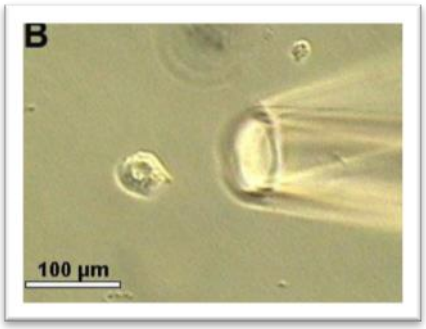
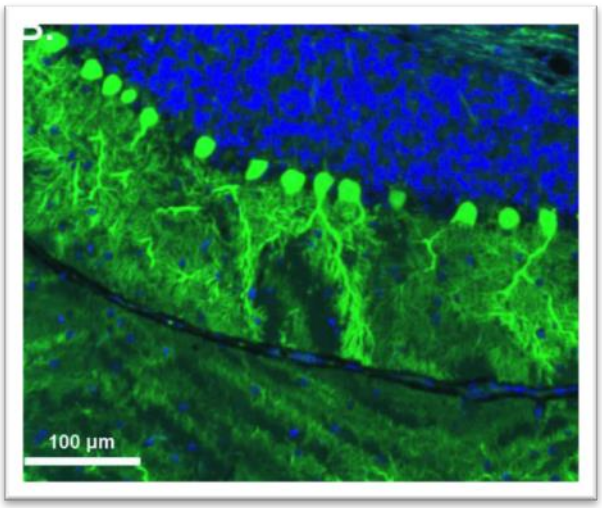
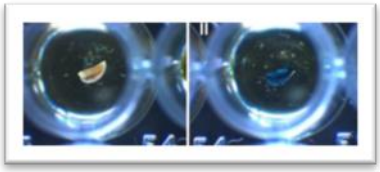



# Biomedical Sciences Research Projects 2020



School of Biomedical Sciences
Queensland University of Technology

## Contents

# Welcome

Dear Potential Biomedical Sciences Research Student,

The Honours year is a rewarding and challenging year that provides you with an insight to the excitement of the scientific journey. It is a period of intensive personalised scientific training, where you have the opportunity to design, implement and interpret scientific experiments, under the guidance of your supervisors. An accompanying program of interactive seminars, workshops, forum discussions and written tasks enhances your potential as a reliable, resourceful, ethical and self-motivated researcher who is able to perform independently and as part of a team. Successful completion of the Honours year may enable you to pursue higher degree studies, or seek employment in a research laboratory of a university or specialised institute, or in a commercial company.

This Booklet provides some general information on the Bachelor of Biomedical Science (Honours) program, and gives details of research projects that are available at the current time. **Research Projects for the Master of Philosophy course are also included here. Please ask potential supervisors if they are offering a project for Honours or Masters entry.**

**Master of Philosophy Entry requirements and further information can be found at: https://www.qut.edu.au/research/study-with-us**

If you are interested in any of the projects or research areas listed in this Booklet, you should contact the Project Leader for further discussion. Additional projects also may be available, so if a topic interests you, it is worthwhile discussing this with potential supervisors or any member of the Honours Coordination Team.

## Details of HL53 Bachelor of Biomedical Science (Honours) Course

### Admission Enquiries

Before submitting an application for admission, please contact the relevant Project Leader or Contact to discuss your participation in the project. Full details on available Honours projects offered are available at the information session and on line through the School of Biomedical Sciences Website.

Remember: supervisors are always enthusiastic about their projects. It is important to recognise that you will be working with them on a project for a reasonably long period. **Discuss widely and choose carefully.**

If you have any questions, please ask around, and the Course coordinator can also discuss these with you.

Professor Kirsten Spann
HL53 Course Coordinator
Email: kirsten.spann@qut.edu.au

| HL53 Bachelor of Biomedical Science (Honours) Course | |
|---|---|
| **Course duration (full-time):** | 1 year |
| **Domestic fees (indicative):** | 2018: $5,400 per Study Period (full-time) (subject to annual review) |
| **International fees (indicative):** | 2017: $21,550 per Study Period (full-time) (subject to annual review) |
| **Total course credit points (CP):** | 96 |
| **Standard CP per full time semester:** | 48 |

- Students need to support themselves for 12 months
- Possibility of obtaining H1 for scholarship consideration
- CAN change from Honours into Masters Research (before census best)
- Coursework/training involves critiquing manuscripts, writing Grant Proposal, Manuscript prepared for Final paper, Oral presentations

## Entry Requirements

- A completed recognised bachelor degree in a relevant area with a minimum grade point average (GPA) of 5.0 on QUT's 7-point scale; and
- An application must be made within 18 months of completing the Bachelor degree.

## Program Overview

The Faculty of Health offers an Honours course as a *one-year full-time course* available to students who have completed a Bachelor degree with a focus in the appropriate discipline, either from QUT or another tertiary institution.

There are a number of important advantages to completing an Honours degree:

* An Honours degree offers the opportunity to *develop advanced expertise* in a chosen discipline
* An Honours degree is *held in high regard* by employers as a measure of advanced knowledge and skills
* An Honours degree offers students the opportunity to *explore their potential* ability for research
* An Honours degree is a *favoured entry point* to PhD programs.

### *Full-Time Course Structure*

The Honours course consists of the following units:

| | | |
|---|---|---|
| HLH101 | Research Funding Proposal | 12cp |
| HLH104 | Manuscript Critique | 12cp |
| HLH105 | Research Strategies 1 | 12cp |
| HLH106 | Research Strategies 2 | 12cp |
| HLH107 | Research Project | 48cp |

The units complement each other and, in conjunction with one-on-one training of students by

supervisors of the research projects, provide the skills required for achieving the aims and learning outcomes of the course.

The Honours course will consist of the following units:

**Semester 1**

| | | |
|---|---|---|
| HLH101 | Research Funding Proposal | 12cp |
| HLH104 | Manuscript Critique | 12cp |
| HLH105 | Research Strategies 1 | 12cp |
| HLH107-1 | Research Project | 12cp |

**Semester 2**

| | | |
|---|---|---|
| HLH106 | Research Strategies 2 | 12cp |
| HLH107-2,3,4 | Research Project 2-4 | 36cp |

### *Unit Synopses*

**HLH105 Research Strategies 1 and 2**
**HLH106**

These units run over two semesters and involve a number of different components:

- informal and formal oral presentations
- training in writing of a grant proposal and in analysing scientific writing
- a series of specialised lectures dealing with topics relevant to research
- attendance and reflective journal accounts of attendance at and participation in Discipline and Institute Seminar series
- assessment of laboratory workbooks or work journals generated from the student's research project
- a formal seminar of about 20 minutes which describes the background, hypothesis, aims, methods and significance of the research project.

**HLH101 Research Funding Proposal**

This unit involves the presentation of a written grant proposal based on the research project you are undertaking, including a critical analysis of literature related to the research topic.

**HLH104 Manuscript Critique**

This unit involves the presentation of a written critique of a scientific paper which is related to your research project.

**HLH107 Research Project**

The unit covers the research project development and outcomes. It requires the preparation of a paper reporting the background, methods, results, analysis and discussion of investigations in a research project carried out during a period of about eight months. Additionally, a formal seminar of about 25 minutes reporting

these aspects orally, and an assessment by the project supervisor contribute to this unit.

### *Assessment of Honours Course*

QUT's award of Honours is based on your Honours course GPA, according to the University's Manual of Policies and Procedures (MOPP) C/5.2.6:

**Honours 1 GPA 6.50 – 7.00**
**Honours 2A GPA 5.50 – 6.49**
**Honours 2B GPA 4.50 – 5.49**
**Honours 3 GPA 4.00 – 4.49**

Note: The grade for HLH107 Project will be weighted to reflect its 48 credit point value.

Graduates who successfully complete the Honours course should be able to:

- demonstrate an understanding of advanced theories, concepts, and techniques appropriate to their area of specialisation
- recognise worthwhile scientific problems and seek solutions to these by using appropriate research strategies
- demonstrate independence of thought and critical analysis skills appropriate to solving novel problems in their chosen discipline area or specialisation
- employ research methods and technology relevant to their chosen discipline
- contribute effectively to work and research groups
- communicate at a high level in both written and oral forms
- demonstrate a commitment to lifelong learning and to professional and ethical practice

These learning outcomes are linked to the QUT teaching and learning and research goals:

- To ensure that QUT graduates possess knowledge, professional competence, a sense of community responsibility and a capacity to continue their professional and personal development throughout their lives
- To advance and apply knowledge germane to the professions, and to the communities, with which QUT interacts and relevant to the enhancement of economic, cultural and social conditions.

## How to apply

Applicants for HL53 Bachelor of Biomedical Science (Honours) are required to submit the following documents to Student Business Services by the deadline of 31 January 2019.

- PG Form (PDF file, 232.74 KB) for domestic applicants or F Form (PDF file, 249.27 KB) for international applicants. These can be found at: https://www.qut.edu.au/study/postgraduate-study/postgraduate-coursework-applications

- Once you have made a decision, fill out the Honours Project Preference form (please see last page of this booklet), have it signed by the appropriate supervisor/s and attach it to your PG or Application form. Also email this form to the Honours Course Coordinator:
    - Kirsten.Spann@qut.edu.au
- You will need a co-supervisor, so please talk to you principal supervisor to identify a co-supervisor to be named on your preference form

**Early submission of forms is recommended** to allow time for the application to be processed, an offer of a place to be made, and information on O-Week Activities to be sent to you.

Forms must be completed, signed and returned to QUT Admissions:

By mail: QUT Admissions
Student Business Services
Victoria Park Road
Kelvin Grove, Qld, 4059, Australia

In person: HiQ Service Centre
Gardens Point Campus, V Block, Level 1
Kelvin Grove Campus, R Block, Level 1
Caboolture Campus, J Block

By email: apply@qut.edu.au for domestic applicants or
gut.intadmission@qut.edu.au for international applicants

## Honours (HL53) Information Session

## Semester 2, 2020

**Meet Researchers – Discuss Projects**

**Thursday 26th September 3pm-5pm**

**The Cube, P Block, GARDENS POINT CAMPUS**

## Honours/Masters Projects For 2020

Full details on available Honours projects offered are available at the information session and within this booklet. Some projects are also advertised on the START database. http://start.health.qut.edu.au. Please talk to prospective supervisors about your interests as there may be some flexibility in project topic by January 2019.

## **Field of Research**: Applied allergy research; molecular allergology

**Project Title:** Mapping antibody specificity for grass pollen allergens for targeted subtropical grass pollen allergen immunotherapy vaccines

**Research Group:** Allergy Research Group
**Principal Supervisor:** Prof Janet Davies
**Principal Supervisor Contact and Location:** IHBI at QIMRB labs, j36.davies@qut.edu.au
**Masters or Honours project:** Both

**Background to the project:**
Grass pollen allergens are the major outdoor allergen trigger for allergic asthma and rhinitis (hayfever) that affect up to 20% of Australians as well as 500 million people globally. Whilst allergen specific immunotherapy vaccine treatments are effective at reducing symptoms of hayfever and reduce progression to asthma, tests and treatments are based on the temperate grass pollens. However, our research shows that patients with grass pollen allergy from subtropical regions show higher sensitisation and specific IgE and T cell recognition of allergens from the subtropical Bahia and Johnson grass pollens than temperate grass pollens. There is a need to develop more specific tests and treatments for diagnosis and treatment of patients primarily sensitized to subtropical grass pollens.

**Hypothesis/Aims:**
Knowledge of the molecular basis of antibody specificity for subtropical grass pollen allergen components will aid the design of more specific allergen immunotherapy reagents for subtropical grass pollen allergy.

The aim of this project is to express and purify newly discovered allergen components of subtropical *grass pollens and map reactivity of allergen-specific human and murine antibodies.*

**Approaches / Skills and techniques:**
The student will gain an appreciation for applied allergy research and have the opportunity to engage in collaborative research involving industry partners. This project will involve the student applying and consolidating experience with a number of molecular biology, protein chemistry and serological assays. The student will tailor established methods to develop optimal expression and purification strategies for grass pollen allergen components that will then be used in epitope mapping of the specificity and affinity of reactivity of patient IgE and a panel of murine antibodies.

Students with a background in infection and immunity and molecular methods will be suited to this project. The successful student will be invited to join the multidisciplinary QUT Allergy Research Group that is funded by NHMRC and ARC as well as government and competitive foundation grants.

**References / key papers:**

Nony et al. Specific IgE recognition of pollen allergens from subtropic grasses in patients from the subtropics. Ann Allergy Asthma Immunol. 2015 114; 214-220.

Campbell et al. Total transcriptome, proteome, and allergome of Johnson grass pollen, which is important for allergic rhinitis in subtropical regions. J Allergy Clin Immunol 2015; 135; 133-142.

Timbrell et al. An ImmunoCAP assay for quantitation of specific IgE to the major allergen of Bahia grass pollen Int. Arch. Allergy Immunol. 2014; 165; 219- 228. DOI:10.1159/000369341

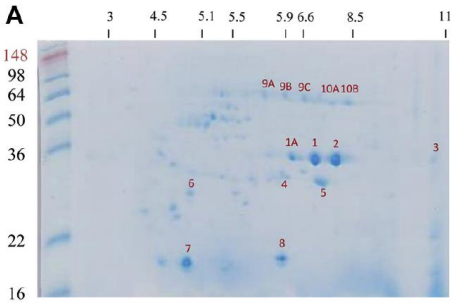
## **Field of Research**: Applied allergy research; molecular allergology

**Project Title:** Tracking Stability of allergen extracts used clinically for diagnosis and therapy of patients with grass pollen allergy

**Project Leader & Contacts**
Prof Janet Davies, QIMRB labs, j36.davies@qut.edu.au

**Collaborators**: Dr Zi Tan, Clinical Immunologist at the Royal Brisbane and Women's Hospital.

**Honours project**



2D gel of JGP stained with Coomassie

**Background**
Grass pollen allergens are the major outdoor allergen trigger for allergic asthma and rhinitis (hayfever) that affect up to 20% of Australians as well as 500 million people globally. Whilst allergen specific immunotherapy vaccine treatments are effective at reducing symptoms of hayfever and reduce progression to asthma, some skin prick test and allergen immunotherapy reagents are not standardized.

**Hypothesis/Aims**
Mixing of aqueous allergen extracts of grass pollen and house dust mites leads to loss of allergen content.

The aim of this project is to establish an allergen stability test of controlled combinations of aqueous allergen extracts and evaluate the change in content of key allergen components over time. .

