practice

Emily Reeve

Quality use of pathology

Marianne Gillam, 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

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.

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## Independent Researchers

[Emeritus Professor Mary Barton](#)

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

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

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

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[Dr Brian Dale](#) (Senior Lecturer in Haematology)

Dr Brian Dale has research interests in the area of haemostasis. This encompasses the investigation of

bleeding and thrombotic disorders as well as the development and application of assays for diagnosis and assessment of treatment including evaluation of the anticoagulant effects of direct oral anticoagulants. Current areas of interest that could generate Honours projects include: investigation of the thrombogenic properties of cellular microparticles in haematological malignancy; the role of platelet mitochondria in myeloproliferative neoplasms; clinical applications of a recently developed Overall Haemostasis Potential assay; the role of Factor XIII and the fibrinolytic system in the coagulopathy of trauma and in thrombohaemorrhagic disease; evaluation of the haemostatic effects of new treatments for haemophilia.

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[Dr Cameron Phillips](#) (Adjunct Lecturer)

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

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