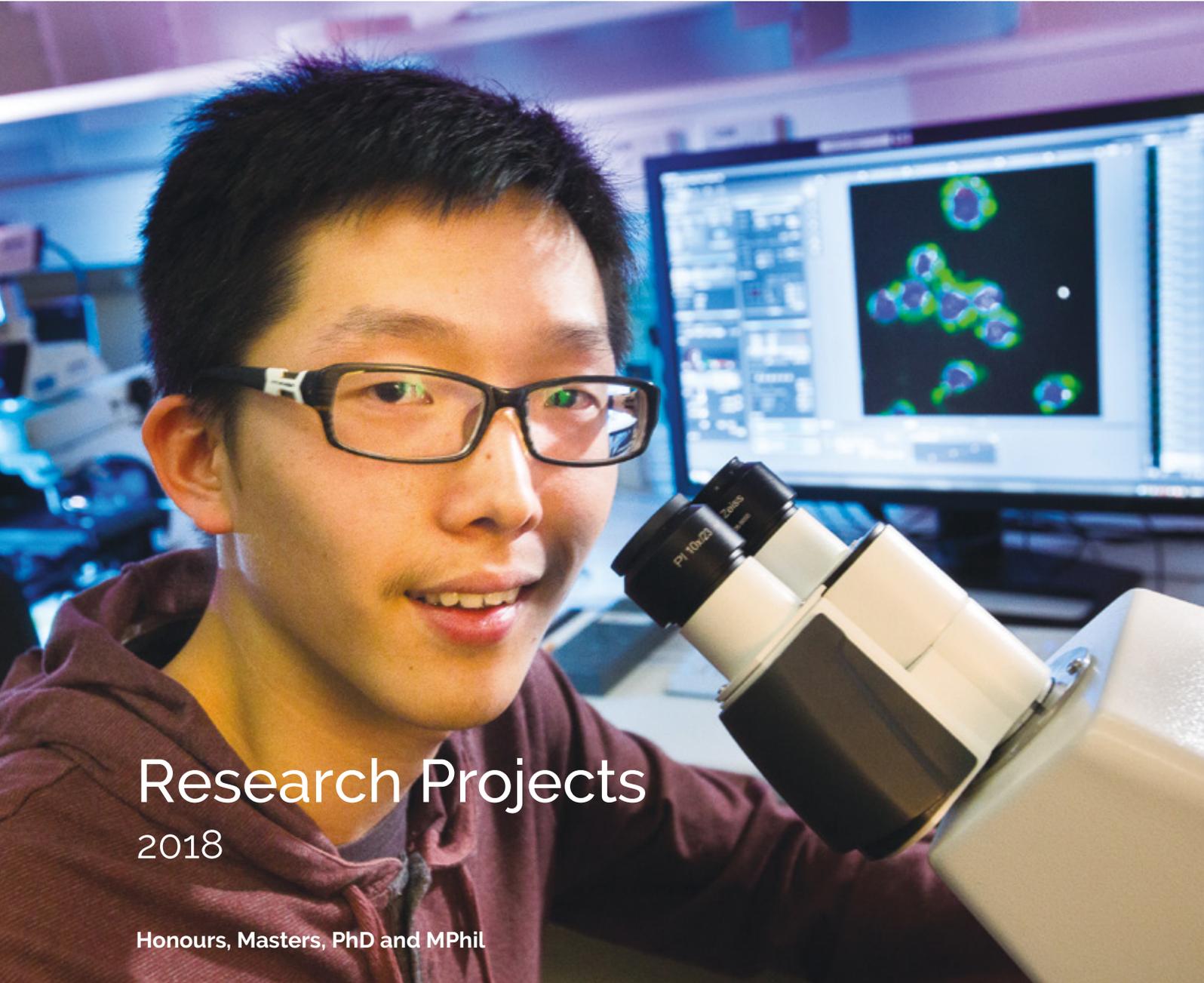




Doherty  
Institute



# Research Projects 2018

Honours, Masters, PhD and MPhil



THE UNIVERSITY OF  
MELBOURNE



The Royal  
Melbourne  
Hospital

A joint venture between The University of Melbourne and The Royal Melbourne Hospital

# About the Doherty Institute

Finding solutions to prevent, treat and cure infectious diseases and understanding the complexities of microbes and the immune system requires innovative approaches and concentrated effort.

This is why The University of Melbourne – a world leader in education, teaching and research excellence – and The Royal Melbourne Hospital – an internationally renowned institution providing outstanding care, research and learning – have partnered to create the Peter Doherty Institute for Infection and Immunity, a centre of excellence where leading scientists and clinicians collaborate to improve human health globally.

Located in the heart of Melbourne's Biomedical Precinct, the Doherty Institute is named in honour of Laureate Professor Peter Doherty, winner of the 1996 Nobel Prize for discovering how the immune system recognises virus-infected cells. Under the expert guidance of Director, University of Melbourne Professor Sharon Lewin, a world leader in research and clinical management of HIV and infectious diseases, the Doherty Institute employs more than 700 staff who conduct a broad spectrum of activities – from discovery research; to the diagnosis, surveillance and investigation of disease outbreaks; and the development of ways to prevent, treat and eliminate infections.

The Institute is home to over 100 Honours, Masters and PhD students obtaining high-level training in microbiology, immunology, epidemiology and clinical infectious diseases research.

## The Doherty Institute vision

To improve health globally through discovery research and the prevention, treatment and cure of infectious diseases.

## The Doherty Institute mission

The Doherty Institute will be an inspiring, innovative and enabling environment. We are dedicated to identifying and addressing fundamental challenges in all aspects of infection and immunity. Through our leadership, advocacy and education we will shape policy, practice and research both nationally and internationally.

## The Doherty Institute values

**Discover:** we break new ground and innovate

**Deliver:** we work to improve health practice and outcomes

**Inspire:** we develop the highest calibre people to achieve excellence

**Connect:** we engage locally and globally with our partners, stakeholders, colleagues and community



The Doherty Institute specialises in the following themes and cross-cutting disciplines:

## Themes

- Immunology
- Viral infectious diseases
- Antimicrobial resistance and healthcare associated infections
- Host-pathogen interactions

## Disciplines

- Public health
- Epidemiology
- Translational and clinical research
- International health
- Education and professional development
- Indigenous health
- Genomics
- Discovery research

The Doherty Institute is home to the following units:

### The University of Melbourne

- Department of Microbiology and Immunology, including the Microbiological Diagnostic Unit Public Health Laboratory
- Department of Medicine

### The Royal Melbourne Hospital

- Victorian Infectious Diseases Reference Laboratory (VIDRL)
- Victorian Infectious Diseases Service (VIDS)
- WHO Collaborating Centre for Reference and Research on Influenza
- VICNISS – the Victorian Healthcare Associated Infection Surveillance System

# About the Department of Microbiology and Immunology

The University of Melbourne's Department of Microbiology and Immunology is a research and research-led teaching department of the School of Biomedical Sciences in the Faculty of Medicine, Dentistry and Health Sciences located at the Doherty Institute. The Department delivers specialised courses in bacteriology, virology and immunology along with more generalist infection and immunity subjects.

The Department comprises more than 270 staff including 21 Professors/Associate Professors and around 30 research groups that are actively involved in microbiology and immunology research and teaching. It has close interactions with clinical and public health researchers, who are involved in translating basic science into direct patient care and policy outcomes.



# Study at the Doherty Institute

Through the Department of Microbiology and Immunology, the Doherty Institute offers undergraduate (Honours) and graduate (Masters, PhD, MPhil) courses. Students will generally be based at the Doherty Institute, however, in certain cases students may be based at affiliated institutes with a co-supervisor at the Doherty Institute, including (but not limited to) the Burnet Institute, the Peter MacCallum Cancer Centre, the Murdoch Children's Research Institute and St Vincent's Institute.

Note: Students wishing to study at the Doherty Institute and enrol in undergraduate or graduate research degrees through other University of Melbourne departments will need to seek further information on the application process directly from the departments and/or by contacting Rebecca Whitsed: [rwhitsed@unimelb.edu.au](mailto:rwhitsed@unimelb.edu.au)

## Honours program

Honours is a fourth-year undergraduate course that involves coursework worth 25 subject points and an intensive research project worth 75 subject points. Bachelor of Biomedicine (B.Biomed) and Bachelor of Science (B.Sc.) students who obtain faculty honours in their third year will be welcome to join the Department of Microbiology and Immunology as B.Biomed/BSc (Honours) candidates provided a supervisor is available.

The course, which runs from late February until mid-November, is designed to develop the research student's capacity to solve problems, to analyse data, to read and think critically, and to communicate clearly. A research project is undertaken in close collaboration with a supervisor. In addition, the coursework component will involve 30 hours of contact for the study of advanced microbiology and immunology.

## Masters program

The Master of Biomedical Science is a two-year graduate degree with a major in a relevant discipline and a weighted average mark of at least H3 (65%), or equivalent. This program is an alternative to the Honours to PhD pathway involving 75 subject points and a 125-point research project.

## PhD/MPhil program

Postgraduate training through the Department of Microbiology and Immunology allows students to develop advanced skills in carrying out independent research on a particular topic under academic supervision. PhD program students also get exposed to unique training opportunities beyond their immediate research topic, including a diverse range of workshops, seminars, and internships.

## Choosing a supervisor and research area

A critical element of success during your studies is choosing a research area that interests you. The Institute website and this brochure have information on the range of research areas on offer, as well as areas of interest of academic staff members who can supervise your project.

It is very important for you to talk to supervisors and current/previous research students. It is one thing to be interested in the project but you need to get along with your supervisor too. If possible, familiarise yourself with the environment and your chosen laboratory group.



# How to apply

## Honours

1. For more detailed information, visit the Faculty of Medicine, Dentistry and Health Sciences Honours webpage: <http://mdhs-study.unimelb.edu.au/degrees/honours/overview>
2. Visit the Department of Microbiology and Immunology webpage for further information: <http://go.unimelb.edu.au/pgx6>
3. Review the list of prospective projects and supervisors in this handbook.
4. Identify projects of interest and contact the project supervisor to explain your research interests and provide your curriculum vitae (CV) and academic transcripts. In some cases, supervisors may be willing to offer you a provisional place in their laboratory (a provisional offer indicates that you have a place in the Honours course providing you satisfy all the entry requirements).
5. Lodge an online application to The University of Melbourne for admission to Honours at <http://go.unimelb.edu.au/ww6a>
6. Once you have submitted an online course application, you will receive an email with login details to access the Honours project preference system - SONIA. Follow the instruction in the email to set up your own password and select your preferences for projects offered within MDHS departments. You may select up to ten project preferences. You must only preference projects after making contact with the relevant supervisor(s).

## PhD, MPhil or Master of Biomedical Sciences

1. Review the list of prospective projects and supervisors in this handbook.
2. Identify projects of interest and contact the project supervisor to explain your research interests and provide your curriculum vitae (CV) and academic transcripts.
3. Apply online at: <http://futurestudents.unimelb.edu.au/admissions/applications/research> or for Master of Biomedical Science via: <https://futurestudents.unimelb.edu.au/admissions/applications/grad-dom>
4. For PhD visit: <http://mdhs-study.unimelb.edu.au/degrees/doctor-of-philosophy/overview>
5. For MPhil visit: <http://mdhs-study.unimelb.edu.au/degrees/master-of-philosophy/overview>
6. Apply for a scholarship from The University of Melbourne: <http://futurestudents.unimelb.edu.au/admissions/scholarships>

## Scholarships

Honours applicants who accept and enrol in an honours course will automatically be considered for available Honours scholarships. These are awarded on academic merit.

Students with a high average in their third year marks will be awarded a Department of Microbiology and Immunology Honours scholarship of \$5000.

### Frances Elizabeth Thomson Trust Scholarship

The scholarship is offered to highly-ranked full-time students who have enrolled in an MDHS program through the Bachelor of Biomedicine (Degree with Honours) and the Bachelor of Science (Degree with Honours) and demonstrated a level of financial needs. The scholarship will award eligible students with a one-off payment of \$5000.

### Doherty Institute Host-Pathogen Interactions Honours Award

The Doherty Institute Host-Pathogen Interactions theme is offering a \$2000 award to one honours student in 2018.

## Department of Microbiology and Immunology contacts:

### Honours coordinators

Associate Professor Scott Mueller  
Ph: (03) 8344 9044  
Email: smue@unimelb.edu.au

Professor Damian Purcell  
Ph: (03) 8344 6753  
Email: dfjp@unimelb.edu.au

Professor Katherine Kedzierska  
Ph: (03) 8344 3384  
Email: kkedz@unimelb.edu.au

### Postgraduate coordinators

Ms Rebecca Whitsed (Academic Programs Officer)  
Ph: (03) 8344 5679  
Email: rwhitsed@unimelb.edu.au

Dr Marie Greyer (PhD Programs Officer)  
Ph: (03) 8344 40875  
Email: doherty-phdprogram@unimelb.edu.au



# Bedoui group

**Contact:** Associate Professor Sammy Bedoui  
**Email:** sbedoui@unimelb.edu.au

Number of vacancies available: 1



Immunology



Host-pathogen Interactions



Associate Professor Sammy Bedoui's research has defined how particular types of T cells protect the host from bacterial infections, uncovering that these responses are regulated through the stimulation of protein complexes within dendritic cells; the so-called inflammasomes. His work on virus infections has identified how different dendritic cell types contribute to the initiation of virus-specific immunity and has delineated how specific viral fragments augment these responses. Ongoing work interrogates the mechanisms by which T cells 'help' dendritic cells in driving immune responses. Overall, A/Prof Bedoui's work has shed new light onto understanding how dendritic cells integrate multiple signals into protective immunity against infections.