**Approaches:**
The student will gain an appreciation for applied allergy research and have the opportunity to engage in collaborative research involving clinical research partners. This project will involve the student applying and consolidating experience with a number of protein chemistry and serological assays including one and two dimensional gel electrophoresis and immunoblotting. The student will apply established methods to address a specific research question leading to publishable outcomes of clinical relevance within the duration of this Honours project.

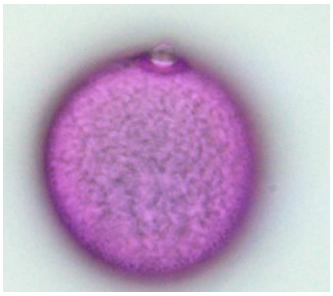
Students with a background in infection and immunity and molecular methods will be suited to this project. The successful student will be invited to join the multidisciplinary QUT Allergy Research Group that is funded by NHMRC and ARC as well as government and competitive foundation grants.

Campbell et al. Total transcriptome, proteome, and allergome of Johnson grass pollen, which is important for allergic rhinitis in subtropical regions. J Allergy Clin Immunol 2015; 135; 133-142.
Nelson et al., Studies of allergen extract stability: The effects of dilution and mixing. J. Allergy Clin. Immunol. 1996; 98, 382–388.
Plunkett G. Curr Opin Otolaryngol Head Neck Surg. Update: stability of allergen extracts to establish expiration dating. 2016 Jun;24(3):261-9. doi: 10.1097/MOO.0000000000000248.
https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20Management/PM%20Resource%20Guide/Ch-9-Allergen-Immunotherapy-Extract-Preparation-Manual-correction-July-19-12.pdf

## **Field of Research**: Applied allergy research; molecular allergology

**Project Title/Area** Interaction between pollen and rhinovirus immunity in asthma

**Project Leader & Contacts** *Prof Janet Davies, CCHR,* *j36.davies@qut.edu.au*



**Masters project**

Background

Lower respiratory tract infection and atopic status in early life synergistically increase risk of asthma. Rhinovirus (RV) infection is associated with up to two thirds of acute exacerbations of asthma in children requiring hospital care for asthma. Patients with asthma appear to mount inadequate innate anti-viral immune responses to rhinovirus infection. Factors within the allergen source may directly interact with pattern recognition receptors on airway epithelium to exert early effects on innate antiviral immunity and airway inflammation. Moreover, grass pollen exposure has been associated with hospital admissions for asthma and grass pollen allergen challenge can induce acute allergic airway inflammation. Synergy between exposure to allergen sources such as grass pollen and house dusts and human rhinovirus infection has not been investigated.

Hypothesis/Aims

Grass pollen allergen exposure and grass pollen-allergy status influences asthma pathogenesis by exerting direct effects on innate antiviral immunity and indirect effects mediated by allergen-specific IgE.

We aim to investigate innate immune effects of pollen and rhinovirus co-exposure on matching cultures of i) PBMC and ii) primary airway epithelial cells of healthy and asthmatic subjects.

Approaches

During this project the student will gain an appreciation of the immunology of allergic asthma, familiarity with clinical research, handling human blood and nasal biopsy samples, databases and record keeping. In the laboratory a range of techniques will be mastered including cell culture, ELISA, RNA extraction, cDNA synthesis and quantitative real time PCR.

Students with a background in infection and immunity will be suited to this project. The successful student will be invited to join the multidisciplinary QUT Allergy Research Group that is funded by NHMRC and ARC as well as government and competitive foundation grants.

References

Thien F, Beggs P, Csutoros D, Darvall J, Hew M, Davies JM, et al. The Melbourne epidemic thunderstorm asthma event 2016: a multidisciplinary investigation of environmental triggers, health service impact and patient risk factors. Lancet Planet Health 2018; 2: e255–63.

Spann et al., Viral and host factors determine innate immune responses in airway epithelial cells from children with wheeze and atopy. Thorax. 2014 69:918-25.

Erbas et al. Does Human Rhinovirus infection and allergic sensitisation modify the association between outdoor grass pollen and asthma hospital admissions in children? J Allergy Clin Immunol 2015 http://dx.doi.org/10.1016/j.jaci.2015.04.030

BIOMEDICAL SCIENCE RESEARCH PROJECTS 2020

**Field of Research:** Anatomy

**Research Group:** Clinical Anatomy & Paediatric Imaging
**Principal Supervisor:** Associate Professor Laura Gregory
**Co-supervisors:** Ms Mikaela Reynolds
**Principal Supervisor Contact:** l.gregory@qut.edu.au
**Masters or Honours project:** Both

**Background to the project:**

The anatomy of the human body drives how the body functions in health and disease, yet contemporary research into the relationship between anatomical variation and disease presentation is limited. Furthermore children and adolescents are considered miniature adults, and little attention has been given to the study of the anatomy of subadults. Through manipulating digital imaging capabilities of a range of medical imaging modalities including computed tomography, plain radiography and magnetic resonance imaging, we are able to qualitatively and quantitatively investigate the presentation and pattern of variation of major organs in children including blood vessels, major organs such as the heart and kidneys and the skeleton, to determine the effect of sex and age on anatomical presentation.

**Our research group therefore aims to:**

- Investigate paediatric anatomy and development, and clinically relevant anatomical variation in the body to provide personalised patient care to all individuals and improved patient outcomes.

The skeleton is a dynamic living organ, constantly adapting to its environment through complex mechanisms that are sensitive to mechanical perturbations and hormonal regulation. Due to its central role in providing structural support and metabolic homeostasis in the body, skeletal dysfunction results in significant morbidity and economic burden in our ageing population. However current research has only just begun to unravel the complex mechanisms that drive skeletal regulation. Furthermore investigating skeletal variability and development, provides improved standards for forensic practice in the identification of unknown remains and in assessing growth and maturation in clinical contexts. Contemporary, population-specific biological anthropology research in Australia is lacking due to the challenges of obtaining large repositories of physical skeletal material. Our laboratory has overcome this limitation through the collection of clinical and mortuary medical images, providing a virtual platform to study the human body using advanced 3-dimensional modelling and computing capabilities with impressively large, contemporary datasets. The goal of our program is to build upon our current understanding of how bone tissue functions in both health and diseased states; and explore the range of skeletal variability present in modern Australians. Our research addresses this goal by:

- Investigating mechanisms to improve strength in the skeleton;
- Investigating novel treatments for bone disease (including bone metastasis);
- Investigating improved anthropological methods of human identification from skeletal remains of Australian individuals;
- Investigating skeletal variability and bone development in Australian juveniles and adults.

**References / key papers:**

[1] Gregory, LS., McGifford, O., Jones, LV. (2019) '*Differential growth patterns of the abdominal aorta and vertebrae during childhood*'. Clinical Anatomy (first published online May 2019).

[2] Reynolds, MS., MacGregor, DM., Barry, MD., Lottering, N., Schmutz, B., Wilson, LJ., Meredith, M. and Gregory, LS. (2017) *'Standardised anthropological measurement of postcranial bones using three-dimensional models in CAD software'.* Forensic Science International 278:381-7.

[3] Lottering, N., MacGregor, D., Alston, CL. and Gregory, LS. (2015) '*Ontogeny of the Spheno-Occipital Synchondrosis in a Modern Queensland, Australian Population using Computed Tomography'* American Journal of Physical Anthropology 157(1):42-57.

## **Field of Research**: Biotechnology, Molecular Biology, Diagnostics, Clinical Collaboration, Industry Linkages and International Collaborations

**Project Title:** Human Papilloma Virus Associated non-invasive biomarkers in oropharyngeal cancers

**Research Group:** Saliva Translational Research Group
**Principal Supervisor:** Associate Professor Chamindie Punyadeera
**Principal Supervisor Contact and Location:** Translational Research Institute and IHBI, QUT
**Email:** chamindie.punyadeera@qut.edu.au; +61 7 3138 0830
**Masters or Honours project:** Both

**Background to the project:**
This project is with an international industry partner. Student will get the opportunity to work closely with industry.

Head and neck squamous cell carcinoma (HNSCC) is the 6$^{th}$ most common cancer globally with less than 40% survival beyond 5 years. A sub-set of HNSCC is caused by human papilloma virus and it is known as oropharyngeal cancers (OPC). OPC is increasing world-wide and men are at a 4-times risk of developing OPC compared to women. We have published that we can detect HPV DNA in saliva samples collected from patients with 93% sensitivity and 100% specificity. In addition, we have also demonstrated that method of saliva collection does not affect HPV-16 genotyping (Tang et al., under revision). It is known that micro RNA (miRNAs) are regulated by HPV-16. In addition, it is also known that telomere length is shorten in cells that are affected by HPV-16. It is interesting then to understand the HPV-16 driven changes at the cellular level (miRNA and telomere) during the development of OPC.

**Hypothesis:**
HPV-16 infections has an affect at the cellular level and this is reflected at the miRNA and telomere lengths.

**Aims**

1. Transfects head and neck cancer cells with viral oncogenes to determine changes in miRNA and telomere lengths
2. Discern the molecular pathways affected by HPV-16 integration in OPC cells

**Approaches /skills and techniques:**
Samples will be collected from cancer patients across two major academic hospitals. In the first instance, we will use molecular and cell biology techniques (such as cloning, PCR and RNA expression studies). Mammalian cell cultures will also be used. We will also use advance bioinformatics algorithms to develop diagnostic and prognostic "cut-off" levels.

**References / key papers:**

1. Chaturvedi AK, Engels EA, Anderson WF and Gillison ML. J Clin Oncol. 2008; 26(4):612-619.
2. Chai RC, Lambie D, Verma M and Punyadeera C. Current trends in the etiology and diagnosis of HPV-related head and neck cancers. Cancer Med. 2015; 4(4):596-607.
3. Chai RC, Lim Y, Frazer IH, Wan Y, Perry C, Jones L, Lambie D and Punyadeera C. BMC Cancer. 2016; 16:178.
4. Salazar C, Nagadia R, Pandit P, Cooper-White J, Banerjee N, Dimitrova N, Coman WB and Punyadeera C. Cell Oncol (Dordr). 2014; 37(5):331-338.

**Field of Research**: Biotechnology, Molecular Biology, Diagnostics, Clinical Collaboration, Industry Linkages and International Collaborations

**Project Title:** The Development of Salivary Exosome as Biomarkers for Heart Failure

**Research Group:** Saliva Translational Research Group
**Principal Supervisor:** Associate Professor Chamindie Punyadeera
**Principal Supervisor Contact and Location:** Translational Research Institute and IHBI, QUT
**Email:** chamindie.punyadeera@qut.edu.au; +61 7 3138 0830
**Masters or Honours project:** Masters and/or Honours

**Background to the project:**
This project is a multidisciplinary and translational research project. Student will get the opportunity to work closely with both clinical collaborators across two large hospitals.

Heart Failure (HF) is a severe complication that affects 26 million people across the globe. HF is prevalent in both in the developed and developing countries. Currently, there is no early screening program for HF. This prohibits most HF patients from receiving early treatment and sadly contributes to the mortality of HF. To reduce the societal burden of HF, we require effective screening strategies to allow early detection and management of structural heart disease prior to the development of clinical HF.

Human saliva contains a large number of circulating proteins that can serve as indicators of the body's health and wellbeing. Previous study suggested circulating peptide biomarkers are secreted into saliva in a manner that might enables highly specific detection of HF. However, the mechanism of how these biomarkers are transported to saliva is still uncertain. Recent studies have suggested that exosomes, a cell-derived vesicle with diameters between 30 and 100 nm, may be the key component of biomarker transportation between saliva and circulation.

**Hypothesis:**
Salivary exosomes link systemic disease with oral health
Exosomes contains biomarkers that can be used for HF disease management.

**Aims:**
1. To develop a robust method to isolate and characterise exosomes from human whole saliva
2. To determine exosome changes with aging
3. Compare exosome protein profiles between blood and saliva from controls and patients

**Approaches /skills and techniques:**
This project is funded by the Heart Foundation. Human whole saliva will be collected from HF patients and healthy controls (QUT HREC approval: 1400000616B). We will use state of the art technologies to develop a method to detect proteins abundance in salivary exosomes. Ultracentrifugation coupled with multiple steps of pre-centrifugation will be used to isolate exosomes from human whole saliva samples. The proteomics profile of exosomes will be investigated with state of the art technologies such as next gen sequencing, SWATH-Mass Spectrometry. Specific proteins will be quantified with immunoassay such as ELISA or AlphaLISA® technology.

**References /key papers:**
1. Pfaffe, T., et al., Diagnostic potential of saliva: current state and future applications. Clinical Chemistry, 2011. 57(5): p. 675-87.
2. Zheng, X., et al., Exosome analysis: a promising biomarker system with special attention to saliva. J Membr Biol, 2014. 247(11): p. 1129-36.

## **Field of Research**: Burn injury; biomarkers

**Project Title:** Biomarkers of burn wound healing

**Research Group:** QUT Burns and Trauma Research Group
**Principal Supervisor:** A/Prof Leila Cuttle,
**Co-supervisors:** A/Prof Tony Parker, Dr Dan Broszczak
**Principal Supervisor Contact and Location:** leila.cuttle@qut.edu.au, 07 3069 7208, Centre for Children's Health Research, South Brisbane
**Masters or Honours project:** Masters

**Background to the project:**
It can be difficult for clinical teams to determine the severity of burn injuries when the patient first presents to the hospital. Wounds may be very deep and require aggressive surgical treatment e.g. grafting, or the burns may be less deep, and they can be managed conservatively with the application of different dressings. We have previously found that certain proteins present in burn wound fluid may be used to help predict burn depth and the time taken to heal. We have also found that certain proteins and metabolites are related to wounds that heal faster and with a better outcome. In this project, these proteins will be validated using different techniques and to help develop an assay which can be used in the clinic.

**Aims:**
Several different aims could be investigated, depending on the interest/background of the student:

- Measuring the levels of specific proteins in burn wound fluid samples
- Testing the effect of proteins or metabolites on skin cell monolayers or using skin in vitro models
- Developing mass-spectrometry-based assays to detect proteins of interest in burn wound fluid samples.

**Skill and techniques to be developed:**
The student will be validating the presence and effect of different proteins using mass spectrometry, ELISA, western blotting or skin cell culture techniques.

**References / key papers:**

1. Zang T, Cuttle L, Broszczak DA, Broadbent JA, Tanzer C,Parker TJ. Characterisation of the blister fluid proteome for pediatric burn classification. Journal of Proteome Research 2019;18 (1): 69-85
2. Zang T, Broszczak DA, Broadbent JA, Cuttle L, Tanzer C, Parker TJ. Blister fluid proteome of paediatric burn patients. Journal of Proteomics; 2016 June; 146:122-132
3. Zang T, Broszczak DA, Broadbent JA, Cuttle L, Lu H, Parker, TJ. The biochemistry of blister fluid from paediatric burn injuries: proteomics and metabolomics aspects

## **Field of Research**: burn injury; tissue engineering

**Project Title:** Replacement of skin using tissue engineering techniques

**Research Group: QUT Burns and Trauma Research Group**
**Principal Supervisor:** A/Prof Leila Cuttle
**Co-supervisor**: A/Prof Tony Parker
**Principal Supervisor Contact and Location: leila.cuttle@qut.edu.au, 07 3069 7208, Centre for Children's Health Research, South Brisbane**
**Masters or Honours project:** Masters

**Background to the project:**
The replacement of skin after burn injuries is important for children and adults. Large or deep burn injuries are common and devastating for children, especially if the burns take a long time to heal and result in scarring. Adult burn injuries are often large, with the need to replace skin quickly to ensure survival. A new skin scaffold has recently been developed which will be investigated in this project, to optimise the replacement of skin for burn patients.

**Aims:**
Several different aims could be investigated, depending on the interest/background of the student:

- Examining the ability of tissue engineered skin to withstand infection
- Investigating the potential of using donor (allogeneic skin) skin cells in tissue engineered constructs
- Testing different structures and forms of the skin scaffold for optimum cell growth

**Skill and techniques to be developed:**
The student will be using tissue culture techniques to grow the skin cells (keratinocytes and fibroblasts) on scaffolds. Cell growth will be examined using microscopy, histology and assays for cell proliferation and differentiation.

**References / key papers:**

1. Greenwood J.E. The evolution of acute burn care – retiring the split skin graft. Ann R Coll Surg Engl 2017; 99:432-438
2. Dearman B.L., Li A., Greenwood, J.E. Optimization of a polyurethane dermal matrix and experience with a polymer-based cultured composite skin. Journal of Burn Care and Research. 2014; 35(5):437-48

## **Field of Research**: Cell biology and biochemistry / cell development, proliferation and death

**Project Title:** DNA repair mechanisms in aging adult stem cells

**Research Group:** Cancer and Aging Research Program (CARP)
**Principal Supervisor:** Dr Karsten Schrobback
**Co-supervisors:** Prof Derek Richard
**Principal Supervisor Contact and Location:**
Translational Research Institute
Level 6, 37 Kent Street, Woolloongabba, Brisbane, QLD, 4102
Ph: +61 7 3443 7314, email: k.schrobback@qut.edu.au
**Masters or Honours project:** Masters or Honours

**Background to the project:**
The DNA repair systems of a cell function to protect the genetic code from deleterious mutations caused by the thousands of DNA lesions a cell experiences in a day. When we age these repair systems become down regulated. This results in reduced DNA repair capacity, enhanced rates of mutation load and may result in the development of chronic aging-associated diseases including osteoporosis, Alzheimer's and cancer(1). So it is no surprise that genome instability and stem cell exhaustion, which also strongly correlates with the accumulation of DNA damage, are considered hallmarks of aging(2). However, we still lack a clear understanding on how the decrease in DNA repair fidelity affects the maintenance and differentiation of adult stem cells and their ability to contribute to tissue homeostasis and regeneration. We also lack a comprehensive understanding of which specific pathways and proteins are involved in the DNA repair of skeletal stem cells and how the decline of repair processes with age contributes to musculoskeletal diseases such as osteoporosis and osteoarthritis. This project is therefore aimed at characterising the differences in DNA damage responses in young and aged skeletal progenitor cells and how the DNA repair mechanism are affected by cell cycle exit and differentiation.

**Aims:**
1. Comparison of DNA repair processes in bone marrow-derived mesenchymal stromal cells (MSC) derived from young and old donors in response to oxidative agents and irradiation?
2. Characterisation of the main DNA repair processes in dividing and non-dividing (differentiating) MSC in response to DNA damage?

**Skill and techniques to be developed:**
- Culture and transfection of human adult stem cells incl. differentiation in 3D culture models(3),
- Immunofluorescence staining and high-throughput confocal microscopy,
- Other biological and biochemical techniques such as Western blotting, life dead assays, qPCR
- Mass spectrometry-based proteomics

**References / key papers:**
1. V. Tiwari, D. M. Wilson, 3rd, DNA Damage and Associated DNA Repair Defects in Disease and Premature Aging. *Am J Hum Genet* **105**, 237-257 (2019).
2. C. Lopez-Otin, M. A. Blasco, L. Partridge, M. Serrano, G. Kroemer, The hallmarks of aging. *Cell* **153**, 1194-1217 (2013).
3. K. Schrobback, T. J. Klein, T. B. Woodfield The importance of connexin hemichannels during chondroprogenitor cell differentiation in hydrogel versus microtissue culture models. *Tissue Eng Part A* **21,** 1785-1794 (2015)

## **Field of Research**: Cancer

**Project Title:** Evaluating critical nodes of therapy resistance in advanced prostate cancer

**Research Group:** GU PRECISION CANCER MEDICINE GROUP
**Principal Supervisor:** PROFESSOR DAVID WAUGH
**Co-supervisors:** DR NATALIE BOCK, DR JOAN ROHL
**Principal Supervisor Contact and Location:** Translational Research Institute, Level 3
D6.waugh@qut.edu.au
**Masters or Honours project:** either

**Background to the project:**
Advanced prostate cancer is treated using systemic androgen deprivation therapy (ADT). This strategy attempts to block the effects of androgen signalling in malignant cells located either within the prostate gland or in metastatic lesions located principally within the skeleton of patients [1]. Our research has identified that use of androgen signalling inhibitors such as enzalutamide not only affects the viability of prostate cancer cells but also has profound effects on the viability of vascular endothelial cells (in preparation). Consequently, the administration of ADT results in a significant and profound hypoxia which we propose underpins a novel mode of therapeutic resistance.
Loss of the tumour suppressor gene PTEN is a frequent and early onset event in the pathogenesis of prostate cancer. Over 50% of metastatic prostate cancer is identified as lacking in PTEN expression [2]. PTEN-deficient tumours also exhibit diminished response to ADT [3]. Our prior laboratory work suggests that PTEN-deficient cells have a more profound response to hypoxia [4], however we have yet to conduct a comprehensive analysis of hypoxia-induced transcriptomic and/or proteomic responses.
We hypothesise that "adaptation to treatment-induced microenvironmental hypoxia results in malignant cells acquiring molecular properties that render them less sensitive to ADT".

**Aims:**

1. Using PTEN-deficient and PTEN-expressing isogenic prostate cancer cells, we will characterise the effects of hypoxia upon signalling pathways and downstream effects on transcriptomic and proteomic profiles.

2. Using PTEN-deficient models, we will determine whether hypoxia disrupts apoptosis focusing on the regulation of the intrinsic and extrinsic signalling pathways and decreases the efficacy of ADT.

3. Determine whether hypoxia alters the signalling communication between malignant prostate cancer cells and resident osteoblasts using an engineered model of the bone microenvironment.

**Skill and techniques to be developed:**
Skills: Cell culture, organoid and advanced co-culture systems; transcriptomic, proteomic and data analytics; Cell survival and viability assays; analysis of apoptosis and signalling pathways
Pharmacological and phenotypic analysis of ADT and targeted combinations.
Presentation, writing and data interpretation skills; critical review and analysis of literature

**References / key papers:**

**1.** Ferraldeschi R, Welti J, Luo J, Attard G, de Bono JS. Targeting the androgen receptor pathway in castration-resistant prostate cancer: Progresses and prospects. Oncogene 2015;34:1745-57.

**2.** Cancer Genome Atlas Network. The Molecular Taxonomy of Prostate Cancer. Cell 2015;163:1011-1025

**3.** Maxwell PJ, Coulter J, Walker SM, McKechnie M, Neisen J, McCabe N, Kennedy RD, Salto-Tellez M, Albanese C, Waugh DJ. Potentiation of inflammatory CXCL8 signalling sustains cell survival in Pten-deficient prostate carcinoma. Eur Urol 2013;64:177-188

## **Field of Research**: Cancer Biology

**Project Title:** Post-translational modification of proteins important in cancer

**Research Group:** Protein Ablation Cancer Therapies (PACT) group
**Principal Supervisor:** A/Prof Sally Stephenson
**Co-supervisors:** Dr Aaron Smith, Dr Mohanan Maharaj
**Principal Supervisor Contact and Location:** s.stephenson@qut.edu.au, Translational Research Institute, PA Hospital, Woolloongabba.
**Masters or Honours project:** Masters and/or Honours

**Background to the project:**
Many proteins are modified after they are made through various means collectively called post-translational modifications. Some of these modifications contribute to protein function, protein-protein interactions, protein localisation and protein stability/turnover. We are interested in identifying cancer-associated proteins that have modifications that are required for their cancer promoting functions. Preventing these modifications using small molecules may provide new options for the development of anti-cancer treatments.

**Aims:**

1) Select a target protein of interest from experimental data already available in our laboratory.
2) Clone coding sequence of gene corresponding to target protein into mammalian expression vector.
3) Predict amino acid residues that may be important for modification using on-line motif prediction software.
4) Use site-directed mutagenesis to alter predicted key amino acid residues.
5) Express wildtype and mutant proteins in human cancer cells after transfection/transduction.
6) Analyse protein localisation/stability using microscopy and Western analysis/Immunoprecipitation/Subcellular fractionation.
7) With assistance, use *in silico* modelling and screening to identify small molecules targeting key amino acid motifs that may be potential inhibitors.
8) *In vitro* test inhibitor molecules analysing protein levels and localisation.
9) *In vitro* test inhibitor molecules analysing cell proliferation, viability, migration and invasion

**Skill and techniques to be developed:**
Cell biology - Cell culture, Lentivirus production, Transfection/Transduction, Small molecule inhibitor screening, Immunofluorescence/Fluorescence microscopy, Cell growth assays – proliferation, viability, migration and invasion.
Molecular biology – Cloning, Site directed mutagenesis, Bacterial transformation, Plasmid minipreps, Restriction digests, Gel Electrophoresis, Polymerase chain reaction, Protein lysate preparation, SDS-PAGE, Western analysis, Immunoprecipitation, Subcellular fractionation
*In silico* - Various bioinformatics programs, Protein modelling, Inhibitor screening

**References / key papers:**
Please contact A/Prof Stephenson for more information.

## **Field of Research**: Cancer

**Project Title:** Assessment of DKLS02 activity in breast cancer cell lines

**Research Group:** Cancer and Ageing Research Program (CARP), IHBI, SoBS
**Principal Supervisor:** Dr Laura Croft
**Co-supervisor:** Prof Derek Richard
**Principal Supervisor Contact and Location:**
laura.croft@qut.edu.au
Translational Research Institute , 37 Kent street, Woolloongabba 4102
**Masters or Honours project:** Masters/Honours

**Background to the project:**
Cancer is one of the biggest clinical problems facing the world. It has been estimated that by 2030 half of all deaths worldwide will be from cancer. There is a great need for more effective, less toxic cancer therapeutics. Our group has developed a new class of therapeutics targeting a critical DNA repair protein hSSB1[1], which is overexpressed in lung and breast cancers. The lead compound named DKLS02, shows broad-spectrum anticancer activity in several cell line models including melanoma, osteosarcoma, breast, prostate, pancreatic, cervical, ovarian, lung and head and neck cancers. Breast cancer is the leading cause of cancer-related mortality in women worldwide. While survival has increased in recent years, nearly 500 women die each year from breast cancer in Queensland alone. There are several molecular subtypes of breast cancer including Luminal A, Luminal B and triple-negative breast cancer (TNBC). TNBC is defined by the lack of expression of human epidermal growth factor receptor 2 (HER2), estrogen receptor (ER), and progesterone receptor (PR). Relative to other breast cancer subtypes, TNBC is a particularly aggressive disease, associated with a higher incidence of recurrence, metastasis and a poorer survival. In this project we will delineate the efficacy of DKLS02 in a panel of breast cancer cell lines covering the different molecular subtypes, including TNBC. We will determine the half maximal inhibitory concentration (IC50), in order to identify if DKLS02 efficacy varies among the different breast cancer subtypes. We will also investigate hSSB1 protein and transcript levels, which will help determine if hSSB1 protein and/or mRNA levels could be used as a DKLS02 response-predicting measure in patients.

**Aims:**
1. To assess the efficacy of DKLS02 in a panel of breast cancer cell lines of various molecular subtypes
2. To measure the expression levels of hSSB1 mRNA in the breast cancer cell line panel
3. To measure the expression levels of hSSB1 protein in the breast cancer cell line panel

**Skill and techniques to be developed:**
Cell culture, cell viability assay, cell proliferation assay, drug treatments, IC50 determination, holographic imaging, protein extraction, western blotting, RNA extraction, quantitative real time PCR (qPCR).

**References / key papers:**
Croft, L. V.; Bolderson, E.; Adams, M. N.; El-Kamand, S.; Kariawasam, R.; Cubeddu, L.; Gamsjaeger, R.; Richard, D. J., Human single-stranded DNA binding protein 1 (hSSB1, OBFC2B), a critical component of the DNA damage response. *Seminars in cell & developmental biology* **2018**.

## **Field of Research**: Breast Cancer


**Project Title:** Targeting Epithelial Mesenchymal Plasticity for Therapy Resistance in Breast Cancer

**Research Group:** Invasion and Metastasis Unit

**Co-supervisors:** Laura Bray, Elizabeth Williams and Christine Chaffer

**Principal Supervisor:** Erik (Rik) Thompson, PhD; Professor in Breast Cancer Research, School of Biomedical Sciences and Associate Director, Institute of Health and Biomedical Innovation (IHBI) @ Translational Research Institute (TRI)

**Principal Supervisor Contact and Location:** TRI Rm 7031, 37 Kent St, Woolloongabba, QLD 4102, Australia
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**Masters or Honours project:** Both

**Background to the project:** Therapy resistance is a critical factor underpinning the metastatic progression and treatment failure resulting in death of ~2,200 women annually in Australia from breast cancer. New treatment options are urgently needed to increase survival and reduce suffering. MDA-MB-468 human breast cancer (BC) cells are one of several models that demonstrates intrinsic epithelial mesenchymal plasticity (EMP) in vitro and in vivo [1, 2], and thus represents a good model in which to search for EMP-associated factors influencing therapy resistance. Similarly, the PMC42-LA cells harbour intrinsic EMP in vitro and in vivo [3], as do HCC-38 cells [4]. A polarity / EMP - enriched shRNA library screening was performed in these cells to identify and target the genes that might contribute to drug resistance against three currently employed BC drugs: doxorubicin, docetaxel and eribulin. Using Connectivity Map, we identified partner inhibitors targeting these gene families that may induce cell death in combination with doxorubicin. Our shRNA screen strategy has rationally identified novel treatment combinations that could benefit these patients. The project has commercial potential due to novelty and opportunity to develop IP.