## Project: Interaction between microbiota and CD8+ T cell immunity

Autoimmune disease development has been linked to disturbances in the microbes that normally colonise our body surfaces (microbiota). Precisely how these microorganisms and the resulting stimulation of the immune system impact on T cells remains elusive. Building on exciting new findings in the lab, this project will investigate how the microbiota influences particular cytokine responses linked to our understanding of T cell-mediated autoimmune disease, such as type-1 diabetes. Conceptually, this work will provide novel insights into innate regulation of adaptive immune responses. This project would suit a student interested in working at the intersection of Immunology and Microbiology.

### Project supervisor

Associate Professor Sammy Bedoui

### Project availability

- PhD
- MSc
- Honours

### Further information

<http://go.unimelb.edu.au/kge6>

# Brooks group

**Contact:** Professor Andrew Brooks  
**Email:** agbrooks@unimelb.edu.au

Number of vacancies available: 1



Immunology



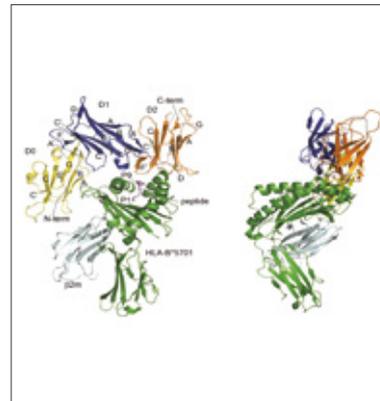
Viral Infectious Diseases



Host-pathogen Interactions



The Brooks lab has a broad array of interests, largely centered on the role of immunoreceptors in the regulation of lymphocyte activation. In particular, we are interested in how natural killer cell receptors regulate NK cell and T cell activation and how genetic variation in these receptors along with their HLA-encoded ligands impacts on clinical outcomes in the settings of infection and transplantation.



Interactions between the NK receptor KIR3DL1 and its high-affinity ligand HLA-B57 are associated with improved control of HIV infection.

## Project: Understanding how NK cell receptors regulate target cell recognition.

Unlike T cells and B cells, natural killer (NK) cell activation is regulated by the balance of signals received by numerous activating and inhibitory receptors. The expression of the ligands for these receptors varies with the nature of infection and/or across tumour cell types. Additionally, genetic variation in these ligands further modulates their capacity to regulate NK cell activation. This project will assess the contribution of distinct receptor/ligand interactions to target cell recognition and the nature of the subsequent NK cell response.

### Project supervisor

Professor Andrew Brooks

### Project availability

- PhD
- MSc



# Brown group

**Contact:** Professor Lorena Brown  
**Email:** lorena@unimelb.edu.au

Number of vacancies available: 1-2



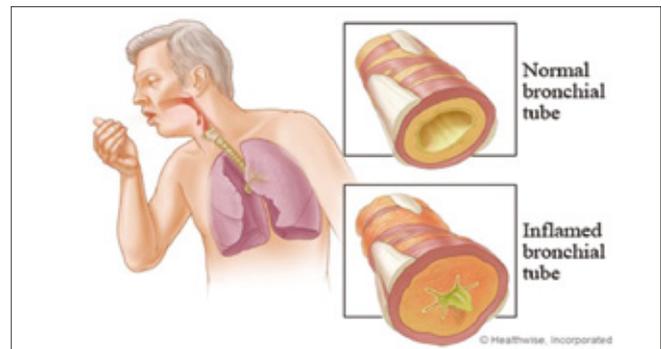
Immunology



Host-pathogen Interactions



The Brown Lab has a long history of research into influenza virus and is committed to understanding and controlling influenza infections. The breadth of our work encompasses determining the intricacies of viral replication, understanding how novel viral gene constellations arise and the impact of these, elucidating the major virulence factors of the virus that result in lethal infection, understanding B and T cell immunity to the virus and designing and evaluating new vaccines and antivirals.



During influenza, hyperinflammation restricts breathing and patients may experience Acute Respiratory Distress Syndrome.

## Project: Discovering the mechanistic basis of hyperinflammatory disease due to influenza infection

Our discovery of influenza PB1-F2 as a trigger of the NLRP3-inflammasome has led us to explore the impact of PB1-F2 sequence on the capacity to induce severe inflammatory disease. We have shown that triggering the inflammasome depends on the ability of PB1-F2 to form aggregates, which in turn depends on critical residues within the C-terminal end of the protein. The student will create viruses with mutations in the proposed “inflammatory residues” of PB1-F2 and test their ability to activate the inflammasome and cause severe disease in mice. The information will be used in surveillance of viruses in the avian reservoir.

### Project supervisor

Professor Lorena Brown

### Project co-supervisor

Dr Julie McAuley

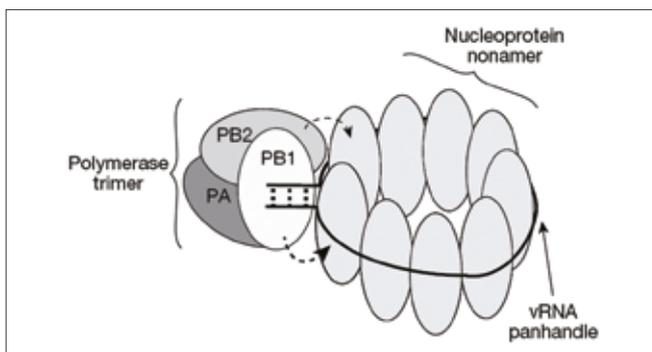
### Project availability:

- Honours

### Further information

<http://go.unimelb.edu.au/3ge6>

<http://go.unimelb.edu.au/qge6>



PB1 and NP work together

**Project: Understanding the critical interactions between influenza RNA polymerase and nucleoprotein that determine replicative fitness.**

We previously created influenza viruses that have the HA, NA and polymerase (PB1) genes from one strain (Udorn) and the remaining five genes from a different strain (PR8). The virus replicates very poorly and we have shown that this is due to incompatibility between Udorn PB1 and PR8 nucleoprotein (NP). In this project the student will use reverse genetics to create viruses that encode the Udorn PB1 together with chimeric NPs made up of sections derived from Udorn and PR8. The replicative capacity of these viruses will pinpoint the region of the NP interacting with PB1 for optimal polymerase function.

**Project supervisor**

Professor Lorena Brown

**Project co-supervisor**

Dr Brad Gilbertson

**Project availability:**

- Honours

# Davies group

**Contact:** Dr Mark Davies  
**Email:** mark.davies1@unimelb.edu.au

Number of vacancies available: 3



Antimicrobial Resistance and Healthcare Associated Infections



Host-pathogen Interactions



Public Health



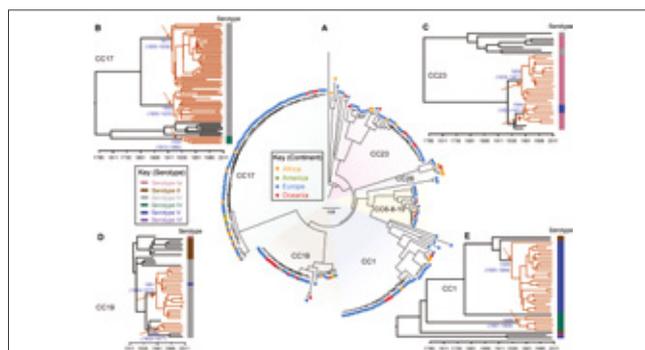
Epidemiology



Indigenous Health



Genomics



Population structure of Group B Streptococcus is driven by the acquisition of tetracycline resistance

The Davies Lab applies genome sequencing methodologies and bioinformatic approaches to understanding the evolution and transmission of bacterial pathogens. This knowledge can help facilitate a global understanding of pathogen evolution in addition to informing public health intervention to reduce the disease burden associated with bacterial pathogens. Current projects address key questions such as, "Is there a genetic difference between strains causing different disease manifestations?", "What is driving the emergence and dissemination of bacterial pathogens?", and "How do host immune factors govern disease severity?". Our research closely aligns with key International collaborators, including the Wellcome Trust Sanger Institute, UK.

## Project: Population genomics of endemic Streptococcus pyogenes

*Streptococcus pyogenes* is one of the leading infectious disease agents in the world. The disease burden is alarmingly high within the Top End of Australia, where the epidemiology of infection contrasts with other geographical regions. Through linking genomics with epidemiology, we aim to examine the evolutionary relationship between disease causing *S. pyogenes* clones within remote communities of Australia. Furthermore, we will apply statistical genetic models to identify genetic signatures associated with different disease stats and tissue tropism. Unlocking these mysteries is key to informing public health intervention strategies, including the development of informed vaccine programs within disease-endemic regions.

### Project supervisor

Dr Mark Davies

### Project co-supervisor

Associate Professor Steven Tong

### Project availability

- PhD
- MSc
- Honours

### **Project: Application of systems informatics to analysing the dynamics of *Streptococcus pyogenes* infection**

The relationship between, and integration of, genomics, transcriptomics, proteomics and metabolomics lies at the heart of understanding how organisms, including bacteria, respond to environmental changes, and especially stress, be it physical, immunological or nutritional. This is generically termed systems biology. This project will examine the systems biology of *Streptococcus pyogenes* subject to a major and important stress, transition from the ex-vivo environment to blood. The research will use various aspects of molecular biology and especially bioinformatics to address the key research questions. Avenues are available to expand this research into systems biology approaches within a controlled human challenge study.

#### **Project supervisor**

Dr Mark Davies

#### **Project co-supervisor**

Professor Dick Strugnell

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: Worldwide molecular analysis of *Streptococcus pyogenes* scarlet fever outbreaks**

Outbreaks of scarlet fever associated with multi-drug resistant Group A Streptococci have occurred recently in both Asia and the United Kingdom, placing a serious strain on health systems. We recently examined the genomic basis behind the scarlet fever outbreak in Hong Kong. This project expands on these findings to examine the emergence and transmission of GAS clones and associated mobile genetic elements within a global context. Specifically, we will examine the population structure of scarlet fever associated lineages, apply statistical genetic models to identify common disease signatures and examine the movement of mobile genetic elements to this alarming health problem.

#### **Project supervisor**

Dr Mark Davies

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: Typhoid in the Pacific**

Typhoid fever is caused by *Salmonella* Typhi, one of many bacteria now showing increased antimicrobial resistance (AMR). Alarmingly, the incidence of typhoid is very high in many Pacific Island states. To determine what impact AMR *S. Typhi* might have on the Pacific Island states, a genomic study of *S. Typhi* isolates from the Pacific is being conducted. This study uses historical and more recent isolates to track the movement of the bacterium around the region, and to study potential introductions. Techniques involved include bioinformatics related to genomics, micro-epidemiology using rich metadata, and detailed mapping of drug resistance loci.

#### **Project supervisor**

Dr Mark Davies

#### **Project co-supervisor**

Professor Dick Strugnell

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: Evolution of streptococcal pathogens**

*Streptococcus dysgalactiae* subspecies *equisimilis* is a human pathogen, mirroring the disease profile and colonising the same ecological niche as the well-documented human pathogen, *Streptococcus pyogenes*. The overlap in both pathogen lifestyle and disease repertoire along with evidence of gene transfer between these pathogens suggests that they may share common genetic mechanisms for causing disease. The primary aim of this project is to apply various bioinformatics approaches within global genome databases to identify candidate genes that drive streptococcal invasive disease and other pathogenic processes. This will also inform vaccine approaches to combat streptococcal disease.

#### **Project supervisor**

Dr Mark Davies

#### **Project co-supervisor**

Associate Professor Steven Tong

#### **Project availability**

- PhD
- MSc
- Honours



# Fazakerley group

**Contact:** Lukasz Kedzierski  
**Email:** lukasz@unimelb.edu.au

Number of vacancies available: 2



Immunology



Viral Infectious Diseases



Host-pathogen Interactions



The Fazakerley lab main interest is in the pathogenesis of infections with RNA viruses, in particular arboviruses and virus infections of the central nervous system. Our main focus is to understand arbovirus encephalitis and arbovirus persistence in mammalian systems and the response to these viruses of arthropod cells and mosquitoes.

## Project: SOCS proteins as controllers of persistent viral infection

The suppressor of cytokine signalling (SOCS) proteins are key negative regulators of the JAK/STAT pathway and are involved in fine-tuning the cytokine networks responsible for an efficient innate and adaptive immune response. SOCS are expressed by the CNS and by the cells infiltrating the CNS. Hence, SOCS have the potential to impact immune responses, and while limiting inflammatory responses in the brain, may enhance the ability of neuroinvasive viruses to cause a persistent infection. This project aims to explore a possible role for SOCS4 and 5 during Semliki Forest virus-induced encephalitis in a mouse model.

### Project supervisor

Professor John Fazakerley

### Project co-supervisor

Lukasz Kedzierski

### Project availability

- Honours

## Project: Vertical transmission of Alphaviruses in mosquito vectors

Chikungunya virus is an *alphavirus* currently experiencing severe outbreaks in the Americas and South East Asia, with over five million suspected and confirmed cases. *Alphaviruses* such as Chikungunya and Semliki forest virus are transmitted by mosquito vectors between susceptible vertebrate hosts. Recently it has been suggested that vertical transmission of alphaviruses might play a role in maintaining the virus circulating in the mosquito population.

Using recombinant alphaviruses expressing fluorescent proteins, we will investigate the role of vertical transmission in mosquito infection as well as the implications of having two alphavirus co-infecting the same mosquito.

### Project supervisor

Professor John Fazakerley

### Project co-supervisor

Dr Julio Rodriguez

### Project availability

- Honours

# Godfrey group

**Contact:** Professor Dale Godfrey  
**Email:** godfrey@unimelb.edu.au

Number of vacancies available: 4



Immunology



Translational and Clinical Research



The Godfrey Lab has a strong track record in the field of unconventional T cells with a focus on CD1 restricted (NKT cells); MR1-restricted T cells (MAIT cells) and gamma delta T cells (1). The ultimate aim of this research is to understand the mechanisms with which these unconventional T cell populations specifically contribute to the immune response and how they can be harnessed for immunotherapy.

## Further information

1. Godfrey, D. I., A. P. Uldrich, J. McCluskey, J. Rossjohn, and D. B. Moody. 2015. The burgeoning family of unconventional T cells. *Nat Immunol* 16: 1114-1123.
2. Gorini et al. 2017. Invariant NKT cells contribute to chronic lymphocytic leukemia surveillance and prognosis. *Blood e-pub ahead of print*. doi.org/10.1182

## Project: The therapeutic potential of unconventional T cells in Chronic Lymphocytic Leukemia (CLL)

CLL is one of the most common types of leukemia in adults, but the role that different immune cells play in combating this cancer is unclear. A recent study suggested a key role for CD1d-restricted NKT cells in controlling growth and survival of human CLL cells (2), but the study was limited in scope and mechanistic understanding.

Using an extensive tissue bank of blood samples from CLL patients from various stages of disease, this project will examine the status of unconventional T cells and the potential for unconventional T cells to target and kill CLL cells in vitro.

## Project supervisor

Dr Adam Uldrich

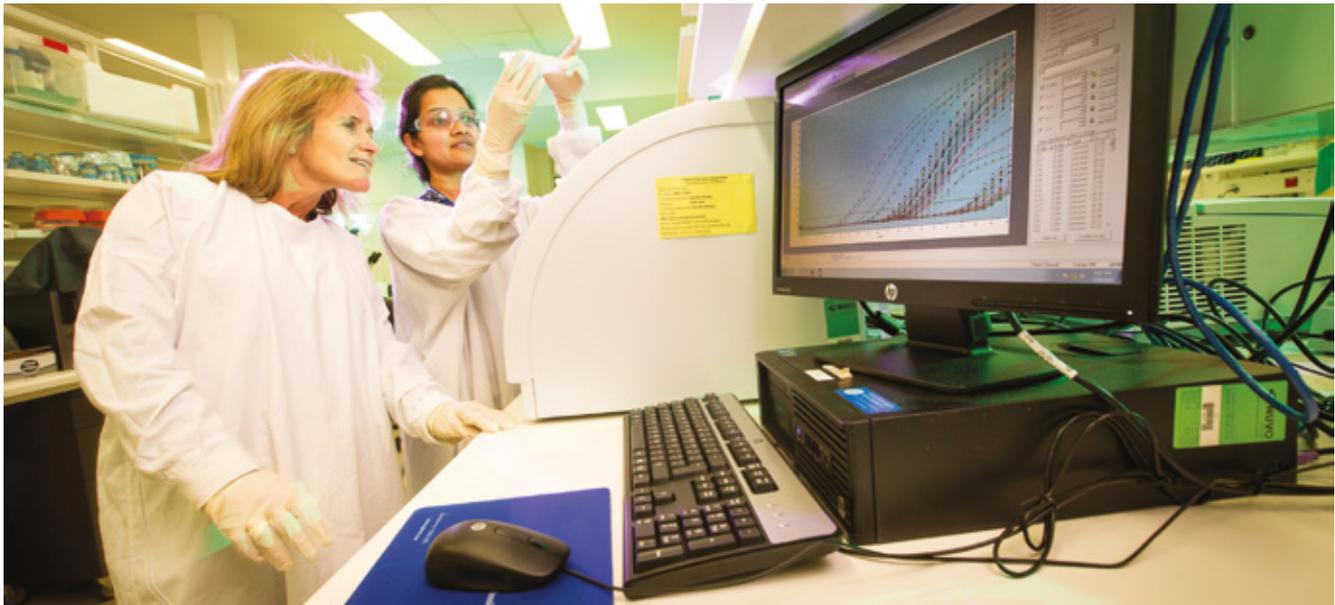
## Project co-supervisors

Nick Gherardin, David Ritchie, Professor Dale Godfrey

## Project availability as follows

- PhD
- MSc
- Honours





### **Project: Development and function of atypical MR1-restricted T cells.**

We recently determined that some T cells can recognise the antigen-presenting molecule MR1 with a TCR usage and transcription factor expression profile not typically associated with the classical MR1-restricted MAIT cell population (2). These data suggest the existence of new types of MR1-restricted human T cells and highlight the fact that we are still discovering new types of human immune cells which are likely to play unique roles in immunity and immunotherapy. This project will explore the developmental origins, antigen-reactivity and functional potential of these unconventional MR1-restricted T cells.

#### **Project supervisor**

Garth Cameron

#### **Project co-supervisor**

Dr Hui-Fern Koay, Professor Dale Godfrey

#### **Project availability**

- PhD
- MSc
- Honours

#### **Further information**

1. Godfrey, D. I., A. P. Uldrich, J. McCluskey, J. Rossjohn, and D. B. Moody. 2015. The burgeoning family of unconventional T cells. *Nat Immunol* 16: 1114-1123.
2. Gherardin, N. A., A. N. Keller, et al. D. P. Fairlie, A. P. Uldrich, D. G. Pellicci, J. McCluskey, D. I. Godfrey, and J. Rossjohn. 2016. Diversity of T Cells Restricted by the MHC Class I-Related Molecule MR1 Facilitates Differential Antigen Recognition. *Immunity* 44: 32-45.

### **Project: Development of Mucosal-Associated Invariant T (MAIT) cells**

MAIT cells play an important role in host immunity and represent the largest population of T cells with a single specificity within the human body. Yet MAIT cell numbers vary widely between individuals. Thus it is vital we understand the factors that regulate their development and function. We recently mapped out the development pathway for MAIT cells, identifying new populations of thymic MAIT cells in humans and mice (1). This project will use RNA-seq in combination with flow cytometry and real time PCR to decipher the factors that are critical for the development and function of MAIT cells.

#### **Project supervisor**

Professor Dale Godfrey

#### **Project co-supervisor**

Dr Hui-Fern Koay, Dr Daniel Pellicci

#### **Project availability**

- PhD
- MSc
- Honours

#### **Further information**

1. Godfrey, D. I., A. P. Uldrich, J. McCluskey, J. Rossjohn, and D. B. Moody. 2015. The burgeoning family of unconventional T cells. *Nat Immunol* 16: 1114-1123.
2. A three-stage intrathymic development pathway for the mucosal-associated invariant T cell lineage. Koay HF, Gherardin NA, Enders A, Loh L, Mackay LK, Almeida CF, et al. Fairlie DP, Rossjohn J, Chong MM, Kedzierska K, Berzins SP, Belz GT, McCluskey J, Uldrich AP, Godfrey DI, Pellicci DG. *Nat Immunol.* 2016 Nov;17(11):1300-1311.

## **Project: Identification and characterisation of type-2 NKT cells using CD1d tetramers**

NKT cells play a role in cancer, autoimmunity, infection, allograft rejection and graft versus host disease. Most studies have focused on Type-1 NKT cells that express a semi-invariant T cell receptor (TCR) and recognise the prototypic antigen  $\alpha$ -GalCer, whereas much less is known about Type-2 NKT cells, which express diverse TCRs and have different antigen specificities. This project utilises novel CD1d tetramers that we have developed to identify and characterise Type-2 NKT cells in humans and mice. These studies will lay the foundation for understanding the role of Type-2 NKT cells in human immunity.

### **Project supervisor**

Dr Daniel Pellicci

### **Project co-supervisor**

Catarina Almeida, Professor Dale Godfrey

### **Project availability**

- PhD
- MSc
- Honours



# Heath group

**Contact:** Lynette Beattie  
**Email:** lynette.beattie@unimelb.edu.au

Number of vacancies available: 1



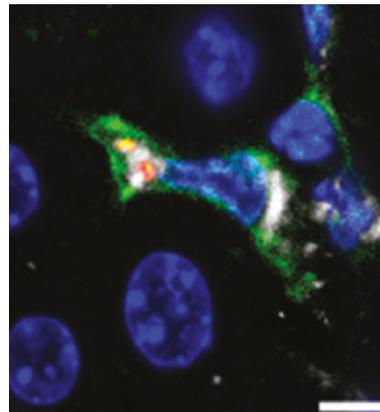
Immunology



Host-pathogen Interactions



Lynette Beattie is a senior research officer within Professor William Heath's laboratory, where she focuses on understanding the immune responses that are generated in the liver in response to infection with leishmania or malaria parasites. Lynette is particularly interested in host-pathogen interactions with a focus on observing the dynamic interactions that occur, via a technique known as 2-photon intravital imaging. We utilise this technique to study the development and mode of action of immune cells in the control of parasites, in order to better inform vaccine development programs.



## **Project: Determining the role of CD8 resident memory T cells in the control of Leishmania infection**

CD8 memory T cells that are resident in peripheral organs (Trm) have been shown to play a clear role in host protection from a number of pathogens. The Heath Lab has designed an experimental vaccine regimen that generates robust, antigen-specific CD8 Trm in the liver that are capable of protecting against an experimental plasmodium infection in vivo. This project will determine if this regimen also induces Trm capable of protecting against Leishmania infection. The characterisation of the Trm and the investigation into their mechanism of action will give novel insights into the control of Leishmania in vivo.

### **Project supervisor**

Lynette Beattie

### **Project availability**

- PhD
- MSc
- Honours

# Howden group

**Contact:** Benjamin Howden  
**Email:** bhowden@unimelb.edu.au

Number of vacancies available: 3



Antimicrobial Resistance and Healthcare Associated Infections



Host-pathogen Interactions



Public Health



Epidemiology



Genomics



The Howden Lab is an established research group, embedded in a State Public Health Laboratory, with expertise in pathogen genomics and antimicrobial resistance, including functional genomics technologies and models of disease. We complement these molecular biology studies with epidemiological and clinical studies to address a broad range of issues related to invasive bacterial diseases in humans, especially those caused by staphylococci, enterococci and other antimicrobial-resistant species (CPE). Working closely with scientists in the MDU PHL, we investigate the epidemiology, evolution, and spread of bacterial pathogens of public health significance such as *Neisseria gonorrhoea*, *Listeria monocytogenes*, *Legionella* spp., and *Salmonella* spp..

## Project: The gut microbiota in health and nutrition

The first two to three years of life represent a crucial period for establishing a healthy gut microbial community, which plays an important role in nutritional and child growth outcomes, including cognitive function and social behaviours. This study will utilise high-throughput sequencing, metagenomic analyses, and epidemiology (including correlations with early-life determinants and child health outcomes) to interrogate two large study cohorts. The study cohorts include children from Arnhem Land (NT, Australia), and Ha Nam province (Vietnam). The expected outcomes from this study include developing cross-disciplinary skills in laboratory-based and bioinformatic techniques in public health and epidemiology.

### Project supervisor

Dr Sarah Hanieh, Dr Andre Mu

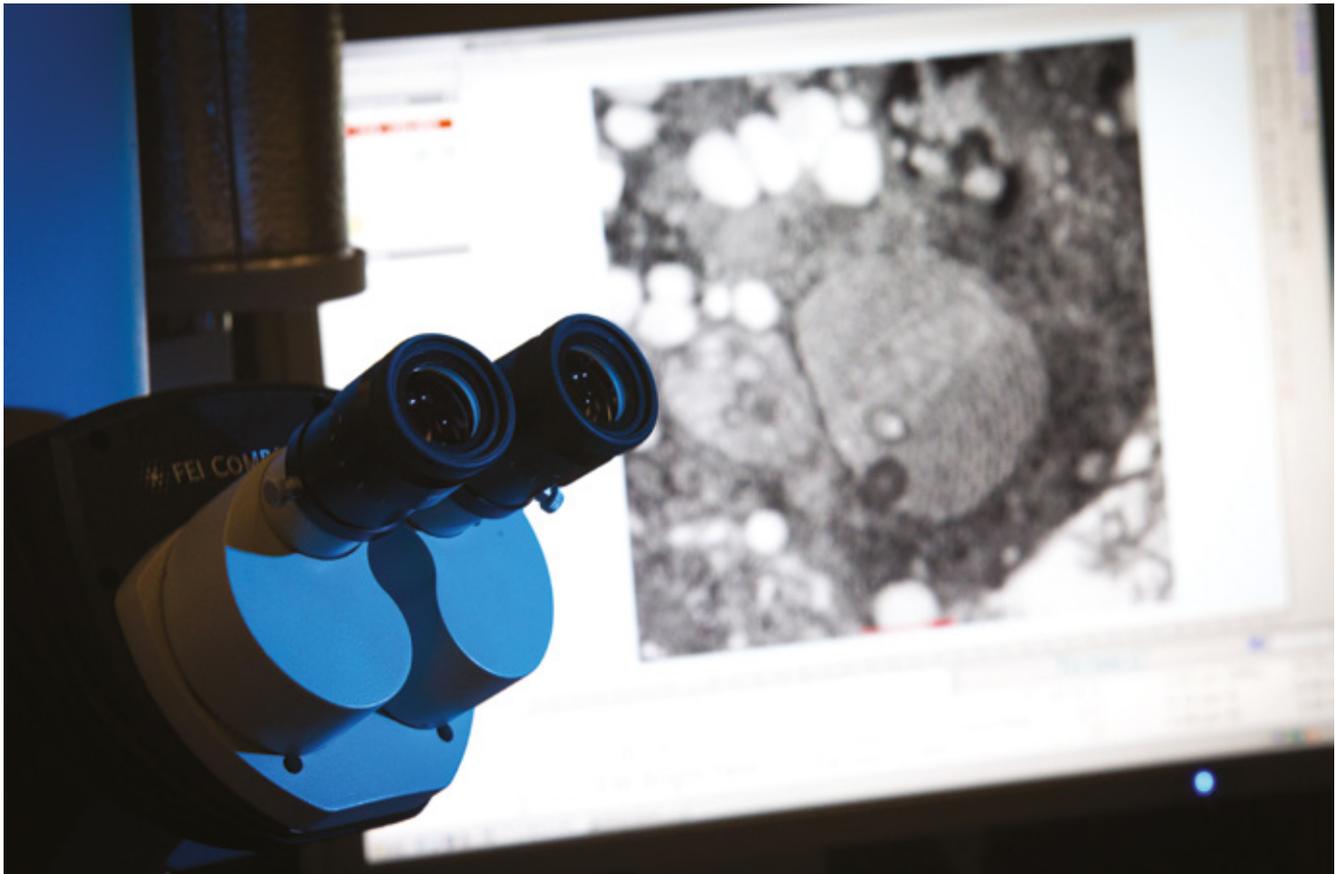
### Project co-supervisor

Professor Benjamin Howden, Professor Beverley-Ann Biggs

### Project availability

- PhD





### **Project: Stopping the spread of the superbug VRE in Australian hospitals**

Enterococci emerged in terrestrial animals about 450 million years ago, and are frequent commensal bacteria in the human gut. In the past 50 years, pathogenic strains have emerged in our hospitals, such as *Enterococcus faecalis* and *Enterococcus faecium* (VRE), that are highly persistent and resistant to multiple antibiotics. We have established a mouse model of VRE colonisation and RNAseq expression profiling to identify bacterial persistence factors. This project will apply molecular biology approaches to define factors essential for gut colonisation and persistence.