**Hypothesis:** That novel therapy opportunities can be identified using shRNA screening in the EMP-positive MDA-MB-468 and PMC42-LA

**Aim 1.** To further assess individual gene product targets (shRNA / small molecules) and C-Map-identified candidates from the screen for therapy responses in MDA-MB-468, PMC42-LA and HCC-38 cultures

**Aim 2.** To extend these studies into appropriate in vivo models

**Aim 3.** To assess responses in material obtained clinically through the CPAC collaboration

**Skill and techniques to be developed:** 2D and 3D culture systems, shRNA (or CrispR) functional screen, target validation, C-Map / other bioinformatics for drug discovery, In vivo testing in NSG mice with breast cancer cell lines and PDX models; Aim 3, breast cancer metastasis-derived 3D tumouroid models for clinically-representative testing.

**References / key papers:**

1. Cursons, J., et al., Stimulus-dependent differences in signalling regulate epithelial-mesenchymal plasticity and change the effects of drugs in breast cancer cell lines. Cell Commun Signal, 2015. 13(1): p. 26.
2. Hugo, H.J., et al., Epithelial requirement for in vitro proliferation and xenograft growth and metastasis of MDA-MB-468 human breast cancer cells: oncogenic rather than tumor-suppressive role of E-cadherin. Breast Cancer Research: BCR, 2017. 19: p. 86.
3. Bhatia, S., et al., Interrogation of phenotypic plasticity between epithelial and mesenchymal states in breast cancer. J Clin Med, 2019. 8(6).
4. Yamamoto, M., et al., Intratumoral bidirectional transitions between epithelial and mesenchymal cells in triple-negative breast cancer. Cancer Sci, 2017. 108(6): p. 1210-1222.

## **Field of Research**: Cancer, stem cells and tissue engineering


Dr. Mike Doran

**Project Title:** Three projects available: (1) Cartilage tissue engineering, (2) wound repair, or (3) cancer models and drug screening.

**Research Group:** Doran Laboratory.
**Principal Supervisor:** A/Prof Mike Doran
**Co-supervisors:** Co-supervisors will vary depending on the specific project.
**Principal Supervisor Contact and Location:** mike@mikedoranlab.com at The Translational Research Institute (TRI).
**Masters or Honours project:** Masters or Honours – recruiting 2 candidates.

**Please ask us for more information about the projects below:**

**Project 1: Cartilage Tissue Engineering:** Our group developed a microtissue model for studying bone marrow mesenchymal stem/stromal cell (BMSC) chondrogenic differentiation. This system provides enormous capacity to tease out the factors that influence chondrogenesis. Our system is underpinned by the Microwell-mesh (see ref below), a technology developed by our team, enabling manufacture of thousands of uniform cartilage microtissues simultaneously, followed by characterisation of cellular behaviour in complex culture conditions. Through extensive gene expression comparison of BMSCs and articular chondrocytes (ArtCH) we have identified targets to genetically override intrinsic hypertrophy programming in BMSCs. In this project you will use genetic engineering technologies to prevent BMSC hypertrophy, and generate a cell population suitable for the repair of cartilage defects.

**Acquired and Developed Skills throughout Project: Biochemical analysis, histology,** Microscopy, compressive mechanical testing, cell culture (human bone marrow stem cells), mouse models, genetic modification, gene expression (rtPCR, RNA-seq), analytical software (ImagJ, GraphPad Prism).

Related paper – PMID: 26010218

**Project 2: Wound Healing:** Optimisation and characterisation of manufacturing processes in the production of a more biomimetic multilayer scaffold for wound repair dermal tissue regeneration. This novel scaffold will consist of a biodegradable knitted mesh, produced from a biodegradable synthetic biomaterial called poly (lactic-co-glycolic acid, PLGA), that will then be embedded within a porous scaffold sponge produced from collagen. This collagen porous sponge will be fabricated using a scaffold manufacture referred to as thermally induced phase separation (TIPS). The outcome of project has further research applications that will involve the application of the scaffolds to animal models.

and

this

**Acquired and Developed Skills throughout Project:** Microscopy (Scanning Electron Microscope (SEM), Confocal, MicroCT), tensile mechanical testing, cell culture (keratinocytes/fibroblasts), and analytical software (ImagJ, GraphPad Prism).

**Related paper** - PMID: 31476748

**Project 3: Prostate Cancer:** Capacity to procure standarised materials, such as culture medium or cell lines, has led to booms in scientific output. Studies are becoming increasingly complex, and the next revolution in cancer research productivity and reproducibility will be enabled by the capacity to share sophisticated standardised experimental tissues. This project will contribute to major innovations that will lead to completely new tools for the study of prostate cancer (PCa). We AIM to contribute to a paradigm shift in

how complex research tools are shared around the world, facilitating critical standardisation and output. Project detail available in person.

**Acquired and Developed Skills throughout Project:** Microscopy (Confocal Fluorescence Microscopy), mammalian cell culture (prostate cancer cells, human stromal cells), genetic modification, mouse models, and analysis and analytical software (ImagJ, GraphPad Prism).

Related paper - PMID: 25380249 or PMID: 29321576

## **Field of Research**: Genetics, cell and molecular biology

**Project Title:** Investigating genetic variants involved in Wilson disease and copper metabolism using genome editing

**Principal Supervisor:** Dr Daniel Wallace
**Co-supervisors:** Prof Nathan Subramaniam**,** Dr Gautam Rishi
**Principal Supervisor Contact and Location:**
Dr Daniel Wallace (d5.wallace@qut.edu.au) Institute of Health and Biomedical Innovation (IHBI) , Kelvin Grove Tel. 31380052
**Masters or Honours project:** Masters or Honours

**Background to the project:**
Wilson disease (WD) is a genetic disorder of copper metabolism. It can present with hepatic and neurological symptoms, due to copper accumulation in the liver and brain (1). WD is caused by compound heterozygosity or homozygosity for mutations in the copper transporting P-type ATPase gene ATP7B. Over 700 ATP7B genetic variants have been associated with WD. Estimates for WD population prevalence vary with 1 in 30,000 generally quoted. Early diagnosis and treatment are important for successful management of the disease. Diagnosis can sometimes be difficult but may be enhanced by molecular genetic testing for ATP7B mutations and knowledge of variant penetrance. Recent research from the laboratory has estimated a much higher genetic prevalence of the disease based on WD-associated variant frequencies in the general population (2). Our results suggest that there are several low penetrant WD variants that may lead to milder or later onset forms of WD that may go undiagnosed.

We hypothesise that the penetrance of ATP7B variants involved in WD is variable and related to the phenotypic variability of the disease. The more prevalent, lower penetrant variants may lead to milder abnormalities in copper homeostasis and/or later onset forms of the disease.

**Aims:**
The aims of this project are to (1) to develop a cellular model to study human ATP7B function, (2) use molecular techniques including CRISPR-Cas9 to introduce WD-associated variants and (3) measure their functional consequences on copper metabolism.

**Skill and techniques to be developed:**
The following cellular and molecular techniques may be included in this project: cell culture, PCR, real-time PCR, DNA cloning, transformation of bacteria, transfection of mammalian cell lines, immunofluorescence microscopy, flow cytometry, CRISPR-Cas9 mediated genome editing, DNA sequencing and Western blotting.

**References / key papers:**
(1) Ala A, Walker AP, Ashkan K, Dooley JS, Schilsky ML. Wilson's disease. Lancet 2007;369:397-408. doi: 10.1016/S0140-6736(07)60196-2
(2) Wallace DF, Dooley JS. Analysis of the frequency and pathogenicity of ATP7B variants in a genomic dataset: implications for Wilson disease prevalence and penetrance. Biorxiv 2019. doi: https://doi.org/10.1101/499285

## **Field of Research**: Genetics and Neuroscience

**Project Title:** Tackling heterogeneity in major depressive disorder through genetics

**Research Group:** Genetic Epidemiology at QIMR Berghofer Medical Research Institute
**Principal Supervisor:** Prof Nick Martin
**Principal Supervisor Contact and Location:** QIMR Berghofer Medical Research Institute
**Email:** Nick.Martin@qimrberghofer.edu.au
**Co-supervisor:** Dr. Miguel E. Rentería (Miguel.Renteria@qimrberghofer.edu.au)


Prof. Nick Martin

**Background to the project:** Major depressive disorder (MDD) is a common complex disease that results from genetic and environmental factors. According to the World Health Organisation, it is currently the fourth leading cause of disability worldwide, and its prevalence is projected to rise in the upcoming years. Characterising the genetic architecture of MDD has been challenging, even compared to other psychiatric conditions such as schizophrenia and bipolar disorder. This is in part due to the highly heterogeneous and polygenic nature of MDD. A wide array of differences exists in symptom profiles, age of onset and triggers across patients. For instance, not all patients experience sleep dysfunction, fatigue or suicidal ideation in the same way. Importantly, patients respond differently to specific antidepressants. An antidepressant that is very effective for a patient, might have adverse side effects in another one and vice versa. These differences arise due to multiple molecular pathways implicated in the genetic architecture of the disease.

**Aims:** This project aims to characterise the genetic heterogeneity that underlies individual variation in both symptom profiles, comorbidities, and treatment response across patients with MDD.

**Skill and techniques to be developed:**
The students will learn and apply a number of computational (genome-wide association, polygenic risk scoring, Mendelian randomisastion, bioinformatics, machine learning, ) approaches to analyse a recently collected dataset of >20,000 Australian MDD patients and >18,000 healthy controls. Cases have been extensively phenotypes for depression symptoms, response to antidepressant medication and a wide range of comorbid features (e.g. anxiety, obsessive compulsive disorder, migraine, post-traumatic stress disorder, etc.). All participants have been genome-wide genotyped. Opportunities for national and international collaboration with leading scientists and consortiums are possible.

**References / key papers:**
Byrne EM et al (2019) **The Australian Genetics of Depression Study: Study Description and Sample Characteristics** *bioRxiv 626762*: https://doi.org/10.1101/626762

Howard DM et al (2018) **Genome-wide meta-analysis of depression identifies 102 independent variants and highlights the importance of the prefrontal brain regions** *Nature Neuroscience* 22, *343–352:* https://www.nature.com/articles/s41593-018-0326-7

## **Field of Research**: Immunology; autoimmunity

**Project Title:** Effect of biologic treatments on immune cell function in ankylosing spondylitis

**Research Group:** Experimental Rheumatology Group
**Principal Supervisor:** A/Prof Tony Kenna
**Co-supervisors:** Dr Darrell Bessette
**Principal Supervisor Contact and Location:** tony.kenna@qut.edu.au, IHBI at QIMRB
**Masters or Honours project:** Either

**Background to the project:**
Ankylosing spondylitis (AS) s a common form of arthritis affecting joints of the spine and pelvis. AS affects about 1 in 200 of the population and is genetically and immunologically complex. Our group has mapped much of the genetics of the disease and has discovered important roles for the inflammatory cytokines IL-23 and IL-17. Current gold standard treatments in AS include use of monoclonal antibodies that block the effects of IL-17. Somewhat surprisingly treatment of patients with anti-IL-23 antibodies has little effect on disease. A recent paper demonstrated that different immune cell types respond very differently to triggers through IL-23 or IL-17 receptors. Understanding how different immune cells respond to inflammatory signals is important for better understanding of disease processes which, in turn, helps better define how to treat disease.

**Aims:**
Determine what cell types respond to signalling through IL-23 or IL-17 pathways
Determine the nature of responses of immune cell subsets to stimulation with IL-23 or IL-17
Define molecular regulation of response to IL-23 versus IL-17 signalling.

**Skill and techniques to be developed:**
Cell culture
Working with primary human cells
High content flow cytometry
qPCR
Statistical analysis

**References / key papers:**
Omenetti S, Bussi C, Metidji A, Iseppon A, Lee S, Tolaini M, Li Y, Kelly G, Chakravarty P, Shoaie S, Gutierrez MG, Stockinger B. The Intestine Harbors Functionally Distinct Homeostatic Tissue-Resident and Inflammatory Th17 Cells. Immunity. 2019 Jul 16;51(1):77-89.e6. doi: 10.1016/j.immuni.2019.05.004.

Kenna TJ, Hanson A, Costello ME, Brown MA. Functional Genomics and Its Bench-to-Bedside Translation Pertaining to the Identified Susceptibility Alleles and Loci in Ankylosing Spondylitis. Curr Rheumatol Rep. 2016 Oct;18(10):63. doi: 10.1007/s11926-016-0612-x.

Brown MA, Kenna T, Wordsworth BP.Genetics of ankylosing spondylitis--insights into pathogenesis. Nat Rev Rheumatol. 2016 Feb;12(2):81-91. doi: 10.1038/nrrheum.2015.133.

Vecellio M, Cohen CJ, Roberts AR, Wordsworth PB, Kenna TJ.RUNX3 and T-Bet in Immunopathogenesis of Ankylosing Spondylitis-Novel Targets for Therapy? Front Immunol. 2019 Jan 10;9:3132. doi: 10.3389/fimmu.2018.03132.

## **Field of Research**: Infection and immunity, and cancer

**Project Title:** Understanding the immunological basis of increased mortality driven by a respiratory syncytial viral infection after stem cell transplantation

**Research Group:** Transplantation Immunology Laboratory
**Principal Supervisor:** Associate Professor Antiopi Varelias
**Principal Supervisor Contact and Location:** QIMRBerghofer MRI
**Email:** A/Prof Antiopi.varelias@qimrberghofer.edu.au
**Masters or Honours project:** Masters and/or Honours

**Background to the project:**
Viral infection and reactivation following stem cell transplantation (SCT) is a common complication following this procedure, which is performed for the treatment of blood cancers. One such pathogen is respiratory syncytial virus (RSV), a common community-acquired infection that leads to significant morbidity in immunocompromised SCT patients. Current treatment strategies for patients infected with RSV is the use of anti-viral agents however these are ineffective. Thus, this complication remains a significant clinical problem where new treatments are desperately needed. To address this, a better understanding of the immunological mechanisms that underlie this disease are essential.

**Aim:**
The specific aim of this project is to establish a robust model of RSV infection in the stem cell transplant setting using Pneumonia Virus of Mice (PVM), the murine relative of RSV. This will enable the contribution of host innate and acquired mucosal immune responses to the viral infection to be dissected.

**Approaches / Techniques to be utilised**
This project is not limited to, but will involve, extensive animal work, flow cytometry, immunological assays, molecular and viral techniques.

**References / Key papers**
Martins JP, Andoniou CE, Fleming P, Kuns RD, Schuster IS, Voigt V, Daly S, **Varelias A**, Tey SK, Degli-Esposti MA and Hill GR. *Strain-specific antibody therapy prevents cytomegalovirus reactivation after transplantation.* ***Science***. 363(6424):288-293 (2019).

**Varelias A,** Gartlan KH, Kreijveld E, Olver SD, Lor M, Kuns RD, Lineburg KE, Teal BE, Raffelt N, Cheong M, Alexander KA, Koyama M, Markey KA, Sturgeon E, Leach J, Reddy P, Kennedy GA, Yanik G, Blazar BR, Tey S-K, Clouston AD, MacDonald KPA, Cooke KR and Hill GR. *Lung parenchyma–derived IL-6 promotes IL-17A–dependent acute lung injury after allogeneic stem cell transplantation.* ***Blood.*** 125(15):2435-44 (2015).

**Varelias A*,** Bunting MD*, Ormerod KL, Koyama M, Olver SD, Straube J, Kuns RD, Robb RJ, Henden AS, Cooper L, Lachner N, Gartlan KH, Lantz O, Kjer-Nielsen L, Mak JYW, Fairlie DP, Clouston AD, McCluskey J, Rossjohn J, Lane SW, Hugenholtz P and Hill GR. *Recipient Mucosal-Associated Invariant T Cells control GVHD within the colon.* ***J Clin Invest.*** 128(5):1919-1936 (2018). *Joint first authors.

**Varelias A,** Ormerod KL, Bunting MD, Koyama M, Gartlan KH, Kuns RD, Lachner N, Locke KR, Lim CY, Henden AS, Zhang P, Clouston AD, Hasnain SZ, McGuckin MA, Bruce R Blazar, MacDonald KPA, Hugenholtz P and Hill GR. *Acute graft-versus-host disease is regulated by an IL-17-sensitive microbiome.* ***Blood.*** 129(15):2172-2185 (2017).
Kennedy GA*, **Varelias A***, Vuckovic S, Le Texier L, Gartlan KH, Zhang P, Thomas G, Anderson L, Boyle G, Cloonan N, Leach J, Sturgeon E, Avery J, Olver SD, Lor M, Misra AK, Hutchins C, Morton AJ, Durrant STS, Subramoniapillai E, Butler JP, Curley CI, MacDonald KPA, Tey SK and Hill GR. *Addition of IL-6 inhibition to standard GVHD prophylaxis after allogeneic stem cell transplantation: a phase I/II trial.* ***Lancet Oncol.*** 15(13):1451-9 (2014). *Joint first authors.

## **Field of Research**: Infection and Immunity, neuro and ocular immunology

**Project Title:** Characterisation of parasite invasion into the eye and brain in a mouse model of cerebral and ocular toxoplasmosis

**Research Group:** Neuroimmunology and Infection Group
**Principal Supervisor:** Dr Samantha Dando
**Co-supervisor:** Dr Fatemeh Chehrehasa
**Principal Supervisor Contact and Location:** samantha.dando@qut.edu.au, QIMR Berghofer
**Masters or Honours project:** Honours

**Background to the project:**
*Toxoplasma gondii* is a ubiquitous protozoan parasite that is estimated to infect at least 30% of the world's population. The parasite can invade the central nervous system (CNS, comprising the brain, retina and spinal cord) where it converts into a slowly replicating form enclosed within a cyst. In most healthy people, *T. gondii* cysts persist as a life-long CNS infection that remain latent (dormant) for many years. However, in immunocompromised individuals latent *T. gondii* can reactivate and cause severe disease such as encephalitis or retinochoroiditis, leading to neurological impairment and blindness. More recently, latent *T. gondii* infection has been associated with neuropsychiatric (schizophrenia) and neurodegenerative (Alzheimer's) conditions, suggesting that chronic infection with this parasite has more significant effects on human health than previously thought. Our lab has established a mouse model of cerebral and ocular toxoplasmosis in order to study the host-pathogen interactions within the brain and the eye. The overall aim of this project is to characterise parasite invasion into the brain and retina in order to: (i) advance our understanding of how *T. gondii* interacts with its host and (ii) determine the consequences of *T. gondii* infection on brain and ocular health.

**Aims:**
1. To determine where *T. gondii* localises within the brain and retina following CNS invasion
2. To determine how microglia (CNS resident macrophages) respond to *T. gondii* infection
3. To determine if *T. gondii* invasion of the CNS supporting tissues (meninges, choroid) precedes invasion of the neural parenchyma

**Skill and techniques to be developed:**
Tissue dissection
Cryotomy and histology
Immunostaining (wholemount tissues and tissue sections)
Confocal microscopy and advanced image analysis

**References / key papers:**
1. Forrester JV, McMenamin PG, Dando SJ. 2018. CNS infection and immune privilege. *Nature Reviews Neuroscience* 19(11): 655-671.
2. Schluter and Barragan. 2019. Advances and challenges in understanding cerebral toxoplasmosis. *Frontiers in Immunology* 10: 242.
3. Dando SJ, Kazanis R, Chinnery HR, McMenamin PG. 2019. Regional and functional heterogeneity of antigen presenting cells in the mouse brain and meninges. *Glia* 67: 935-949.

## **Field of Research**: Infection and Immunity

**Project Title:** Infection kinetic and genetic changes that occur within macrophage-adapted *Chlamydia*.

**Research Group:** Beagley *Chlamydia* Research Group
**Principal Supervisor:** Prof Kenneth Beagley
**Principal Supervisor Contact and Location:**
E: k2.beagley@qut.edu.au; P: (07) 3138 6195; L: QUT@QIMR-B, 300 Herston Road, Herston, QLD 4006
**Co-supervisors:**
Associate Supervisor: Dr Alison Carey; alison.carey@qut.edu.au, (07) 31386259
Associate Supervisor: Dr Emily Bryan; er.bryan@qut.edu.au, (07) 3138 6260
**Masters or Honours project:** Honours

**Background to the project:**
*Chlamydia trachomatis* is an obligate intracellular, bacterial pathogen. *C. trachomatis* infections of the human reproductive tract affect approximately 131 million people globally each year. The major concern of *C. trachomatis* infections is their ability to cause infertility in both men and women, by damaging the upper reproductive tracts. However, we are still lacking information about how *Chlamydia* travels around the reproductive tract, and reaches the upper tract (ovaries and testes in particular) to cause this damage. Recent research has shown that macrophages are a key cell type responsible for harbouring and transmitting *Chlamydia* within the reproductive tract. Macrophages are generally thought of as an immune cell responsible for fighting infections. However, in the case of *Chlamydia*, this does not always occur. *Chlamydia* possesses molecular mechanisms that allow it to avoid macrophage-mediated killing and under some circumstances survive and replicate within these cells. Research has shown that during chlamydial infection, cells undergo genetic and transcriptional changes. However, limited information exists about changes that occur within the *Chlamydia* during growth within immune cells and macrophages. This project aims to elucidate the kinetics of chlamydial growth within macrophages and to delineate the chlamydial genetic and transcriptional changes that occur during infection.

**Aims and Hypothesis:**
Hypothesis: *Chlamydia* that has been grown long-term in macrophages undergoes infectivity and genetic changes that promote its survival.

Aim 1: To harvest *Chlamydia* for infectivity assays and chlamydial RNA from RAW 264.7 macrophage cells infected with passage one or passage 30 *Chlamydia* previously grown in macrophages.

Aim 2: To analyse RNAseq data to identify genes that are differentially expressed between the passage one and passage 30 macrophage-adapted *Chlamydia*.

Aim 3: To map differentially expressed genes to biological pathways/systems to posit the effects of long-term growth of *Chlamydia* in macrophages.

**Skill and techniques to be developed:**
Mammalian cell culture, chlamydial cell culture, immunocytochemistry, epifluorescent microscopy, RNA isolation, RNAseq, differential gene analysis, KEGG pathway mapping, biological system analysis, written and oral communication skills.

**References / key papers:**
Bryan *et al*. 2019, Hematogenous dissemination of *Chlamydia muridarum* from the urethra in macrophages causes testicular infection and sperm DNA damage, *Biology of Reproduction*, ioz146, https://doi.org/10.1093/biolre/ioz146

## **Field of Research**: Infection and Immunity

**Project Title:** Testing of novel antibiotic-loaded nanoparticles for treatment of *Chlamydia* infection.

**Research Group:** Beagley Chlamydia Research Group
**Principal Supervisor:** Prof Kenneth Beagley
**Principal Supervisor Contact and Location:**
E: k2.beagley@qut.edu.au
P: (07) 3138 6195
L: QUT@QIMR-B, 300 Herston Road, Herston, QLD 4006
**Co-supervisors:**
Associate Supervisor: A/Prof Tim Dargaville, t.dargaville@qut.edu.au, (07) 3138 2451
Associate Supervisor: Dr Alison Carey; alison.carey@qut.edu.au, (07) 31386259
Associate Supervisor: Dr Emily Bryan; er.bryan@qut.edu.au, (07) 3138 6260
**Masters or Honours project:** Honours

**Background to the project:**
*C. trachomatis*, sexually transmitted infections of both the female and male human reproductive tract, affects approximately 127 million people globally each year. The major concerning sequela of *C. trachomatis* infection is infertility in both men and women. This occurs by damaging the upper reproductive tracts, the ovaries and testes most importantly. The majority of research has been focussed on female disease, and male disease has been underestimated and understudied, particularly therapeutics for male infections. Antibiotic therapy is the only therapy currently available and this is not effective in all cases with significant treatment failure. However, recent data shows that male *Chlamydia* infections frequently reside within testicular macrophages, an immune cell type that requires 10 times more antibiotics to clear an infection compared to infected epithelial cells; levels that are not achievable using the currently recommended oral doses of Azithromycin or doxycycline. The aim of this project is to compare conventional and a novel, nanoparticle-delivered antibiotic therapy to eliminate infection in macrophages. The novel approach will need to achieve clearance of infection at an antibiotic concentration comparable to that needed to clear epithelial infections, with no cytotoxic effects on the host cells.

**Aims and Hypothesis:**
Hypothesis: Antibiotic-loaded nanoparticles will have increased uptake and chlamydial clearance efficiency in macrophages compared to conventional antibiotic treatment.

Aim 1: To assess the cytotoxicity of the nanoparticles for macrophages in cell culture.

Aim 2: To assess the ability of standard versus nanoparticle-contained antibiotics to clear chlamydial infection in macrophages.

Aim 3: To develop assays for detection of nanoparticle-contained antibiotics within macrophages.

**Skill and techniques to be developed:**
Mammalian cell culture, chlamydial cell culture, immunocytochemistry, epifluorescent microscopy, light microscopy, flow cytometry, DNA/RNA extraction, qPCR, gel electrophoresis, data analysis using GraphPad Prism, written and oral communication skills.

**References / key papers:**
Bryan *et al*. 2019, Hematogenous dissemination of *Chlamydia muridarum* from the urethra in macrophages causes testicular infection and sperm DNA damage, *Biology of Reproduction*, ioz146, https://doi.org/10.1093/biolre/ioz146

## **Field of Research**: Infection and Immunity; inflammation

**Project Title:** Using hookworm-derived products to protect from asthma and inflammatory bowel disease

**Research Group:** Mucosal Immunology Group, QIMRBerghofer MRI
**Principal Supervisor:** A/Prof Severine Navarro
**Principal Supervisor Contact and Location:** Severine.navarro@qimrberghofer.edu.au. Located at QIMRBerghofer Medical Research Institute.
**Masters or Honours project:** Both. This project is suitable for up to 3 three students.

**Background to the project:**
Nearly one billion people globally suffer from allergies, representing a considerable social and economic impact, significant morbidity and reduced quality of life. Allergic diseases most commonly develop in infancy, meaning that children are exposed to life-long treatments that can cause considerable and irreversible side effects. Compelling evidence suggests that sensitisation occurs within the first two years of life when the gut microbiome establishes. Over this period, a delicate balance linking the microbiome and the immune system exists, which, if perturbed, results in heightened allergen-specific Th2 responses. These observations imply a "window of susceptibility" for the development of sensitisation that could be explored as an intervention opportunity to prevent atopy.

We have recently described that a hookworm recombinant protein, named Anti-Inflammatory Protein (AIP)-2, is able to suppress allergic responses in both mice (in vivo) and humans (ex vivo), and to promote sustained immune regulation in mice. We have found that AIP-2 administered via breastmilk (BM) within the first week of life, modified the composition of the gut microbiome and protected pups from asthma onset into adulthood. Our central hypothesis is that AIP-2 and BM co-factors prevent sensitisation by modifying the immune and microbiome landscape promoting sustainable tolerance.

The project is designed around the characterisation of the responses induced in lung and intestinal epithelial cells when exposed to hookworm-derived products. The techniques employed to determine these responses will be: aseptic cultures, gene and protein expression, flow cytometry, confocal microscopy, real-time PCR/gene arrays/nanostring.

**Skill and techniques to be developed:**
Students will gain extensive knowledge in immunology, allergy and chronic inflammatory disorders, as well as drug development. The skills employed for this project are sought-after know-hows for any higher professional degrees in research. Students will be provided skills for efficient literature search and analysis.
Students will participate in routine journal club/lab meetings and will be asked to present an original article as part of the journal club, as well as a project plan and final placement presentations.