#### **Project supervisor**

Professor Ben Howden, Professor Tim Stinear

#### **Project co-supervisor**

Dr Glen Carter

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: Applying synthetic biology to unravel the virulence of the hospital-adapted clones of *Staphylococcus epidermidis***

*Staphylococcus epidermidis* is a predominant coloniser of human skin, but also termed the “accidental pathogen” as it can cause life-threatening infections upon skin breach. Despite the diversity in *S. epidermidis* strains, the majority of infections are caused by a single sequence type (ST2). Until recently this clone has been refractory to genetic manipulation. Through bioinformatic analysis of over 300 Australian/international isolates, we have developed techniques to genetically manipulate clinically relevant ST2 clones. Using synthetic biology, this project will develop CRISPR (gene deletion/knockdown), phage integrase vectors and TNseq to uncover the molecular basis of enhanced pathogenicity within ST2 clones.

#### **Project supervisor**

Professor Ben Howden, Professor Tim Stinear

#### **Project co-supervisor**

Dr Ian Monk

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: Defining the impact of antibiotic resistance on staphylococcal pathogenesis and host-pathogen interactions**

*Staphylococcus aureus* is one of the major causes of human bacterial infection, with increasing antibiotic resistance making treatment difficult. Our laboratory has discovered a critical link between resistance, and changes in host-pathogen interactions. In this project, techniques including directed mutagenesis, RNAseq, reporter assays, whole genome sequencing and bioinformatics, and phenotype screening, will be used to unravel the complex relationship between resistance, virulence and host immunity in this important human pathogen. This information is critical for further defining the consequences of inappropriate antibiotic use and antibiotic resistance, and refining treatment approaches to avoid these negative consequences in the pathogen.

#### **Project supervisor**

Professor Ben Howden, Professor Tim Stinear

#### **Project co-supervisor**

Dr Romain Guerillot

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: Evolution in *Staphylococcus aureus* – what makes a successful hospital-adapted clone?**

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the major causes of hospital-acquired infections globally. Our laboratory has been investigating the genomic and phenotypic evolution of the major MRSA clones and has now uncovered a major shift in the clonal structure of MRSA in Australia. Little is known about why some clones of *S. aureus* are successful, and how they become embedded in our healthcare institutions. This project will use techniques including genomics and bioinformatics, statistical genetics, phenotypic comparisons (including models of infection) and mutagenesis to reveal the mechanisms and predictors of successful MRSA clones.

#### **Project supervisor**

Professor Ben Howden

#### **Project co-supervisor**

Sarah Baines

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: Genomic modelling and machine learning to reveal genomic mediators of disease in *Staphylococcus aureus***

*Staphylococcus aureus* is responsible for significant human disease and mortality, with bacteraemia one of the most devastating. We have collected over 800 invasive *S. aureus* bacteraemia isolates from around Australia, completed genome sequencing of all isolates, and collated detailed clinical information. This project will apply evolving statistical genomics approaches (such as machine learning) to identify genomic mediators of disease in *S. aureus*, and predictors of poor clinical outcomes. Identified targets will be validated through a directed mutagenesis and infection model. This project will provide novel insights into *S. aureus* pathogenesis and mediators of mortality in bacteraemia.

#### **Project supervisor**

Professor Ben Howden, Professor Tim Stinear

#### **Project co-supervisor**

Dr Anders Gonçalves da Silva

#### **Project availability**

- PhD
- MSc

### **Project: Tracking superbugs using genomics**

Bacterial whole genome sequencing is a new technology allowing high-resolution tracking of the emergence and spread of antimicrobial resistant pathogens (such as MRSA, VRE and KPC-producing bacteria). In this project, this technology will be applied to clinical drug-resistant bacterial isolates from hospitals where patients with these infections are presenting. Genomic approaches, including identification of resistance elements, phylogenetics and evolutionary modelling, will be applied to reveal how superbugs are emerging and spreading in our region, and will help design strategies to combat them.

#### **Project supervisor**

Professor Ben Howden

#### **Project co-supervisor**

Dr Jason Kwong

#### **Project availability**

- PhD
- MSc
- Honours



## Howden group

### **Project: Metagenomics for infectious diseases diagnostics and identifying antimicrobial resistance**

Metagenomics (the sequencing of all genetic material in a sample) is an exciting new technology that can be applied to the diagnosis and characterisation of infectious diseases. Using state-of-the-art sequencing technology available in the MDU public health laboratory, and access to clinical samples from complex infectious diseases cases, this project will use this new technology to understand how it can be best applied to inform the management of patients with serious infections. Additionally, the technology will be applied to uncover the repertoire of antimicrobial resistance elements in clinical samples to improve the tracking and treatment of resistant pathogens.

#### **Project supervisor**

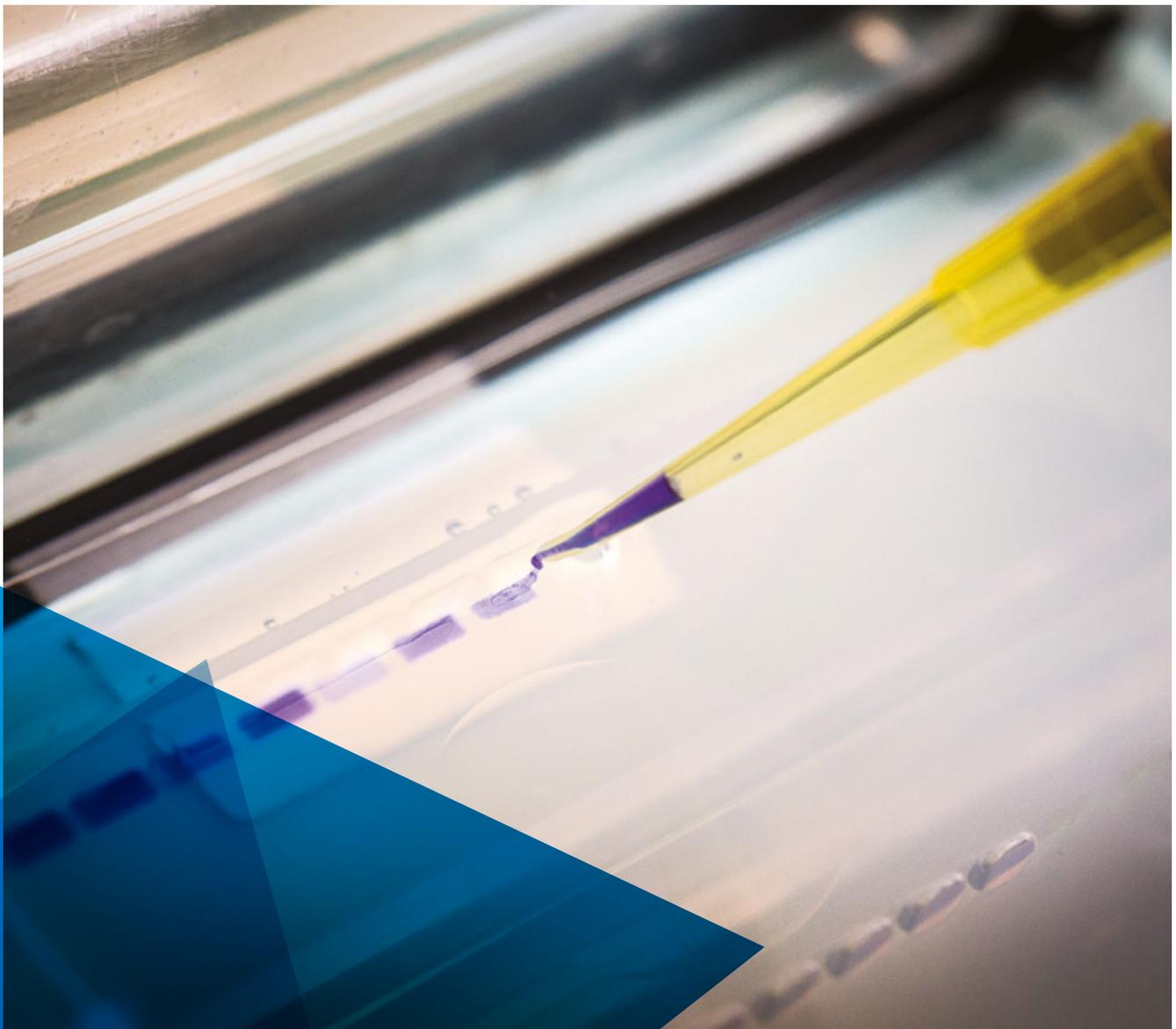
Professor Ben Howden

#### **Project co-supervisor**

Dr Jason Kwong

#### **Project availability**

- PhD
- MSc
- Honours



# Jackson group

**Contact:** Dr Brendon Chua  
**Email:** bychua@unimelb.edu.au

Number of vacancies available: 1



Immunology



Host-pathogen Interactions



Translational and Clinical Research



Our research interests centre around the discovery and rational development of innovative therapeutic and vaccine candidates to improve both innate and adaptive immunity against a variety of disease indications, from infectious diseases such as influenza, hepatitis B and tuberculosis, to hormone and small molecule blockade. Many of these translation research programs are well aligned with the needs of industry. A dominant strategy of these research efforts is to also understand the mechanisms involved in the biological action of these candidates, utilising immunological, biochemical and genome-based approaches in both human and animal disease models.

## **Project: Myeloid-derived suppressor cells and their influence on antiviral CD8+ T cell immunity**

Myeloid-derived suppressor cells (MDSCs) are a heterogenous cell population that share the ability to suppress various T cell functions. Their accumulation in lymphoid organs and many tumour microenvironments is associated with many cancers as well as chronic viral infections, but their role in acute viral infections such as influenza has yet to be systematically studied. This project aims to examine whether MDSC accumulation in the lung following infection by different influenza virus strains affects ensuing anti-viral T cell responses and will extend to defining the MDSC population(s) and mechanisms associated with the suppression of these responses.

### **Project supervisor**

Dr Brendon Chua

### **Project co-supervisor**

Professor David Jackson

### **Project availability**

- Honours



# Kallies group

**Contact:** Professor Axel Kallies  
**Email:** axelk@unimelb.edu.au

Number of vacancies available: 3



Immunology



Viral Infectious Diseases



Host-pathogen Interactions



Translational and Clinical Research



Genomics



The work of the Kallies lab focusses on understanding the molecular regulation of immunity. Our research has established the important functions of several transcription factors and discovered key molecular circuits in lymphocyte differentiation. Current studies focus on molecular regulation of immune cell differentiation and function in non-lymphoid tissues, including tumors, and on metabolic control of lymphocyte differentiation. For our research, we are using preclinical models of infection and malignant disease combined with next generation sequencing technology and bioinformatics. Our discoveries have opened new avenues to targeting plasma cells as well as T cells in autoimmunity, metabolic disease and cancer.

## **Project: Molecular control of T cell responses to chronic infections and tumors**

Chronic infections and tumors are characterised by the persistence of antigen, leading to impaired T cell responses. Thus, improving T cell functionality in these diseases is a major research goal. Recent studies, including our own, described that T cell responses in chronic infections and tumors are sustained by memory-like T cells, which are key successful cancer immunotherapy. This project will delineate the molecular attributes that regulate long-term T cell responses using preclinical models, state-of-the-art sequencing technology and gene targeting approaches. Our studies will aid the development of new strategies to improve T cell responses to chronic infections or tumors.

### **Project supervisor**

Professor Axel Kallies

### **Project co-supervisor**

Dr Sarah Gabriel

### **Project availability**

- PhD
- Honours

### **Project: The role of cellular metabolism in immune cell function**

In response to antigen, T cells undergo rapid proliferation and differentiate into distinct effector and memory populations. Changes to cellular metabolism, in particular an increase in aerobic glycolysis and glutaminolysis are hallmarks of rapidly dividing cells. This metabolic reprogramming is now recognized as a crucial requirement for immune cell differentiation and function, and considered a promising target for therapeutic intervention. This project will delineate the metabolic characteristics of lymphocytes responding to persistent antigen, in particular those residing in non-lymphoid tissues such as tumors. Our studies will aid the development of new strategies to improve T cell responses to chronic infections or tumors.