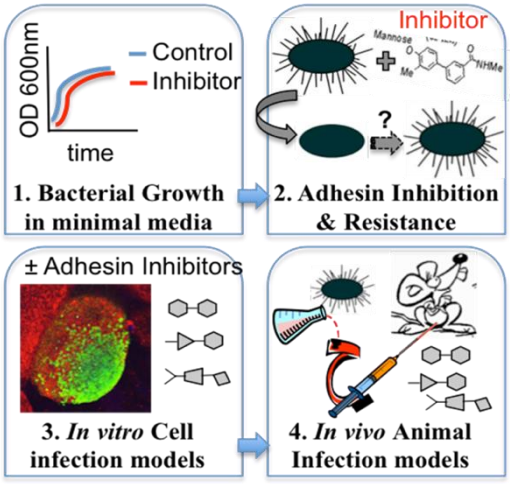
## **Field of Research**: Infection and Immunity; microbiology

**Project Title:** A preclinical evaluation pipeline for new antivirulence drugs targeting multidrug resistant infections

**Research Group:** Bacterial Pathogenesis (Totsika)
**Principal Supervisor:** A/Prof Makrina Totsika
**Principal Supervisor Contact and Location:** Infection and Immunity Program | Institute of Health and Biomedical Innovation (IHBI) | Queensland University of Technology (QUT) | QIMR-Berghofer Medical Research Institute, 300 Herston Rd, Herston, QLD, 4006, Australia | t: +7 3138 0410|e: makrina.totsika@qut.edu.au
**Masters or Honours project:** Suitable for both

**Background to the project:**
'*A post-antibiotic era—in which common infections and minor injuries can kill—far from being an apocalyptic fantasy, is instead a very real possibility for the 21st century.*' -WHO, 2014 (1). Antimicrobial resistance (AMR) is a global public health priority. If no action is taken, AMR is predicted to kill more people than cancer and diabetes combined by 2050, with 10 million deaths estimated each year and a global cost of up to 100 trillion USD. New therapies to tackle multidrug resistant (MDR) pathogens are sorely needed. My lab in collaboration with scientists from Australia and the US has developed novel antimicrobials that aim to disarm (anti-virulence) rather than kill (antibiotics) bacterial pathogens. These novel antimicrobials can offer superior therapeutics, as they can be more evolution-proof and narrow-spectrum than traditional antibiotics (2). These benefits need however to be evaluated in relevant preclinical models before further clinical development (*example figure shown for adhesin inhibitors*).

**Hypothesis**
Antivirulence drugs are effective treatments for common multidrug resistant infections, such as urinary tract infections and diarrhoea.




**Aims:**
1. To establish relevant *in vitro* models of antibiotic resistant infection
2. To evaluate our current virulence inhibitors as therapies in these models

**Skill and techniques to be developed:**
Culture of human cell lines, handling/culturing multidrug resistant bacterial pathogens and GMOs, gene expression analysis (DNA/RNA isolation, protein preparation, PCR, qRT-PCR, DNA/protein gel-electrophoresis, etc), in vitro cell infection assays. You will also receive training in conducting literature searches and critical literature review, research design and methodology, data analysis and presentation in lab meetings.

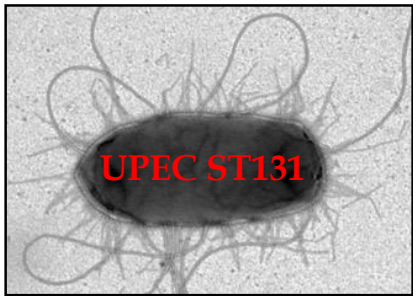
**References / key papers:**
1. World Health Organization, Antimicrobial Resistance: Global Report on Surveillance (2014).
2. **Totsika, M.** (2016) Benefits and Challenges of Antivirulence Antimicrobials at the Dawn of the Post-Antibiotic Era, Drug Delivery Letters 6, 8.

## **Field of Research**: Infection and Immunity; microbiology

**Project Title:** Characterisation of emerging multidrug resistant *E. coli* pathogens

**Research Group:** Bacterial Pathogenesis (Totsika)
**Principal Supervisor:** A/Prof Makrina Totsika
**Principal Supervisor Contact and Location:** Infection and Immunity Program | Institute of Health and Biomedical Innovation (IHBI) | Queensland University of Technology (QUT) | QIMR-Berghofer Medical Research Institute, 300 Herston Rd, Herston, QLD, 4006, Australia | t: +7 3138 0410|e: makrina.totsika@qut.edu.au
**Masters or Honours project:** Suitable for both

**Background to the project:**
The last fifteen years have witnessed an unprecedented rise in the rates of antimicrobial resistance among Gram-negative bacteria, described by the World Health organisation as a global health crisis (1). *Escherichia coli* sequence type 131 (*E. coli* ST131) is a 'high-risk' group of Gram-negative pathogens that have emerged rapidly and spread worldwide in the period of the last 10 years (2). *E. coli* ST131 strains are typically resistant to multiple classes of antibiotics and cause bloodstream and urinary tract infections (UTI) that are extremely difficult to treat. My lab has recently shown that ST131 strains are proficient colonizers of the gut allowing them to persist for long periods of time with the possibility of new hybrid strains emerging (3). This project will investigate newly emerged sub-lineages of ST131 with enhanced pathogenic potential.




**Hypothesis**
*E. coli* ST131 is a versatile MDR lineage with capacity to be pathogenic in and outside the gut.

**Aims:**

1. Comparative genomics of diverse *E. coli* ST131 clinical isolates
2. Identification and characterisation of key virulence factors in newly emerged ST131 isolates

**Skill and techniques to be developed:**
Comparative bacterial genomics and bioinformatics, culture of human cell lines, handling/culturing multidrug resistant bacterial pathogens and GMOs, gene expression analysis (DNA/RNA isolation, protein preparation, PCR, qRT-PCR, DNA/protein gel-electrophoresis, etc), *in vitro* cell infection assays. You will also receive training in conducting literature searches and critical literature review, research design and methodology, data analysis and presentation in lab meetings.

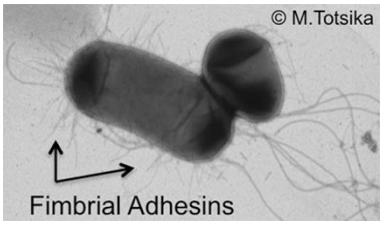
**References / key papers:**
1. World Health Organization, Antimicrobial Resistance: Global Report on Surveillance (2014).
2. Nicolas-Chanoine M-H, Bertrand X, Madec J-Y. Escherichia coli ST131, an Intriguing Clonal Group. *Clinical Microbiology Reviews*. 2014;27(3):543-574.
3. Sarkar S, Hutton ML, Vagenas D, Ruter R, Schüller S, Lyras D, Schembri MA, **Totsika M.** (2018) Intestinal colonisation traits of pandemic multidrug resistant *Escherichia coli* ST131. *Journal of Infectious Diseases,* 218(6):979-990.

## **Field of Research**: Infection and Immunity; microbiology

**Project Title:** Molecular mechanisms of bacterial proteins involved in host recognition and defense

**Research Group:** Bacterial Pathogenesis (Totsika)
**Principal Supervisor:** A/Prof Makrina Totsika
**Principal Supervisor Contact and Location:** Infection and Immunity Program | Institute of Health and Biomedical Innovation (IHBI) | Queensland University of Technology (QUT) | QIMR-Berghofer Medical Research Institute, 300 Herston Rd, Herston, QLD, 4006, Australia | t: +7 3138 0410|e: makrina.totsika@qut.edu.au
**Masters or Honours project:** Suitable for both

**Background to the project:**
Pathogenic bacteria employ a large repertoire of molecular weapons known as virulence factors to infect the host and cause disease. In particular, autotransporter proteins, the largest family of secreted virulence factors in Gram-negative bacteria, promote bacterial colonisation, biofilm formation and host cell invasion and/or damage (1). In response, host cells deploy various antimicrobial strategies, such as the mobilization of copper at the site of infection, which induces bacterial stress. Despite the abundance of autotransporters and their roles in infection, their mechanisms of action remain mostly unknown. In addition, novel bacterial defense proteins to copper stress have been identified (2) but with little mechanistic understanding of how they confer bacterial copper resistance. This project will comprehensively characterize autotransporter and copper resistance proteins from pathogenic bacteria.




**Aims:**
1. Exploring how autotransporter proteins from two different sub-families bind and enter their host targets
2. Define the metal binding and dissect the function of distinct copper resistance systems from two different pathogenic bacteria.

**Skill and techniques to be developed:**
Culture of human cell lines, handling/culturing multidrug resistant bacterial pathogens and GMOs, protein and gene expression analysis (DNA isolation, protein preparation, PCR, DNA/protein gel-electrophoresis, etc), *in vitro* cell infection assays. You will also receive training in conducting literature searches and critical literature review, research design and methodology, data analysis and presentation in lab meetings.

**References / key papers:**
1. Heras B, **Totsika M**, Peters KM, Paxman JJ, Gee C., Jarrott RJ, Perugini MA, Whitten AE, and Schembri MA. (2014) The antigen 43 structure reveals a molecular Velcro-like mechanism of autotransporter-mediated bacterial clumping. *PNAS*, 7;111(1):457-62
2. Furlong EJ, Lo AW, Kurth F, Premkumar L, **Totsika M**, Achard MES, Halili MA, Heras B, Whitten AE, Choudhury HG, Schembri MA, Martin JL. (2017) A shape-shifting redox foldase contributes to *Proteus mirabilis* copper resistance. *Nature Comms,* 8: 16065.

## **Field of Research**: Infection and Immunity; microbiology

**Project Title:** A novel genomics approach to understanding capsular polysaccharide synthesis in *Acinetobacter baumannii*

**Research Group:** Bacterial Polysaccharides Research Group (Kenyon Laboratory)
**Masters or Honours project:** Honours or Masters
**Principal Supervisor:** Dr Johanna Kenyon
**Principal Supervisor Contact and Location:** johanna.kenyon@qut.edu.au; (07) 3138 2552, IHBI@QIMR-B
**Co-supervisors:** Professor Ruth M. Hall OAM FAA (External; University of Sydney)

**Background to the project:**
Capsular polysaccharide (CPS) is a critical virulence determinant currently being targeted in novel vaccine and phage therapies against *Acinetobacter baumannii,* the World Health Organisation's number one critical priority pathogen for therapeutics development. Determination of specific antigen and phage recognition sites relies on knowledge of CPS chemical structures and their biosynthesis pathways. Our team is leading the way in this field using a novel 'genomics-structure' approach that correlates the CPS structures produced by clinical isolates with the genes that direct CPS biosynthesis. This approach has led to the discovery of novel sugars that have not previously been found before in nature and has allowed the functions of numerous biosynthesis enzymes to be assigned without the need for complex and time-consuming biochemistry. This has proven invaluable for enzymes that are notoriously difficult to characterize, such as Wzy integral membrane proteins that are required to link oligosaccharide units together to form the CPS. These proteins remain largely uncharacterized in bacterial systems due to inherent difficulties in working with membrane proteins in the laboratory. However, with the largest collection of sequenced *A. baumannii* strains for representative CPS types and our established NMR structure determination pipeline, we have the unprecedented opportunity to characterise Wzy diversity using the 'genomics-structure' approach. We have also found that *wzy* genes can be carried by phage and other genomic elements to alter the *A. baumannii* cell surface, providing novel insights into the clinical impact of gene movement and subsequent implications for phage therapy and vaccine research.

**Aims:** To utilize the novel 'genomics-structure' approach to correlate CPS structures produced by clinical isolates with the genes that direct CPS biosynthesis; to consolidate information on Wzy linkages to build connections between Wzy properties and substrate specificities; and to mine *A. baumannii* genome sequences for new related sets of CPS gene clusters to identify new Wzy proteins.

**Skill and techniques to be developed:** CPS structural data will be correlated with genetic sequences using a wide range of bioinformatic tools to deduce the function of Wzy proteins in *A. baumannii*.

**References / key papers:**
1. **Kenyon JJ***, Arbatsky NP*, Sweeney EL, Shashkov AS, Shneider MM, Popova AV, Hall RM, Knirel YA. (2019). Production of the K16 capsular polysaccharide by *Acinetobacter baumannii* ST25 isolate D4 involves a novel glycosyltransferase encoded in the KL16 gene cluster. *Int J Biol Macromol.* 128: 101-106.
2. **Kenyon JJ**, Notaro A, Hsu LY, De Castro C, Hall RM. (2017). 5,7-Di-N-acetyl-8-epiacinetaminic acid: A new non-2-ulosonic acid found in the K73 capsule produced by an *Acinetobacter baumannii* isolate from Singapore. *Sci Rep*, 7, 11357.
3. **Kenyon JJ**, Shneider MM, et al. (2016). The K19 capsular polysaccharide of *Acinetobacter baumannii* is produced via a Wzy polymerase encoded in a small genomic island rather than the KL19 capsule gene cluster. *Microbiol*, 162, 1479-1489.
4. **Kenyon JJ** & Hall RM. (2013). Variation in the complex carbohydrate biosynthesis loci of *Acinetobacter baumannii* genomes. *PLoS One* 8: e62160.

## **Field of Research**: Infection and Immunity; microbiology

**Project Title:** Pneumococcal capsular genotyping using bioinformatics

**Research Group:** Molecular Microbial Pathogenesis Group and the Bacterial Polysaccharides Research Group
**Principal Supervisor:** Prof Flavia Huygens
**Co-supervisor:** Dr Johanna Kenyon
**Principal Supervisor Contact and Location:** f.huygens@qut.edu.au; IHBI at QIMR Berghofer, Herston
**Masters or Honours project:** Both

**Background to the project:**
*Streptococcus pneumoniae* is a Gram-positive bacterium that is associated with a range of diseases including invasive pneumococcal disease (IPD) including meningitis and septicaemia, pneumonia, and otitis media. It is estimated that approximately 800 000 children under five die each year, worldwide, from pneumococcal diseases (O'Brien *et al.,* 2009). As well as this, *S. pneumoniae* causes high morbidity (estimated 14.5 million episodes of serious pneumococcal disease in 2000) and high economic burden globally, especially in underdeveloped countries (O'Brien *et al.,* 2009). Surveying *S. pneumoniae* is important to detect changes in the population, particularly after the introduction of the vaccine Prevenar13® (13vPCV; Pfizer) in Australia in 2011. A number of genotyping methods have been used worldwide to study the pneumococcal population, however, current methods are either too expensive for routine use or fail to completely genetically profile all pneumococcal strains. There is no universally accepted genotyping method to date. This project will utilise a novel bioinformatics approach to develop a robust and comprehensive pneumococcal genotyping method that will incorporate all known serotypes of pneumococcal strains globally.

**Aims:**
To consolidate available genetic information for *S. pneumoniae* capsule gene clusters to establish a complete compendium of data to facilitate rapid pneumococcal genotyping; to compare the new genotyping technique to existing methods.

**Skill and techniques to be developed:**
A wide range of bioinformatics techniques including database creation and use of python scripts

**References / key papers:**

1. O'Brien, K. L., Wolfson, L. J., Watt, J. P., Henkle, E., Deloria-Knoll, M., McCall, N., . . . Cherian, T. (2009). Burden of disease caused by *Streptococcus pneumoniae* in children younger than 5 years: global estimates. *Lancet, 374*(9693), 893-902.
2. Rayner, E.R. Investigating the population structure of Queensland invasive Streptococcus pneumonia isolates in children: using a modified multi-locus variable number of tandem repeat analysis and a novel Minimum SNPs capsular typing method. PhD Thesis, QUT, 2015.
3. Rayner, E.R., Savill, J., Hafner L.M., Huygens F. (2015). Genotyping Streptococcus pneumonia. *Future Microbiology, 10(4),* 653-664.