#### **Project supervisor**

Professor Axel Kallies

#### **Project co-supervisor**

Patrick Gubser

#### **Project availability**

- PhD
- Honours

### **Project: Molecular regulation of tissue-resident T cell differentiation**

Tissue-resident memory T cells (TRM) reside in non-lymphoid tissues and localise to sites of pathogen entry where they provide protection against reinfection; however, they are also implicated in protection against cancer. Thus, understanding the determinants that control their differentiation and function is critical to devise new therapies. We recently identified a transcriptional module consisting of the transcription factors Blimp1 and Hobit that is required for TRM. Using a series of new genetic models, we will delineate their precise function, determine the contribution of TRM to protection against reinfection and cancer, and will identify signals that determine TRM development.

#### **Project supervisor**

Professor Axel Kallies

#### **Project co-supervisor**

Dr Laura Mackay

#### **Project availability**

- PhD
- Honours

### **Project: Regulatory T cell differentiation and function in disease**

Regulatory T (Treg) cells are indispensable for the maintenance of immune homeostasis and the prevention of autoimmunity. They also play critical roles in cancer and inflammatory diseases. We and others have shown that Treg cells undergo a distinct differentiation program that is essential to acquire a fully suppressive effector phenotype. This process is paralleled by increasing specialization of the Treg cells and their migration to non-lymphoid organs where they play critical roles in maintaining tissue health. Using a number of new preclinical models and cutting-edge technology, this project aims to uncover new molecular regulators of Treg cell differentiation and function.

#### **Project supervisor**

Professor Axel Kallies

#### **Project co-supervisor**

Dr Ajith Vasanthakumar

#### **Project availability**

- PhD
- Honours

### **Project: Immune regulation adipose tissue health**

Adipose tissue is an endocrine organ, which not only stores excessive energy but plays an important regulatory role. Thus, obesity and associated complications including insulin resistance and liver disease constitute a serious health-burden. The adipose harbors large numbers of immune cells that control tissue health and organismal metabolism. We have shown that adipose-resident cells express a unique set of molecules including the IL-33 receptor, required for their development and function. This project utilizes novel preclinical models and molecular techniques to unravel the cellular and molecular components of the IL-33-controlled lymphocyte network that controls adipose tissue health and maintains organismal metabolism.

#### **Project supervisor**

Professor Axel Kallies

#### **Project co-supervisor**

Dr Ajith Vasanthakumar

#### **Project availability**

- PhD
- Honours



# Lewin/Cameron group

**Contact:** Professor Sharon Lewin  
**Email:** sharon.lewin@unimelb.edu.au

Number of vacancies available: 3



Immunology



Viral Infectious Diseases



Host-pathogen Interactions



Translational and Clinical Research



Discovery Research



Co-infections with viral or bacterial pathogens cause significant morbidity in people with HIV. In the case of HIV/HBV co-infection, morbidity and mortality secondary to liver disease is greatly increased compared to those infected with HBV or HIV alone. Mortality remains elevated even after treating both the HIV and HBV viruses. The HBV Immunology Lab investigates the mechanism of how HIV can accelerate liver disease in patients co-infected with HBV. They hypothesise that this occurs by combined effects of HIV and HBV on inflammation in the liver. These studies could potentially lead to new treatments for liver disease.

## Project: Understanding the role of B cell activation in curing hepatitis B virus

A higher frequency of antibodies to key HBV proteins are observed following antiviral treatment of individuals with HIV-HBV co-infection. We hypothesise that this is due to higher basal levels of B cell activation. This project involves the development of novel approaches to accurately quantify HBV and HIV-specific B cells ex vivo. At PhD level, the relationship between development of antibodies to HBsAg and HBeAg post-treatment in HIV-HBV co-infection with levels of B-cell activating factor (BAFF), HIV-specific B cells and B cell subtypes will be examined and the effect of a BAFF-HBV fusion protein on production of antibodies to HBsAg determined

### Project supervisor

Professor Sharon Lewin

### Project co-supervisor

Professor Fabienne Mackay, Dr Jennifer Audsley

### Project availability

- PhD
- Honours

### Further information

<https://www.ncbi.nlm.nih.gov/pubmed/24430489>

<https://www.ncbi.nlm.nih.gov/pubmed/23684423>

## **Project: Eliminating HIV latency – towards a cure for HIV**

Despite currently available, highly effective treatments for HIV infection, there is no cure. This is because HIV has a long-lived form of infection called latent infection. Our overall goal is to eliminate latency by activating the latent virus to produce virus protein, which can then be recognized and eliminated by the immune system. We will develop unique tools to measure HIV protein production on the surface of the cell. These tools could then be used to assess activity of latency reversing agents that are currently being evaluated in clinical trials.

### **Project supervisor**

Professor Sharon Lewin

### **Project co-supervisor**

Dr. Jennifer Zerbato

### **Project availability**

- PhD
- MSc
- Honours



# Lewin/Cameron group

**Contact:** Associate Professor Paul Cameron  
**Email:** paul.cameron@unimelb.edu.au

Number of vacancies available: 1



Immunology



Viral Infectious Diseases



Host-pathogen Interactions



Translational and Clinical Research

## Project: HIV integration sites and expansion in antigen specific T cells

Critical for HIV cure is the nexus between integration site selection, antigen-specific TcR signaling at infection and the HIV gene expression required to clear latent infection. The ability to use single cell analysis on rare infection events is limiting, but expression of the CD25 and Ox40 markers after antigen exposure of cells from HIV-infected subjects will be used to sort antigen-specific cells. Clonal expansion of integration sites and distribution in genes expressed in resting/activated cells will be used to identify the gene profile at the time of infection and correlate with response to latency-reversing agents.

### Project supervisor

Associate Professor Paul Cameron

### Project co-supervisor

Dr Jori Symons, Professor Sharon Lewin

### Project availability

- PhD
- MSc

# McVernon group

**Contact:** Professor Jodie McVernon  
**Email:** j.mcvernon@unimelb.edu.au

Number of vacancies available: 1



Immunology



Viral Infectious Diseases



Epidemiology



Professor Jodie McVernon is a physician with subspecialty qualifications in public health and vaccinology. She has extensive expertise in clinical vaccine trials, epidemiologic studies and mathematical modelling of infectious diseases, gained at the University of Oxford, Health Protection Agency London and the University of Melbourne. Her work focuses on the application of a range of cross-disciplinary methodological approaches, including mathematical and computational models, to synthesise insights from basic biology, epidemiological data and sociological research. These models advance understanding of the observed epidemiology of infectious diseases and inform understanding of optimal interventions for disease control.

## **Project: Developing mathematical models of influenza immunity from cohort studies**

Following influenza (flu) infection, antibodies are produced that protect against re-infection with the same flu strain. However, over successive flu seasons, circulating viruses accumulate mutations that render this immunity relatively ineffective (antigenic drift). We have tracked flu infections and illnesses in a cohort of Vietnamese households over 11 years. These rare data documenting infection intervals and antibody responses will be used to develop and validate statistical and mathematical models of influenza infection and immunity, and to better understand the contributions of immune waning, and cross-strain immunity. Insights gained will inform public health strategies for flu prevention, including vaccination.

### **Project supervisor**

Professor Jodie McVernon

### **Project co-supervisor**

Annette Fox, James McCaw

### **Project availability**

- PhD



# Mackay, Fabienne group

**Contact:** Professor Fabienne Mackay  
**Email:** fabienne.mackay@unimelb.edu.au

Number of vacancies available: 3



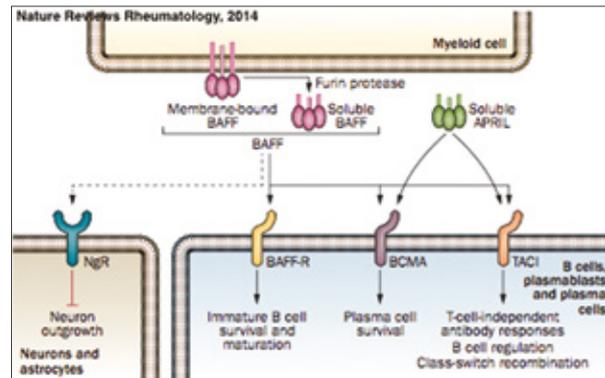
Immunology



Public Health



Translational and Clinical Research



BAFF and APRIL cytokines mediate different functions in B cells.

Professor Mackay's laboratory has an interest in autoimmune diseases and mechanisms leading to loss of immune tolerance, in particular that of B-lymphocytes. Professor Mackay has spent years studying a cytokine from the TNF superfamily named BAFF/BLyS and demonstrated the role of this factor in B cell survival. Excess BAFF leads to autoimmunity in mice and is associated with human autoimmunity, in particular Systemic Lupus Erythematosus (SLE) and Sjögren's syndrome. **Belimumab, a therapeutic BAFF-blocking antibody has been approved for use in SLE in the clinic in March 2011.** This clinical outcome validates over ten years of Prof. Mackay's work on BAFF.

## Further information

<http://go.unimelb.edu.au/a9e6>

[www.doherty.edu.au/people/professor-fabienne-mackay](http://www.doherty.edu.au/people/professor-fabienne-mackay)

## Project: Restoring B cell tolerance in Systemic Lupus Erythematosus

Normally, the immune system effectively fights infections and eliminate cancer cells, however, in autoimmunity, the immune system attacks self-tissues. SWHEL mice, which reveal the fate of autoreactive B cells, will be used to test the requirement for specific signaling pathways for B cell tolerance using crosses to knockout mice. This project will examine autoimmune mice (BAFF-Tg) under various experimental treatments, which may benefit via restored B cell tolerance. This work will also explore the relationship between the gut microbiome and the ability of the innate immune system to select safe B cells into the mature B cell repertoire.

## Project supervisor

Professor Fabienne Mackay

## Project co-supervisor

Dr William Figgett

## Project availability

- PhD
- MSc
- Honours

### **Project: Restoring immunocompetency in Chronic Lymphocytic Leukemia**

Chronic Lymphocytic Leukaemia (CLL) is a blood cancer caused by the malignant expansion of B-cells. CLL cells are able to sabotage the immune system to avoid anti-tumour immunity, but this leaves patients immunocompromised and very vulnerable to infections. We have recently found that CLL cells rely on BAFF/APRIL cytokines to produce the immunosuppressive cytokine IL-10. We want to dissect the contribution of the different BAFF/APRIL receptors in this process to understand how CLL cells shut down the immune system. Our goal is to design therapies able to restore immunity in CLL and hence increase patients' survival.

#### **Project supervisor**

Professor Fabienne Mackay

#### **Project co-supervisor**

Dr Beatriz Garcillan

#### **Project availability**

- PhD
- MSc
- Honours

#### **Further information**

<http://go.unimelb.edu.au/69e6>  
[www.doherty.edu.au/people/professor-fabienne-mackay](http://www.doherty.edu.au/people/professor-fabienne-mackay)

### **Project: The role of CXCR7 in tissue fibrosis**

Chemokines are small molecules that provide guidance cues to cells during embryonic development and are equally critical for the migration of immune cells. The atypical receptor CXCR7 binds the chemokines CXCL12 and CXCL11, which are long-known central players in the immune system during steady state as well as under inflammatory conditions. The clinical potential of targeting CXCR7 is currently under exploration in several clinical trials. However, there are still many open questions and unknowns around the physiological and pathological functions of CXCR7 and our lab investigates the role of CXCR7 in fibrosis.

#### **Project supervisor**

Professor Fabienne Mackay

#### **Project co-supervisor**

Dr Asolina Braun

#### **Project availability**

- PhD
- Honours

#### **Further information**

<http://go.unimelb.edu.au/x9e6>  
[www.doherty.edu.au/people/professor-fabienne-mackay](http://www.doherty.edu.au/people/professor-fabienne-mackay)

### **Project: Elucidating the beneficial and harmful elements of the BAFF/APRIL system in multiple sclerosis**

Multiple Sclerosis (MS) is a chronic neuroinflammatory disease of the brain and spinal cord that causes serious physical disability in young adults. In this disease, self-reactive lymphocytes attack and damage the central nervous system. Our special focus lies on harnessing regulatory B cells, an immunosuppressive subset of B lymphocytes that is essential for decreasing MS severity. BAFF and APRIL are molecules important for the development, activation and survival of conventional as well as regulatory B cells and we are dissecting the role of these cytokines and their receptors in the pathogenesis of MS.

#### **Project supervisor**

Professor Fabienne Mackay

#### **Project co-supervisor**

Dr Beatriz Garcillan

#### **Project availability**

- Honours

#### **Further information**

<http://go.unimelb.edu.au/s9e6>



## Mackay, Fabienne group

### **Project: A new function of the cytokine BAFF in dendritic cell maturation: Implications for immunity and cancers**

Dendritic cells (DCs) are critical players in immunity; they initiate immune responses by capturing, processing and presenting antigens to T cells. Manipulation of DC function is one of several new strategies to improve vaccines and promote anti-cancer immunity. Therefore, understanding the exact processes regulating DC activation and maturation is essential. We have identified TACI, one of 3 receptors for the cytokine BAFF, as a new player in the crosstalk between B cells and DCs. This project aims to elucidate the role of the BAFF system in DC maturation and its impact in the generation of immune responses.

#### **Project supervisor**

Professor Fabienne Mackay

#### **Project co-supervisor**

Dr Beatriz Garcillan

#### **Project availability**

- Honours

#### **Further information**

<http://go.unimelb.edu.au/i9e6>



# Mackay, Laura group

**Contact:** Dr Laura Mackay  
**Email:** lkmackay@unimelb.edu.au

Number of vacancies available: 2



Immunology



Viral Infectious Diseases



The Mackay Group studies cellular immune responses, with a focus on the genes and signals that control resident memory T cell differentiation, with a view to harness these cells to develop new treatments against infection, cancer, and autoimmune disease.

## **Project: The role of tissue-resident memory T cells in immune-mediated pathology**

Tissue-Resident Memory T cells (TRM) rely on distinct molecular mechanisms for their formation and survival within peripheral tissues. Recently, the presence of TRM has been associated with various immune pathologies. This project aims to establish pre-clinical models where TRM cause disease, and will use cutting-edge techniques to target particular genes and/or molecules that will manipulate the TRM population and eliminate these cells from the tissue. Alleviation of TRM-mediated immune pathology will have vast translational consequences that can be applied to a number of autoimmune conditions.