## **Field of Research**: Infection and Immunity; microbiology

**Project Title:** Gene editing against antimicrobial resistance

**Research Group:** Molecular Microbial Pathogenesis Group
**Principal Supervisor:** Prof.Flavia Huygens
**Co-supervisor:** Dr Dimitri Perrin
(School of Electrical Engineering and Computer Science, QUT)
**Principal Supervisor Contact and Location:** f.huygens@qut.edu.au; IHBI at QIMR Berghofer, Herston
**Masters or Honours project:** Both

**Background to the project:**
By 2050, 10 million lives a year and a cumulative $100 trillion of economic output are at risk globally, due to the rise of drug resistant infections [1].
The CRISPR-Cas9 system provides an exciting way to efficiently make accurate modification of the genome, and there has been promising reports on using CRISPR to kill specific bacteria [2]. At QUT, we have expertise in the optimal design of guide RNAs used for CRISPR experiments [3]. In this project, we will leverage this expertise and explore the possible role of CRISPR in the response to antimicrobial resistance.

**Aims:**
1. Antibiotic resistance genes will be selected that confer resistance across several bacterial species.
2. Use QUT developed algorithms to detect efficient CRISPR targets.
3. Package these unique gene editing targets with CRISPR-Cas9 and use AAV for *in vitro* delivery.
4. Use growth-curve experiments to determine the efficiency of the CRISPR system in rendering antibiotic-resistant bacteria susceptible to antibiotics.

**Skill and techniques to be developed:**
1. Application of software algorithms to detect efficient bacterial CRISPR targets.
2. Utilise molecular techniques to package CRISPR-Cas9 into suitable delivery systems such as AAV.
3. Apply bacterial culture methods for testing the restoration of antibiotic susceptibility in bacteria that are resistant to antibiotics.

**References / key papers:**
1. Wellcome Trust and UK Government (2016). "The review on antimicrobial resistance – Tackling drug-resistant infections globally: final report and recommendations". Available online at https://amr-review.org/
2. R.J. Citorik et al. (2014). "Sequence-specific antimicrobials using efficiently delivered RNA-guided nucleases". Nature Biotechnology 32:1146–1150.
3. J. Bradford and D. Perrin. 2019. A benchmark of computational CRISPR-Cas9 guide design methods. PLoS Comput. Biol. 15(8): e10072474.

## **Field of Research**: Microbiology; blood safety

***There are opportunities for part-time employment at the Blood Service in conjunction with this project.***

**Project Title:** Evaluating the risk posed by emerging transfusion-transmitted infectious diseases

**Research Group:** Research and Development, Australian Red Cross Blood Service
**Principal Supervisor:** Prof Robert Flower
**Co-supervisors:** Dr Eileen Roulis (eroulis@redcrossblood.org.au) , Dr Helen Faddy (hfaddy@redcrossblood.org.au)
**Principal Supervisor Contact and Location:** rflower@redcrossblood.org.au; Kelvin Grove
**Masters or Honours project:** Either

**Background to the project:**
There is a risk that transfusion-transmitted infections (TTIs) may occur when blood components for transfusion contain a pathogen/s. The Australian Red Cross Blood Service (Blood Service) currently has mandatory procedures in place to reduce the risk of TTIs. These procedures include a donor eligibility questionnaire and various laboratory screening tests. Although these procedures have been very effective at reducing the incidence of TTIs they do not entirely eliminate all risk (especially for emerging pathogens). The risk of TTIs varies according to biology and local epidemiology of the pathogen in question. The recent spread of Zika virus posed a threat to the blood supply globally and a number of cases of Zika virus transfusion transmission have been reported. This outbreak demonstrated the heightened risk of TTIs when the virus is present in a reservoir host and there is risk of asymptomatic blood donors. This area of research investigates possible risks to the safety of the Australian blood supply. Multiple different student projects are available, and others can be developed depending on student interest.

**Aims:**
To determine if emerging TTIs pose a risk to blood transfusion safety.

**Skill and techniques to be developed:**
Depending on the specific project, this study will:
- Gain experience optimising and performing a range of relevant infectious diseases ELISAs;
- Gain experience with molecular biology techniques, including nucleic acid extraction, real time RT-PCR and next generation sequencing;
- Gain experience in statistical, epidemiological and risk assessment analyses;
- Learn about blood, blood safety and applications of these strategies for ensuring the safety of the blood supply; and
- Gain an understanding of good laboratory practice.

**References / key papers:**
1. Faddy HM et al. No evidence for widespread Babesia microti transmission in Australia. Transfusion. 2019 May 9. doi: 10.1111/trf.15336.
2. Watson-Brown P et al. Epidemic potential of Zika virus in Australia: implications for blood transfusion safety. Transfusion. 2019 Feb;59(2):648-658. doi: 10.1111/trf.15095
3. Hoad VC et al. Hepatitis E virus RNA in Australian blood donors: prevalence and risk assessment. Vox Sanguinis 2017 Oct;112(7):614-621. doi: 10.1111/vox.12559
4. Faddy HM et al. Transfusion risk from emerging pathogens in the Asia-Pacific region. ISBT Science Series 2016;11(Suppl. 2), 143-148

## **Field of Research**: Molecular medicine; liver disease

**Project Title:** Targeting Fibrosis: Identification of novel natural compounds to modulate collagen expression

**Research Group:** Liver Disease and Iron Disorders Research Group, IHBI
**Principal Supervisor:** Prof V. Nathan Subramaniam
(nathan.subramaniam@qut.edu.au)
**Co-supervisors:** Dr Gautam Rishi (gautam.rishi@qut.edu.au)
**Masters or Honours project:** Honours/Research Masters

**Background to the project:**
Liver disease is a huge and increasing burden on society; it can be due to a number of different reasons including excessive alcohol consumption, viral infections, and non-alcoholic liver disease. Each of these causes may have a different molecular pathway of developing the disease pathology, but one common feature is there is an injury or insult to the liver. This injury then results in activation of the wound healing process; when this healing process goes awry liver disease can develop, the first stage of which is liver fibrosis. Although our knowledge and understanding of the molecular pathways involved in liver fibrosis has increased over the past few years, there is still a shortage of effective therapies.

Small molecule libraries have been previously used to try and identify anti-fibrotic molecules but these studies used indirect readouts to measure the effectiveness of the compounds. We have a unique cell line expressing green fluorescent protein (GFP) which can be effectively used to identify external/internal changes in the cells. This project will utilise these cells and natural compound libraries from Compounds Australia to identify molecules that can either increase or decrease collagen expression

**Aim 1:** Identification of small naturally occurring compounds which can increase or decrease the expression of collagen
**Aim 2:** Validation of target identified in Aim 1 in cells treated with fibrotic agents to examine the molecular pathways utilised by the identified targets, using qRT-PCR and western blotting.

**Brief description of methods:**
All compounds will be tested initially to identify the effective target molecules. Cells grown on glass bottom plates will be treated and then be imaged for GFP fluorescence, cell morphology, and nuclei structure to examine the effect of the screening compounds on collagen expression and cell health as well.

This project will utilise the high-throughput imaging facilities at QUT. Instruments like the InCell Analyzer and Deltavision will be used to image collagen and other morphological features of the cell after treatment with the screening compounds. Hepatic cell lines will be utilised to examine the molecular pathways through which the targets identified. This project has the potential of developing into a PhD project.

**Skills and techniques to be developed:**
Cell culture
Transfections
Immunofluorescence
Microscopy
qRT-PCR
Cellular analysis
Western blotting

## **Field of Research**: Molecular medicine; liver disease

**Project Title**: Role of microRNAs (miRNA) in progression and development of liver disease

**Research Group:** Liver Disease and Iron Disorders Research Group, IHBI
**Principal Supervisor:** Prof V. Nathan Subramaniam
(nathan.subramaniam@qut.edu.au)
**Co-supervisors:** Dr Gautam Rishi (gautam.rishi@qut.edu.au),
Dr Michelle Melino (michelle.melino@qut.edu.au)
**Masters or Honours project:** Honours/Research Masters

**Background to the project**:
Liver disease is a significant burden on society, accounting for more than 2 million deaths worldwide. miRNAs can exert causal roles, being pro- or anti-inflammatory, as well as pro- or antifibrotic mediators or being oncogenes as well as tumour suppressor genes. In this project we will identify novel miRNAs which play a role in the progression and development of liver disease and delineate the mechanisms utilised by these miRNAs using cell and mouse models of disease.

**Aim 1:** To identify differentially expressed miRNAs in the liver and serum of mouse models of liver disease.
**Aim 2:** To examine the expression of differentially expressed miRNAs in liver at different stages of liver disease.
**Aim 3:** To delineate the functions of novel miRNAs using cell and mice models of liver disease.

**Brief description of methods:**
In Aim1 miRNA sequencing will be performed on liver and serum samples from mouse models of disease available in the laboratory. The student will then perform bioinformatic analyses on the data generated from this experiment. These miRNA changes will then be validated in mice in Aim 2 at different stages of liver disease to examine the role of these miRNAs in liver disease progression. In Aim 3 we will identify the mechanistic functions of these miRNAs in cell and mouse models using classical and new cell and molecular biology techniques.

**Skills and techniques to be developed:**
miRNA
Next generation sequencing
RNA seq
Bioinformatics
Western blotting
qRT-PCR

## **Field of Research**: Molecular Medicine; liver disease

**Project Title:** Role of Peroxisomes in fatty liver disease

**Research Group:** Liver Disease and Iron Disorders Research Group, IHBI
**Principal Supervisor:** Prof V. Nathan Subramaniam
(nathan.subramaniam@qut.edu.au)
**Co-supervisors:** Dr Gautam Rishi (gautam.rishi@qut.edu.au)
**Masters or Honours project:** Honours/Research Masters

**Background to the project**:
Liver disease is an increasing burden on society, accounting for more than 2 million deaths worldwide. Peroxisomes are multifunctional cellular organelles which are highly enriched in the liver. Our preliminary data shows that defects in a peroxisomal protein affects the ability of the liver to respond to toxic insults. In this research proposal, we build on these important and exciting findings to examine the relationship between peroxisome dysfunction and liver disease.

**Aim 1:** To examine the expression and function of peroxisomal proteins in the liver.
**Aim 2:** To specifically deplete peroxisomal proteins in the hepatocytes of mice and examine its effect on liver function and disease progression.
**Aim 3:** To analyse markers of peroxisomal disorders and peroxisome gene variants in a well-defined cohort of patients with fatty liver disease.

**Brief description of methods:**
In the proposed research, we will identify the cellular roles of peroxisomal proteins in the hepatocytes and their importance in progression of liver disease. The first two aims of the project are to examine the expression of these proteins in the specific cell-types of the liver and examine the consequences of depletion of these genes in vitro on markers of liver disease and iron metabolism. We will use high throughput next generation technologies to identify transcriptomic and proteomic changes in these models to further delineate the molecular mechanisms underlying the role of these protein in liver disease progression. In the third we will develop a genetic panel to be used to identify variants in genes known to affect the progression of liver disease to be used clinically. All resources, equipment and facilities required for the successful completion of the proposed research project are available including animal and cell culture facilities, microscopes, real-time PCR instruments, FACS and histochemical facilities. Knockout mice and conditionally deleted mice are already breeding and the murine models of liver disease are routinely used in the laboratory. This project has the potential of developing into a PhD project.

**Skill and techniques to be developed:**
Cell culture
Microscopy
qRT-PCR
Histology
Flow cytometry
Next generation sequencing
Bioinformatics

## **Field of Research**: Molecular medicine; liver and iron disease

**Project Title:** Understanding the role of TGF signalling intermediates in liver and iron-related disease

**Research Group:** Liver Disease and Iron Disorders Research Group, IHBI
**Principal Supervisor**: Prof V. Nathan Subramaniam
(nathan.subramaniam@qut.edu.au)
**Co-supervisors:** Dr Gautam Rishi (gautam.rishi@qut.edu.au)
**Masters or Honours project:** Honours/Research Masters

**Background to the project**:
Transforming growth factor β (TGFβ) and its family members is involved in many phases of liver disease development and iron regulation. We have identified unexplored players in liver disease and iron-related disorders: TGF signalling intermediates. In this project, we build on our exciting findings to examine the molecular mechanisms involved in TGF signalling intermediates-mediated disease progression and their potential as targets for liver and iron-related disease.

**Aim 1:** To examine the expression of TGF signalling intermediates in the liver.
**Aim 2:** To specifically deplete TGF signalling intermediates in liver cells and examine consequences on liver disease and iron-related disease markers.
**Aim 3:** To generate liver cell-specific deletions in mice and examine consequences on liver disease and iron-related disease markers.
**Aim 4:** To identify TGF signalling intermediates targeting molecules.

**Brief description of methods:**
In the proposed research, we will identify the cellular roles of TGF signalling intermediates and their importance in progression of liver disease and in iron regulation and will develop and test strategies to target TGF signalling intermediates preferentially in specific cell types of the liver. The first two aims of the project are to examine the expression of these proteins in the specific cell-types of the liver and examine the consequences of depletion of these genes in vitro on markers of liver disease and iron metabolism. In the third Aim liver cell-specific deletions of these proteins in mice will be generated. In the fourth aim we will use specific siRNAs identified in Aim 1 to target these genes in vivo. All resources, animal models, equipment and facilities required for the successful completion of the proposed research project are available including animal and cell culture facilities, microscopes, real-time PCR instruments, FACS and histochemical facilities. Knockout mice and conditionally deleted mice are already breeding and the murine models of liver disease are routinely used in the laboratory. This project has the potential of developing into a PhD project.

**Skill and techniques to be developed:**
Cell culture
Transfections
Flow cytometry
Microscopy
qRT-PCR
Histology

## **Field of Research**: Molecular Medicine; iron disorders

**Project Title**: Identification and functional characterisation of genetic modifiers of iron overload

**Research Group:** Liver Disease and Iron Disorders Research Group, IHBI
**Principal Supervisor:** Prof V. Nathan Subramaniam
(nathan.subramaniam@qut.edu.au)
**Co-supervisors:** Dr Gautam Rishi (gautam.rishi@qut.edu.au)

**Background to the project**:
Iron is an element essential for virtually all life forms; aberrant iron metabolism is linked to many diseases. These include cancers, neurodegenerative diseases such as Alzheimer's and Parkinson's disease, iron overload and iron deficiency disorders, iron-loading anaemias, and the anaemia associated with chronic disease. Central to proper iron regulation is the appropriate expression and activity of the liver-expressed regulatory peptide, hepcidin, and the iron exporter, ferroportin (FPN). Modulating the expression and activity of hepcidin and FPN, and their interaction is thus a focus of many therapeutic interventions. We have identified a new mechanism by which ferroportin is regulated. This finding was made possible through the systematic analysis of a cohort of Australian patients with iron overload. Our research proposal builds on this exciting new finding.

**Aim 1:** To analyse the mechanistic role of these novel proteins in iron homeostasis and FPN regulation.
**Aim 2:** To investigate the role of these novel proteins in iron homeostasis in animal models of dysregulated iron homeostasis.
**Aim 3:** To determine the functional consequences of mutations in the se novel proteins and prevalence in subjects with iron overload.

**Brief description of methods:**
In Aim 1 we will perform functional assays to examine the role of these proteins in FPN function and iron homeostasis. We have unique reagents to be able to study the localisation and function of FPN. We will utilise these reagents to examine the effect of loss or gain of function. The experiments outlined in Aim 2 will determine the molecular role of these proteins in systemic iron homeostasis and in conditions known to affect iron homeostasis. These experiments will also aim at developing an animal model to study the mechanism and effect of loss of these proteins on systemic iron homeostasis to recapitulate the human condition that we see in our patients. In Aim 3 Potential iron overload gene variants will be prioritised and those identified through analysis of the ExAC database, and screened for in other cases of atypical iron overload present in the QIMR Berghofer HH Database.

**Skill and techniques to be developed:**
Cell culture
Transfections
Immunofluorescence
Next generation sequencing
Bioinformatics
Flow cytometry

## **Field of Research**: Reproductive Health; medical biochemistry, lipids and protein chemistry

**Project Title:** Early detection of complications in human pregnancy

**Research Group:** Child and Reproductive Health Research
**Principal Supervisor:** Professor Murray Mitchell,
**Principal Supervisor, Contact and Location:**
Institute of Health and Biomedical Innovation (IHBI),
QLD Centre for Children's Health Research (CCHR),
62 Graham Street, South Brisbane
Email: murray.mitchell@qut.edu.au
**Masters or Honours project:** Masters or Honours

**Background to the project:**
Complications of pregnancy, including preterm birth represent the major causes of fetal and neonatal morbidity and mortality and potentially affect childhood and adult susceptibility to both cardiac and metabolic diseases. Early detection of these disorders is, therefore, essential to improve health outcomes for mother and baby.

**Aims:**
Our goal is to elucidate the molecular mechanisms leading to the development of pregnancy complications, to develop diagnostic tests for the early detection of abnormalities in e.g. fertility, pregnancy and childhood development and potentially targets for therapeutic interventions

**Sub-projects available:**

1. **Evaluation of prostaglandins, prostamides, and endocannabinoids as biomarkers for preterm birth.**
2. **Characterisation of inflammatory pathways associated with preterm birth.**
3. **How do prostaglandins, prostamides, and endocannabinoids induce an inflammatory response in the placenta?**

**Skill and techniques to be developed:**
Mass spectrometry, Tissue and cell culture, DNA/RNA/miRNA analyses, PCR Arrays, ELISA,

**References / key papers:**
Mitchell, MD, Rice GE.,Vaswani, K, Kvaskoff, D. and Peiris, HN. Differential regulation of eicosanoid and endocannabinoid production by inflammatory mediators in human choriodecidua PLOS One published 03 Feb 2016, PLOS ONE 10.1371/journal.pone.0148306,2016
Peiris, HN.,Vaswani,K. Almughlliq, F. Koh, YQ. and Mitchell, MD. Eicosanoids in preterm labor and delivery: potential roles of exosomes in eicosanoid functions Placenta doi: 10.1016/j.placenta.2016.12.013,2017

## **Field of Research**: Reproductive Health; medical biochemistry, lipids and protein chemistry, nanomedicine

**Project Title:** Uses of exosomes as therapeutic delivery systems.

**Research Group:** Child and Reproductive Health Research
**Principal Supervisor:** Professor Murray Mitchell,
**Principal Supervisor, Contact and Location:**
Institute of Health and Biomedical Innovation (IHBI),
QLD Centre for Children's Health Research (CCHR),
62 Graham Street, South Brisbane
Email: murray.mitchell@qut.edu.au
**Masters or Honours project:** Masters or Honours

**Background to the project:**
Exosomes are small (40-120 nm), stable, lipid bilayer nanovesicles identified in biological fluids (e.g. in milk, blood, urine and saliva). They contain a diverse array of signalling molecules, including mRNA, microRNA (miR), proteins, lipids and membrane receptors, and they interact with target cells via multiple pathways. The cargo of circulating exosomes can be indicative of a specific tissue's health status, granting the capacity for use of exosomes as a tool for disease diagnosis. Moreover, they have many of the features desirable of an ideal drug delivery system (e.g. long circulating half-life, the intrinsic ability to target tissues and cross species compatibility). Therefore making them an ideal candidate to be investigated as a vehicle for delivering therapeutics.

We hypothesise that exosomes can be manipulated to carry specific cargo and upon their delivery will alter the function of target cells

**Aims**

1. Exosomal loading methods will be tested and isolated exosomes will be loaded with specific cargo (e.g. miRNA) using
2. Loaded exosomes will be incubated with target cells and functional changes (e.g changes in gene or protein expression) evaluated

**Techniques to be utilised**
Exosome isolation and characterisation, Tissue and cell culture, DNA/RNA/miRNA analyses, PCR Arrays, Mass spectrometry, ELISA,

**References / key papers:**
Mitchell, MD, Peiris,HN., Kobayashi, M., Koh, YQ, Duncombe, G., Illanes, SE, Rice, GE, and Salomon, C. Potential uses of placental exosomes in normal and complicated pregnancy American Journal of Obstetrics and Gynecology http://dx.doi.org/10.1016/j.ajog.2015.07.001. S173, 2015

## **Field of Research**: Reproductive Health; medical biochemistry, lipids and protein chemistry, nanomedicine

**Project Title:** Early diagnosis of pregnancy complications using exosomes

**Research Group:** Child and Reproductive Health Research
**Principal Supervisor:** Professor Murray Mitchell,
**Principal Supervisor, Contact and Location:**
Institute of Health and Biomedical Innovation (IHBI),
QLD Centre for Children's Health Research (CCHR),
62 Graham Street, South Brisbane
Email: murray.mitchell@qut.edu.au
**Masters or Honours project:** Masters or Honours

**Background to the project:**

Complications of pregnancy, including preterm birth represent the major causes of fetal and neonatal morbidity and mortality and potentially affect childhood and adult susceptibility to both cardiac and metabolic diseases. Early detection of these disorders is, therefore, essential to improve health outcomes for mother and baby.

Exosomes are small (40-120 nm), stable, lipid bilayer nanovesicles identified in biological fluids (e.g. in milk, blood, urine and saliva). They contain a diverse array of signalling molecules, including mRNA, microRNA (miR), proteins, lipids and membrane receptors, and they interact with target cells via multiple pathways. We hypothesise that the identification and analysis of exosomal cargo isolated from complicated pregnancies will be indicative of a specific tissue's health status, granting the capacity for use of exosomes as a tool for disease diagnosis.

**Aims:**

Employ a discovery approach to evaluate the cargo of exosomes isolated from plasma of women with complicated pregnancies

**Techniques to be utilised:**

Exosome isolation and characterisation, Tissue and cell culture, DNA/RNA/miRNA analyses, PCR Arrays, Mass spectrometry, ELISA,

**References / key papers:**

Mitchell, MD, Peiris,HN., Kobayashi, M., Koh, YQ, Duncombe, G., Illanes, SE, Rice, GE, and Salomon, C. Potential uses of placental exosomes in normal and complicated pregnancy American Journal of Obstetrics and Gynecology http://dx.doi.org/10.1016/j.ajog.2015.07.001. S173, 2015

## **Field of Research**: Animal Reproduction; cell physiology, nanobiotechnology

**Project Title:** Improving cow fertility: targeting exosome-responsive pathways

**Research Group:** Child and Reproductive Health Research
**Principal Supervisor:** Professor Murray Mitchell,
**Principal Supervisor, Contact and Location:**
Institute of Health and Biomedical Innovation (IHBI),
QLD Centre for Children's Health Research (CCHR),
62 Graham Street, South Brisbane
Email: murray.mitchell@qut.edu.au
**Masters or Honours project:** Masters or Honours

**Background to the project:**

Until recently, genetic selection in dairy cows has focused primarily on milk production traits, with very few countries including functional traits such as fertility in selection indices. Poor reproductive efficiency in dairy herds results in fewer calves, reduced milk production, high involuntary culling rates and increased cow maintenance costs. The need for, and utility of, markers of early onset of diseases (or vulnerability to diseases) which often can lead to early intervention and higher survival rates, has increased dramatically with development of methodologies around biomarker discovery.

Exosomes are small (40-120 nm), stable, lipid bilayer nanovesicles identified in biological fluids (e.g. in milk, blood, urine and saliva). They contain a diverse array of signalling molecules, including mRNA, microRNA (miR), proteins, lipids and membrane receptors, and they interact with target cells via multiple pathways. The cargo of circulating exosomes can be indicative of a specific tissue's health status, granting the capacity for use of exosomes as a tool for disease diagnosis.

**Aims**

1. Evaluate plasma derived exosomal cargo from cows with divergent fertility profiles.
2. Determine the effect of the isolated exosomes incubated with target (e.g changes in gene or protein expression)

**Techniques to be utilised**

Exosome isolation and characterisation, Tissue and cell culture, DNA/RNA/miRNA analyses, PCR Arrays, Mass spectrometry, ELISA,

**References / key papers:**

Mitchell, M.D., Crookenden, M.A., Vaswani, K., Roche J.R., and Peiris, H.N., The frontiers of biomedical science and its application to animal science in addressing the major challenges facing Australasian dairy farming. Animal Production Science https;/doi.org/10.1071/AM18579
Almughlliq FB, Koh YQ, Peiris HN, Vaswani K, McDougall S, Graham EM, Burke CR, Mitchell MD. Effect of exosomes from plasma of dairy cows with or without an infected uterus on prostaglandin production by endometrial cell lines. Journal of Dairy Science. 2017;100(11):9143-52. doi: 10.3168/jds.2017-13261.

## **Field of Research**: Vision and Neuroscience

**Research Group:** Medical Retina Laboratory
**Principal Supervisor:** A/Prof Beatrix Feigl, MD, PhD
**Principal Supervisor Contact and Location:**
Email: b.feigl@qut.edu.au, phone: 3138 6147
Location: Institute of Biomedical Innovation (IHBI), 60 Musk Avenue, Kelvin Grove
**Masters or Honours project:** Masters projects

**Background to the projects:**
The Medical Retina Laboratory has two research streams:

1. Basic science investigations relevant to understanding the fundamental mechanisms controlling retinal function.
2. Clinical science studies of the pathomechanisms of retinal eye disease, and the development of new approaches for the early detection of eye and neurodegenerative disease.

**Aims/Projects:**

- Understanding visual processing in the normal eye and how it is affected by healthy ageing and age-related macular degeneration, glaucoma and diabetes
- Understanding how eye and neurodegenerative diseases (i.e. Parkinson's disease) affect circadian rhythms (i.e. sleep/wake)
- Gut-retina axis in eye disease
- Photophobia in migraine

**Skill and techniques to be developed:**
We use custom developed electroretinographic, psychophysical and pupillometric techniques to understand visual processing in the retina. Students will be working with our multidisciplinary collaborators including Ophthalmologists, Optometrists, Geneticists, Physiologists, Molecular Biologists, Psychologists and Chronobiologists.

**References / key papers:**

1. Adhikari P, Zele AJ, Cao D, Kremers J, **Feigl B** (2019). The melanopsin-directed white noise electroretinogram (wnERG). *Vision Research*;doi.or/10.1016/j.vosres.2019.08.007
2. Zele AJ, Adhikari P, Cao D, **Feigl B** (2019). Melanopsin driven enhancement of cone-mediated visual processing. *Vision Research*; 160:72-81
3. Dumpala S, Zele AJ, **Feigl B** (2019). Outer retinal structure and function deficits contribute to circadian disruption in patients with Type II diabetes. *Invest Ophthalmol Vis* Sci; 60: 1870–8.
4. Joyce DS, **Feigl B**, Kerr G, Roeder L, Zele AJ (2018). Melanopsin-mediated pupil function is impaired in Parkinson's disease. *Scientific Reports*; 8:7796
5. Maynard ML, Zele AJ, Kwan A, **Feigl B** (2017). Intrinsically photosensitive retinal ganglion cell function, sleep efficiency and depression in advanced age-related macular degeneration. *Invest Ophthalmol Vis Sci;* 58:990-6.
6. Shokoohmand A, Jeon JE, Theodoropoulos C, Baldwin JG, Hutmacher DW, **Feigl B** (2017). A novel three dimensional cultured model for studying early changes in age-related macular degeneration. *Macromolecular Bioscience*, doi: 10.1002/mabi.201700221.
7. Adhikari P, Zele AJ, Thomas, R. **Feigl B** (2016). Quadrant field pupillometry detects melanopsin dysfunction in glaucoma suspects and early glaucoma. *Scientific Reports*; 6:33373.
8. Maynard ML, Zele AJ, **Feigl B** (2015). Melanopsin mediated post-illumination pupil response in early age-related macular degeneration. *Invest Ophthalmol Vis Sci*; 56:6906-13.
9. Adhikari P, Zele AJ, **Feigl B** (2015). The post-illumination light response (PIPR). *Invest Ophthalmol Vis Sci*; 56:3838-3849. Doi:101167/iovs.14-16233.
10. **Feigl B**, Mattes D, Thomas R, Zele A (2011). Intrinsically photosensitive (melanopsin) retinal ganglion cell function in glaucoma. *Invest Ophthalmol Vis Sci*; 52:4362-7.
11. **Feigl B** (2009). Age-related maculopathy-linking aetiology and pathophysiological changes to the ischaemia hypothesis. *Progress in Retinal and Eye Research;* 28:63-86.

## Honours (HL53) Project Preference Form

| | |
|---|---|
| **Student Name:** | |
| **Student Number** (QUT Students only): | |

| **Preference 1** | |
|---|---|
| Principal Supervisor Name:<br><br>Co-supervisor Name: | |
| Project Title or Area: | |
| Acceptance by Principal Supervisor (signature): | |

| **Preference 2** | |
|---|---|
| Supervisor Name:<br><br>Co-supervisor Name: | |
| Project Title or Area: (including discipline area) | |
| Acceptance by Principal Supervisor (signature): | |

NB: A copy of the completed and signed project preference form is to be submitted with your PG Application Form