### **Project supervisor**

Dr Laura Mackay

### **Project availability**

- PhD
- MSc
- Honours

## **Project: Subset determination of Tissue-Resident Memory**

This project will determine novel regulators of CD8 and CD4 Tissue-Resident Memory cells

### **Project supervisor**

Dr Laura Mackay

### **Project co-supervisor**

Susan Christo

### **Project availability**

- PhD
- MSc
- Honours



# Mackenzie group

**Contact:** Associate Professor Jason Mackenzie  
**Email:** jason.mackenzie@unimelb.edu.au

Number of vacancies available: 2



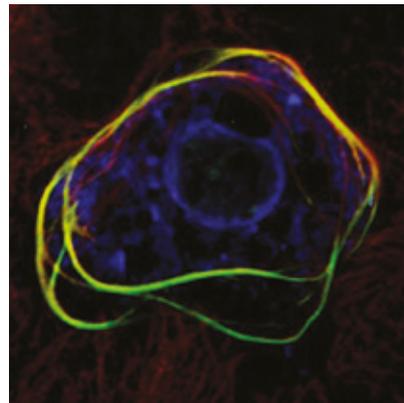
Viral Infectious Diseases



Host-pathogen Interactions



Public Health



Microtubule rearrangements induced during over-expression of host (GEF-H1) and mouse norovirus protein NS1-2

The Mackenzie lab investigates the effects of West Nile, dengue, zika and mouse norovirus infection of host cells. The main goals are to understand the events of virus replication and how these processes influence cellular functions, thus ultimately defining pathological steps generating disease; in particular, the influences of viral replication on metabolic and stress pathways that ultimately lead to immune regulation and dysfunction. We are also exploiting some of these immune evasion strategies to utilise genetic techniques to express immunoactive compounds to prevent infection and disease of human pathogens. Our research centres on molecular virology, cell biology, imaging and innate immunity.

## Project: Can enteric bacteria aid infection by Norovirus?

It has recently been shown that enteric bacteria of our microflora can bind pathogenic Norovirus and facilitate their entry into B cells. We aim to use the bank of bacteria currently available in the MDU to determine the specificity of this interaction i.e., can all bacteria do this or only a select few? We will utilise virus infection models combined with mutant virus-like particle studies to determine interaction domains within the Norovirus particle. Our ultimate goal is to determine if an individual's microbiota has the capacity to influence the outcome and severity of a Norovirus infection.

### Project supervisor

Associate Professor Jason Mackenzie

### Project co-supervisor

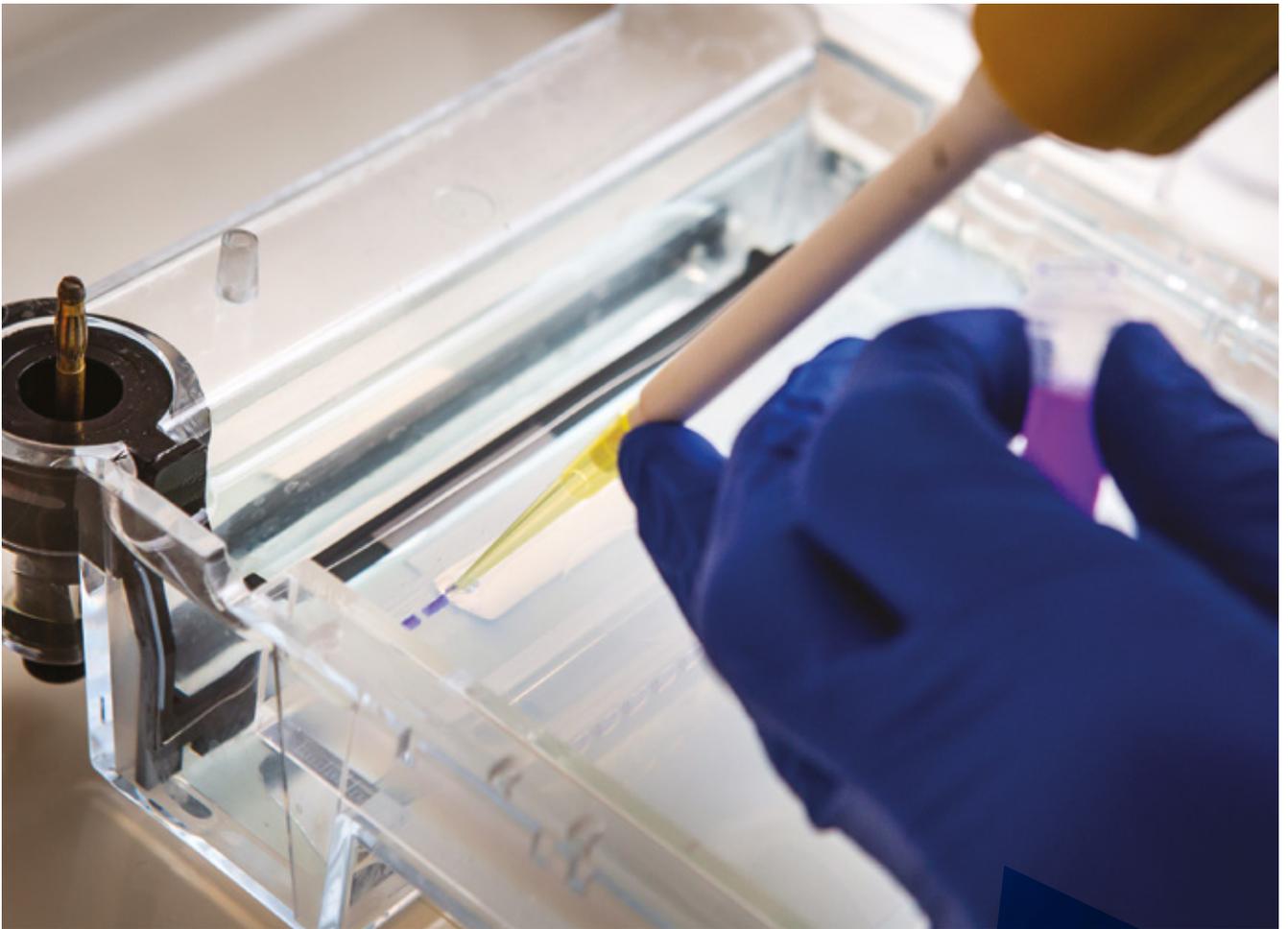
Professor Ben Howden

### Project availability

- Honours

### Further information

<http://science.sciencemag.org.ezp.lib.unimelb.edu.au/content/sci/346/6210/755.full.pdf>



### **Project: Is dengue pathology due to a stressed cell?**

Increasing evidence has indicated that the secreted dengue protein NS1 binds to and activates Toll-like receptor 4 (TLR4) to promote the production of pro-inflammatory cytokines known to be produced during severe dengue disease. However, the exact mechanism of how this occurs is not fully understood. Intriguingly, LPS binding to TLR4 induces a similar response that is mediated via the host stress response. Thus we aim to determine if NS1 is activating the IRE-1/Xbp-1 cellular stress pathway upon TLR4 engagement. We will utilise a variety of KO cell lines to interrogate the hypothesis and immune activation assays.

#### **Project supervisor**

Associate Professor Jason Mackenzie

#### **Project availability**

- Honours

# Mueller group

**Contact:** Associate Professor Scott Mueller  
**Email:** smue@unimelb.edu.au

Number of vacancies available: 1-2



Immunology



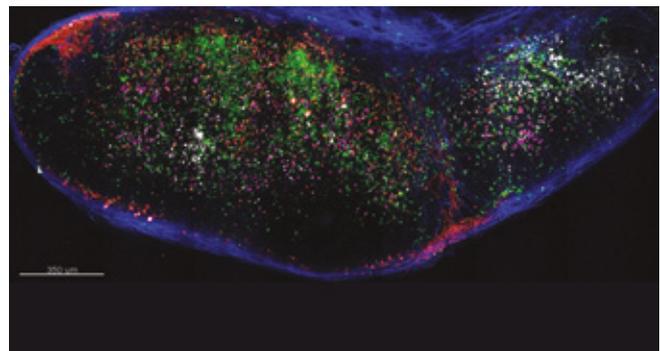
Viral Infectious Diseases



Host-pathogen Interactions



Research in the Mueller lab is focused on examining immune responses to both acute and chronic viral infections using state-of-the-art methods, including intravital 2-photon microscopy to visualise immune cells and pathogens in real time. We are examining how T cells are activated and protect against infections, the induction of immune memory and tissue-resident memory T cells, and the role of stromal cells and neuro-immune interactions for the design of new vaccines and therapeutics.



CD4 and CD8 T cell activation by dendritic cells in lymph nodes during herpes simplex virus infection.

## **Project: Revealing the induction of T cell responses during chronic infection.**

Chronic viral infections induce dysfunctional T cell responses, impaired virus clearance and tissue damage. The early cellular interactions between T cells and antigen-presenting cells that result in impaired responses and uncontrolled viral growth are unknown. Such knowledge is important for the design of therapies to counteract chronic infections, such as HIV. This project will examine these early stages of T cell activation using transgenic mice, multi-parameter flow cytometry and fluorescence confocal microscopy.

### **Project supervisor**

Associate Professor Scott Mueller

### **Project availability**

- MSc
- Honours

### **Further information**

<http://go.unimelb.edu.au/29e6>

### **Project: Regeneration of lymphoid tissues**

In the wake of infectious disease or following lymph node removal, there is little evidence that lymph nodes can regenerate. Lymphoid organs are constructed from heterogeneous subsets of stromal cells that control immune cell survival and immune responses. Using new transgenic mice, this project will examine how lymphoid tissues expand and respond to infection, and how destruction of the tissue environment is regenerated by stromal cells. This will reveal new avenues to repair damage to lymphoid tissues and support immunity. Advanced multi-colour imaging, flow cytometry and molecular techniques will be used to address these questions.

#### **Project supervisor**

Associate Professor Scott Mueller

#### **Project co-supervisor**

Dr Yannick Alexandre

#### **Project availability**

- PhD
- Honours

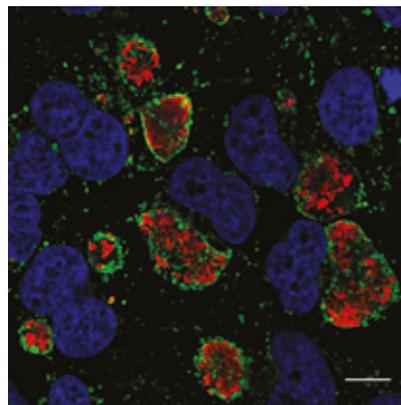
# Newton group

**Contact:** Dr Hayley Newton  
**Email:** hnewton@unimelb.edu.au

Number of vacancies available: 1-2



Host-pathogen Interactions



*Coxiella burnetii* (red) replicates to high numbers in a unique, pathogen-modified lysosome (green) within human host cells.

The Newton Lab investigates the host-pathogen interactions between human cells and intracellular bacterial pathogens. These pathogens have evolved unique and fascinating ways to modulate human processes. By researching the mechanisms used by the pathogens we can gain important insights into how these bacteria cause disease and also use the bacteria as tools to uncover novel understanding of how our cells function. Our main area of interest is *Coxiella burnetii*, the causative agent of Q fever. *Coxiella* uses a secretion system to inject an arsenal of novel proteins into the human cell and establish a replicative niche within the lysosome.

## Project: CCVs: *Coxiella*-containing vacuoles and clathrin-coated vesicles

*Coxiella burnetii* establishes a replicative vacuole, the *Coxiella*-containing vacuole (CCV), by introducing effector proteins into the host cell. We have demonstrated that the effector, Cig57, is essential for intracellular replication of *Coxiella* through its ability to modulate host clathrin-mediated trafficking. We have observed that clathrin is recruited to the CCV and is required for intracellular replication of *Coxiella*.

Here we will examine the relationship between *Coxiella* virulence and clathrin-coated vesicles. This will involve functional analysis of Cig57, identification and characterisation of additional *Coxiella* effectors that manipulate clathrin-mediated traffic and a range of techniques to understand how clathrin-mediated trafficking supports *Coxiella* virulence.

### Project supervisor

Dr Hayley Newton

### Project availability

- PhD
- MSc
- Honours



### **Project: Interplay amongst the *Coxiella burnetii* effector repertoire**

*Coxiella burnetii* injects approximately 150 effector proteins into human cells to remodel the cell and support intracellular replication of the pathogen. Very little is understood about the function of these effectors and how they act to support *Coxiella* virulence. This project will involve investigating both physical and functional interactions between this large cohort of novel proteins. The research will include the use of tissue culture models of infection, imaging technologies and biochemical approaches to examine the relative importance of the effectors and reveal their novel functions.

#### **Project supervisor**

Dr Hayley Newton

#### **Project availability**

- PhD
- MSc
- Honours

# Purcell group

**Contact:** Professor Damian Purcell  
**Email:** dfjp@unimelb.edu.au

Number of vacancies available: 2



Immunology



Viral Infectious Diseases



Host-pathogen Interactions



Translational and Clinical Research



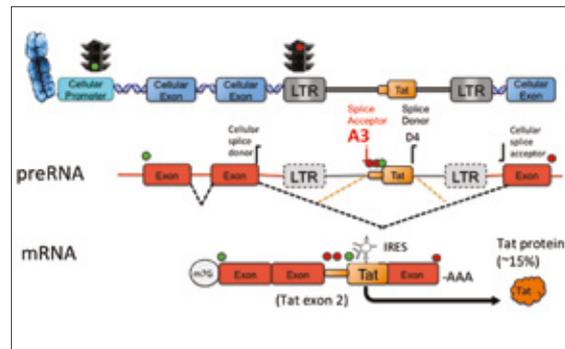
International Health



Indigenous Health



Genomics



Structured RNA controls Tat protein expression to regulate HIV latency

Professor Damian Purcell's research group investigates the HIV-1 and HTLV-1 human retroviruses that cause AIDS and leukaemia/inflammatory pathogenesis respectively. The lab studies their genetic structure and gene expression with a focus on defining the mechanisms that control viral persistence and pathogenesis. The molecular interplay of viral and host factors during viral infection and the innate and adaptive immune responses to viral infection are examined. These molecular insights are used to develop new antiviral and curative therapeutics, preventive prophylactic vaccines and passive antibody microbicides and therapeutics. Some of these patented discoveries have been commercialised and we are assisting with clinical trials.

## Project: RNA control of HIV latency

Long-lived CD4+ T-cells harbouring integrated copies of HIV proviral DNA stand as the barrier to sustained HIV remission without ongoing antiretroviral drug therapy. Multiple mechanisms restrict the viral gene expression needed for immune-detection and clearance. However, RNA transcription from the adjacent highly-active cellular gene reads-through into provirus, whereupon mRNA splicing and other mechanisms recombine HIV Tat RNA into mature cellular RNAs. This project studies these chimeric host-HIV mRNAs and investigates a folded RNA-element that underlies Tat coding RNA, its RNA-epigenetic modifications and the cellular protein binding partners that function to permit Tat-expression through a privileged IRES-translation pathway to regulate HIV-latency.

### Project supervisor

Professor Damian Purcell

### Project co-supervisor

Dr Georges Khoury

### Project availability

- PhD
- MSc
- Honours

### **Project: New drugs to reactivate latent HIV**

Current latency-reversing drugs lack specificity for the latent HIV promoter, and therefore demonstrate reduced safety and potency. We developed a dual-reporter screening cell-line that specifically reactivates HIV-1 gene expression by promoting the HIV RNA-processing and protein-modification pathways that support Tat-activated HIV-1 expression. After screening a 115,000-compound library, we identified and patented a family of Amidothiazol compounds that reactivate latent HIV from primary patient cells as single agents and strongly synergise with the BRD4 inhibitor, JQ1(+). This project will examine the cellular targets of the Amidothiazols and will characterise the novel mechanisms these compounds use to strongly reactivate HIV from latency.

#### **Project supervisor**

Professor Damian Purcell

#### **Project co-supervisor**

Dr Jonathan Jacobson

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: Pathogenesis of HTLV-1 subtype-C infecting remote indigenous Australians**

The HTLV-1 subtype-C is endemic in remote central Australian Indigenous communities with prevalence greater than 50%. Austral-Melanesian HTLV-1c infections with a high proviral load are associated with immunopathogenic conditions, such as bronchiectasis. Sequences from 30 HTLV-1c genomes reveal significant differences in the HBZ and p12 coding-regions compared to the cosmopolitan subtype-A from Africa and Japan that's commonly associated with leukaemia and myelopathy. This project examines p12 and HBZ expression and function during HTLV-1c replication. The role of HTLV-1c provirus-accumulation and immune-dysfunction in diminished health outcomes for Indigenous central Australians will be explored using HTLV-1c integration-site mapping and T-cell receptor clonotyping.

#### **Project supervisor**

Professor Damian Purcell

#### **Project co-supervisor**

Dr Georges Khoury

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: Cow antibodies that potentially neutralize HIV transmission**

Prophylactic HIV vaccines aim to elicit broad neutralising antibody (bNAb) at the sexual mucosa to block virus transmission. The Purcell lab was first to find and publish that vaccination of dairy-cows with HIV Envgp140 trimer vaccines can elicit broad and potent bNAb responses in vast scale in the colostrum milk. This was patented for use as a passive antibody-microbicide prevention against HIV-transmission and has been scaled-up and developed for clinical testing with a commercial partner. This project aims to isolate bovine plasmablasts producing bNAbs for production of monoclonal antibodies to characterise the responses needed for a protective antibody-response in humans.

#### **Project supervisor**

Professor Damian Purcell

#### **Project co-supervisor**

Dr Behnaz Heydarchi

#### **Project availability**

- PhD
- MSc
- Honours

#### **Link for Further information**

<http://dx.doi.org/10.1080/19420862.2016.1270491>



**Contact:** Associate Professor Peter Revill  
**Email:** peter.revill@mh.org.au

Number of vacancies available: 2



Viral Infectious Diseases



Public Health



Translational and  
Clinical Research



International Health



The Revill Lab's work is focused on the molecular virology of hepatitis B virus (HBV), which is one of the most important human pathogens, infecting 257 million people worldwide, including 239,000 Australians. The lab has a particular interest in the contribution of different HBV genotypes and variants to the striking differences in natural history, disease progression and treatment response observed globally. We also have an interest in determining the role of splicing in HBV-mediated liver cancer. Our studies will provide new insights into the role of spliced HBV variants and HBV genotype in liver disease.

## **Project: Characterising the milieu of hepatitis B spliced variants associated with advanced liver disease and liver cancer**

We have previously shown that splice variants of hepatitis B virus are associated with liver cancer and that splice variants are more diverse than previously appreciated. Yet the complexity of splice variants associated with advanced liver disease and liver cancer is unknown. The current quantitative PCR does not detect all known splice variants. This project will develop qPCR protocols to detect all known splice variants, across different HBV genotypes from both cell culture models as well as patient samples. Techniques utilised will include cell culture, real time PCR/digital PCR, next generation sequencing and quantitative serology.

### **Project supervisor**

Associate Professor Peter Revill

### **Project co-supervisor**

Dr Margaret Littlejohn

### **Project availability**

- Honours



**Project: Determining the role of secreted hepatitis B virus (HBV) RNA in the HBV life cycle and pathogenesis.**

Elimination of HBV is difficult, due mainly to the pool of transcriptionally active cccDNA that has to date proven impossible to remove from infected hepatocytes. HBV is a DNA virus, but it has recently been shown that viral RNA is also found in virus particles and secreted from the cell. The role of this RNA in the HBV lifecycle is unclear, but it may be an indirect marker of cccDNA expression. This project will utilise cell culture and patient samples to study the role of secreted viral RNA using Southern and northern blotting, real time PCR/digital PCR and quantitative serology.

**Project supervisor**

Associate Professor Peter Revill

**Project co-supervisor**

Dr Margaret Littlejohn

**Project availability**

- Honours

**Contact:** Professor Roy Robins-Browne  
**Email:** r.browne@unimelb.edu.au

Number of vacancies available: 1-2



Antimicrobial Resistance and Healthcare  
Associated Infections



Host-pathogen Interactions



## Project: Virulence gene activation in *E. coli* that causes oedema disease in pigs

This project aims to investigate the genetic regulation of the biosynthesis of F18 adhesive fimbriae by strains of enterotoxigenic *E. coli* (ETEC) which cause life-threatening postweaning diarrhoea and oedema disease in pigs. The project will take a multidisciplinary approach to generate new knowledge on how virulence is regulated in F18-ETEC and how to interfere with virulence regulation using small molecules. The expected outcome of this project will be important new knowledge on virulence gene regulation, and novel ways to treat and prevent infections with F18-ETEC in pigs. This will provide significant benefits to the pig industry in Australia and worldwide.

### Project supervisor

Professor Roy Robins-Browne

### Project availability

- Honours

## Project: Redefining enteropathogenic *E. coli*

A subtype of enteropathogenic *E. coli*, known as atypical EPEC (aEPEC), is defined in part by the **absence** of bundle-forming pili (BFP) – i.e., a negative criterion. The lack of a positive diagnostic marker precludes us from estimating the overall contribution of aEPEC to disease. We have used sequence data from 185 aEPEC strains obtained from children to identify seven novel fimbrial operons. We hypothesise that these fimbriae perform an analogous role to that of BFP in typical EPEC. If confirmed, these factors will become the diagnostic markers needed to detect pathogenic strains of aEPEC.

### Project supervisor

Professor Roy Robins-Browne

### Project availability

- Honours

# Rogerson group

**Contact:** Professor Stephen Rogerson  
**Email:** sroger@unimelb.edu.au

Number of vacancies available: 2



Immunology



Host-pathogen Interactions



Translational and  
Clinical Research



International Health



The Rogerson laboratory studies the pathogenesis and immunity of malaria in the human host, using in vitro models and clinical samples from individuals in malaria-affected countries.

We study how malaria in the mother affects her placenta, and the growth and development of her baby, and why some children develop life-threatening malaria, while others with similar exposure remain well or develop mild illness.

We are collaborating with engineers to develop new diagnostics for malaria, and we are taking novel approaches to identifying antibody responses that protect pregnant women and young children from malaria, and that block malaria transmission to mosquitoes.

## **Project: Mechanisms of transmission-blocking immunity against malaria**

Transmission of the malaria parasite *Plasmodium falciparum* (Pf) from humans to mosquitos requires the parasite to overcome immune defences in both hosts. Antibodies directed against gametocytes of Pf can directly inhibit their growth.

This project investigates the extent of antibody-mediated immunity against Pf gametocytes, and the functional properties of those antibodies. We will identify malaria-infected individuals who have antibodies to gametocytes

and gametocyte-derived antigens of Pf and determine the biophysical and functional properties of anti-gametocyte antibodies that confer transmission-blocking properties.

Techniques will include flow cytometry, immunofluorescence, antibody subclass analysis, opsonisation, bead phagocytosis assays, NK activation, statistical methods.

### **Project supervisor**

Associate Professor Siddhartha Mahanty

### **Project co-supervisor**

Professor Stephen Rogerson

### **Project availability**

- PhD
- MSc
- Honours

### **Further information**

<http://go.unimelb.edu.au/9qe6>



# Satzke group

**Contact:** Dr Catherine Satzke  
**Email:** catherine.satzke@mcri.edu.au

Number of vacancies available: 2



Host-pathogen Interactions



Epidemiology



Translational and  
Clinical Research



International Health



## Project: Bacterial factors for pneumococcal transmission

*Streptococcus pneumoniae* (the pneumococcus) is a leading killer of children worldwide. Transmission between hosts is a key step of pathogenesis and also underpins herd protection. Despite this importance, little is known about the bacterial factors that mediate transmission. This project will use mutagenesis (targeted, and transposon mutagenesis with next-gen sequencing) to identify the bacterial factors, and to assess their importance in our established *in vivo* transmission model.

### Project supervisor

Dr Catherine Satzke

### Project availability

- PhD
- Honours

### Further information

<http://viin.org.au/member/catherine-satzke>

## Project: Synergistic interactions between *Streptococcus pneumoniae* and respiratory viruses on bacterial pathogenesis

Co-infections with influenza virus and bacterial pathogens (e.g. *Streptococcus pneumoniae*) can lead to severe respiratory infections. Clinical evidence suggests that a similar synergy exists between *S. pneumoniae* (the pneumococcus) and other viruses that are more commonly major causes of respiratory infection and hospitalisation of young infants. Using *in vivo* models, this project will investigate the how respiratory viruses such as influenza, can 1) augment various aspects of pneumococcal pathogenesis and 2) how prevention strategies targeting one pathogen can indirectly impact the other.

### Project supervisor

Dr Catherine Satzke

### Project co-supervisor

Dr Sam Manna

### Project availability

- Honours

### Further information

<http://viin.org.au/member/catherine-satzke>



### **Project: Bacterial gene expression in pneumococcal pneumonia**

*Streptococcus pneumoniae* is the most common cause of community-acquired pneumonia, which is a leading killer of young children worldwide, and can also colonise the upper respiratory tract of healthy children. Our laboratory is interested in identifying genes involved in pneumonia pathogenesis, particularly those that are differentially expressed in disease vs colonisation. These genes could be candidates for novel prevention strategies and improved diagnostics for pneumococcal pneumonia. Using a combination of clinical samples collected from healthy children and pneumonia patients as well as in vitro assays, this project will examine pathogen gene expression and genomics using a variety of molecular methods.

#### **Project supervisor**

Dr Eileen Dunne

#### **Project co-supervisor**

Dr Catherine Satzke

#### **Project availability**

- Honours

#### **Further information**

<http://viin.org.au/member/catherine-satzke>

# Stinear group

**Contact:** Professor Tim Stinear  
**Email:** [tstinear@unimelb.edu.au](mailto:tstinear@unimelb.edu.au)

Number of vacancies available: 3



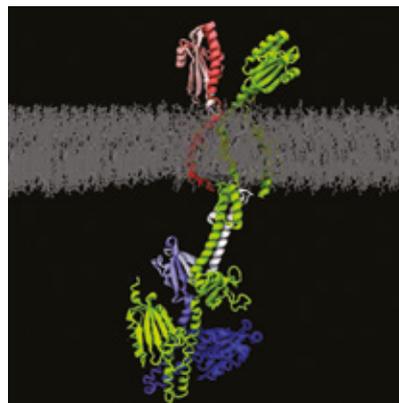
**Antimicrobial Resistance and Healthcare Associated Infections**



**Host-pathogen Interactions**



**Genomics**



Model of the essential *Staphylococcus aureus* two-component regulator, WalkR

The Stinear lab is full of fun-loving microbiologists who make mutants, uncover molecular mechanisms of pathogenesis, discover new antibiotics, make vaccines, create new diagnostic tests, track disease outbreaks, sequence bacterial genomes and expose dodgy science. Our research aims to understand bacterial pathogens in greater detail so that we can develop tools to detect, inhibit or control them. We collaborate with major hospitals and public health labs, so that our research can be rapidly implemented and used to benefit society. If this appeals to you, come and have a chat with our team.

## **Project: Understanding essential gene regulation in *Staphylococcus aureus***

Two component systems (TCS) enable bacteria to respond rapidly to the host environment. Among the 16 two-component systems in *Staphylococcus aureus*, only WalkR is essential, with clinical treatment failure linked to mutations within WalkR (leads to vancomycin resistance). Our laboratory has been investigating the molecular mechanism of WalkR function through the application of next generation DNA sequencing technologies such as RNAseq, ChIPseq, TNseq targeted mutagenesis and suppressor mutant screens. This project will apply the above techniques to determine the molecular basis WalkR essentiality.

### **Project supervisor**

Professor Tim Stinear

### **Project co-supervisor**

Dr Ian Monk

### **Project availability**

- PhD
- MSc
- Honours

### **Project: New drugs from old bugs**

Humans are currently involved in a biological arms race with antibiotic resistant bacteria, due to their worldwide dissemination and a lack of novel antibiotics in the drug discovery pipeline. However, despite being part of the problem, many bacteria are also capable of producing antibiotics. As part of this project, you will hunt for new antibiotics from a range of bacteria, including those in soil (using individual diffusion chambers as shown here: <https://youtu.be/YU5mPUF99BE>) and also human pathogens. Through this project you will learn a combination of microbiology, molecular biology and basic chemistry techniques, to find compounds to kill multi-drug resistant superbugs.

#### **Project supervisor**

Professor Tim Stinear

#### **Project co-supervisor**

Dr Sacha Pidot

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: Towards a new vaccine for Mycobacterium ulcerans infection (Buruli ulcer)**

Buruli ulcer is a neglected tropical disease caused by infection of subcutaneous tissue with Mycobacterium ulcerans, a close relative of Mycobacterium tuberculosis, the agent of human TB. In this project the student will use a novel infection model developed in the Stinear lab and an innovative adjuvant developed in the Jackson lab, to try and develop the world's first effective vaccine against Buruli ulcer.

#### **Project supervisor**

Professor Tim Stinear

#### **Project co-supervisor**

Professor David Jackson, Dr Brendon Chua

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: Finding the factors that make VRE such a successful hospital-adapted pathogen**

Enterococci emerged in terrestrial animals about 450 million years ago, and are frequent commensal bacteria in the human gut. In the past 50 years, pathogenic strains have emerged in our hospitals such as Enterococcus faecalis and Enterococcus faecium (VRE) that are highly persistent and resistant to multiple antibiotics. We have established a mouse model of VRE colonisation and RNAseq expression profiling to identify bacterial persistence factors. This project will apply molecular biology approaches to define factors essential for gut colonisation and persistence.

#### **Project supervisor**

Professor Tim Stinear, Professor Ben Howden

#### **Project co-supervisor**

Dr Glen Carter

#### **Project availability**

- PhD
- MSc
- Honours



### **Project: Applying synthetic biology to unravel the virulence of the hospital-adapted clones of *Staphylococcus epidermidis***

*Staphylococcus epidermidis* is a predominant coloniser of human skin, but also termed the “accidental pathogen”, as it can cause life threatening infections upon skin breach. Despite the diversity in *S. epidermidis* strains, the majority of infections are caused by a single sequence type (ST2). Until recently, this clone has been refractory to genetic manipulation. Through bioinformatic analysis of over 300 Australian/International isolates, we have developed techniques to genetically manipulate clinically relevant ST2 clones. Using synthetic biology, this project will develop CRISPR (gene deletion/knockdown), phage integrase vectors and TNseq to uncover the molecular basis of enhanced pathogenicity within ST2 clones.

#### **Project supervisor**

Professor Tim Stinear, Professor Ben Howden

#### **Project co-supervisor**

Dr Ian Monk

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: What makes a new bacterial pathogen tick?**

*Mycobacterium chimaera* recently burst into the consciousness of public health officials worldwide when it was discovered as the cause of serious post-surgical heart-valve infections and detected in the heater-cooler units used during open heart surgery. Where did this pathogen come from? Why has it spread globally? What makes it such an effective opportunistic pathogen? These questions will be addressed in this research project.

#### **Project supervisor**

Professor Tim Stinear

#### **Project co-supervisor**

Jessica Porter

#### **Project availability**

- PhD
- MSc
- Honours

# Strugnell group

**Contact:** Professor Richard Strugnell  
**Email:** rastru@unimelb.edu.au

Number of vacancies available: 1



Immunology



Host-pathogen Interactions



## Project: Diagnosing salmonella infections

The diagnosis of *Salmonella enterica* infections typically requires some sophisticated blood culture technology, which may not be available in low-income country settings where serious and often life-threatening *Salmonella* infections such as typhoid fever can be common. This project will examine new paradigms for the diagnosis of Salmonella disease. The issues of separating the more generalised inflammation observed in fever settings from the specific immune responses induced by Salmonella infections will be addressed in a murine model. Once proof-of-principle is established in the murine model, attempts will be made to study early-onset typhoid disease in humans. MBIomed project.

### Project supervisor

Professor Dick Strugnell

### Project co-supervisor

Dr Nancy Wang

### Project availability

- MSc

### Further information

<http://emedicine.medscape.com/article/231135-workup>

<https://www.ncbi.nlm.nih.gov/pubmed/24519873>



# Sutton group

**Contact:** Associate Professor Phil Sutton  
**Email:** psutton@unimelb.edu.au

Number of vacancies available: 1



Immunology



Host-pathogen Interactions



Public Health



Translational and Clinical Research



Discovery Research



The Mucosal Immunology research group at the Murdoch Children's Research Institute, is based in the Royal Children's Hospital on Flemington Road, Parkville. The core interests of our group involve studying the host pathogen interactions of bacterial infections at mucosal surfaces and the development of novel vaccine strategies. We have a particular focus on diseases caused by bacteria-induced inflammation such as cystic fibrosis, and gastric cancer caused by *Helicobacter pylori* infection.

## **Project: The immune response to infection in early cystic fibrosis**

Cystic fibrosis (CF) is a genetic disorder, resulting in death from respiratory failure. Disease begins in early life, with diminished lung function related to opportunistic infections. Immunity in the early CF lung is poorly studied despite inflammation playing a critical role in disease progression.

**AIM:** To characterise immunity in the lungs of CF children and how it changes with infection.

**APPROACH:** Lung immune cells will be phenotyped by flow cytometry and stimulated with bacterial pathogens, with cytokine responses measured by ELISA. Results will be related to patients' clinical/infection status.

**SIGNIFICANCE:** Characterising early CF lung immunity may identify potential therapeutic targets.

### **Project supervisor**

Associate Professor Phil Sutton

### **Project availability**

- Honours

# Tong group

**Contact:** Associate Professor Steven Tong  
**Email:** steven.tong@mh.org.au

Number of vacancies available: 3



Antimicrobial Resistance and Healthcare Associated Infections



Public Health



Epidemiology



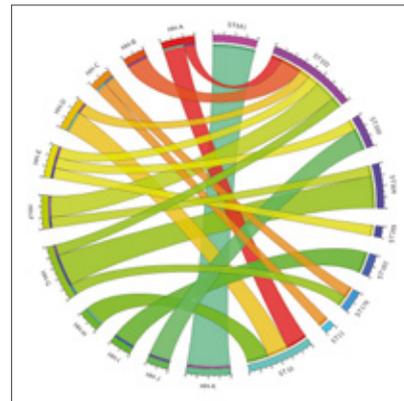
Translational and Clinical Research



Indigenous Health



Genomics



Distribution of Group A streptococcus genotypes in Aboriginal households.

The Tong group encompasses a multi-disciplinary group crossing bacterial and viral genomics, epidemiology, Indigenous health and clinical trials. We are committed to improving Indigenous health with partners in northern Australia, and developing capacity for conducting multi-centre clinical trials using novel methodologies. At the Doherty Institute, we collaborate extensively with the Epidemiology and mathematical modelling groups, and the Doherty Applied Microbial Genomics team.

## Project: Novel adaptive platform trials for *Staphylococcus aureus* bacteraemia

Bayesian adaptive platform trials are novel clinical trial methods that improve trial efficacy and allow multiple subgroups and treatments to be studied concurrently. This project will design and implement an adaptive platform trial for *Staphylococcus aureus* bacteraemia that will build on the infrastructure of a current trial for MRSA bacteraemia that is currently recruiting in 26 centres in Australia and overseas. The PhD student will define appropriate trial endpoints, perform trial simulations using Bayesian methods, and design the trial protocols.

### Project supervisor

Associate Professor Steven Tong

### Project availability

- PhD



## Tong group

### Project: Antimicrobial resistance in Indigenous communities

Indigenous Australians living in remote communities experience an unacceptably high burden of infectious diseases necessitating frequent antibiotic use. The burden of infection, domestic crowding and use of antibiotics drives the emergence of antimicrobial resistance. Rates of MRSA in some communities now constitute over 50% of *Staphylococcus aureus* infections. This project will integrate information from antibiotic-prescribing audits, laboratory surveillance of antimicrobial resistance for key bacteria, and detailed microbiome studies in Indigenous communities, to understand the drivers of antimicrobial resistance and potential means to reduce the emergence and transmission of antimicrobial resistance.

#### Project supervisor

Associate Professor Steven Tong

#### Project co-supervisor

Professor Jodie McVernon  
Dr Katherine Gibney

#### Project availability

- PhD
- MSc

### Project: Genomic epidemiology and antimicrobial resistance of Group A *Streptococcus* and *Staphylococcus aureus* in remote Indigenous communities

Skin infections cause a significant burden of disease in Indigenous communities. This project will analyse the whole genome sequences of hundreds of Group A *Streptococcus* and *Staphylococcus aureus* strains collected from northern Australia to understand the dynamics of transmission, disease associations, and emergence of antimicrobial resistance. The isolates include those collected over more than 20 years in northern Australia, as well those to be collected in planned prospective studies to address specific questions relating to the dynamics of carriage versus infection at skin and throat sites, and the impact of long-term antibiotic use.

#### Project supervisor

Associate Professor Steven Tong

#### Project co-supervisor

Professor Jodie McVernon  
Dr Mark Davies

#### Project availability

- PhD
- MSc
- Honours



# Villadangos group

**Contact:** Professor Jose Villadangos  
**Email:** j.villadangos@unimelb.edu.au

Number of vacancies available: 1-3



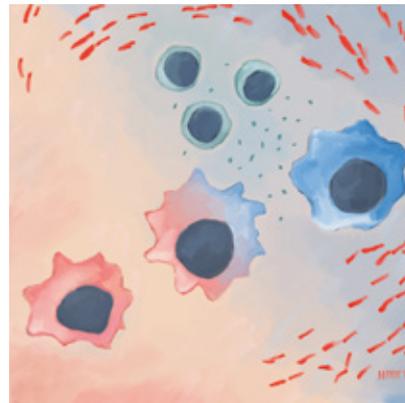
Immunology



Host-pathogen Interactions



The Villadangos group combines immunology, biochemistry and cell biology to study how the adaptive immune system detects pathogens and cancer, a process called Antigen Presentation. Their research is applicable to vaccine development, treatment of critically ill patients and the fight against cancer.



Infection and trauma cause dendritic cell paralysis and lethal immunosuppression

## Project: MR1 – a molecular alarm system for intracellular bacterial infection

MR1 functions as a molecular alarm system to alert the immune system that an intracellular bacterial infection is taking place. It does this by capturing metabolite byproducts from bacteria and presenting them at the cell surface to activate a highly abundant T cell subset, called mucosal-associated invariant T (MAIT) cells, which then secrete inflammatory cytokines to initiate protective immunity. It is currently unknown how the metabolites traffic from the microbes to MR1. This project will investigate these questions using CRISPR/Cas9 gene editing, biochemistry and microscopy, and will be in collaboration with the Strugnell laboratory using unique *Salmonella* Typhimurium strains.

### Project supervisor

Dr Hamish McWilliam

### Project co-supervisor

Professor Jose Villadangos

### Project availability

- PhD
- Honours



## Villadangos group

### **Project: Immunoregulatory functions of the MARCH family of ubiquitin ligases**

Protein localisation in eukaryotic cells is governed by regulatory pathways which remain poorly understood. These regulate changes in protein expression or localization in response to cues such as the presence of pathogens. Addition of the small protein ubiquitin to membrane proteins by the MARCH family of ligases is an important mechanism to control membrane immunoreceptors. This project will employ biochemistry, microscopy, proteomics, and CRISPR-Cas9 to characterise the function of the MARCH family; identify novel MARCH substrates; and characterise the machinery involved in ubiquitination by MARCHs. We aim to develop novel therapeutic approaches to fight infection based on manipulating ubiquitination.

#### **Project supervisor**

Prof. Jose Villadangos

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: Understanding the mechanisms that impair anti-tumour Adoptive Cell Therapy**

Tumour cells express neo-antigens that can be recognized by cytotoxic T lymphocytes (CTL) which can be either isolated from tumour biopsies and expanded and inoculated to kill cancer. Unfortunately, often the tumour "fights back" and inactivates the CTL, compromising the therapy. Using a mouse model of lymphoma, we are performing studies to improve outcomes. We can reproduce successful vs impaired CTL immunotherapy, and have identified genes potentially involved in each outcome. The aims of this project will be to identify further genes that control the outcome of adoptive cell therapy, and characterise the interactions between T cells and the tumour.

#### **Project supervisor**

Prof. Jose Villadangos

#### **Project co-supervisor**

Dr. Sathish Selvaraj

#### **Project availability**

- PhD
- MSc
- Honours

### **Project: How infection and trauma cause dendritic cell paralysis and lethal immunosuppression**

Systemic Inflammatory Response Syndrome (SIRS) is a common condition associated with systemic or severe infections or trauma. After inflammatory cytokines are released to activate the immune system, a period of immunosuppression often follows that can last for weeks. Impairment of dendritic cells (DC), the primary initiators of T cell immunity, plays a prominent role in this immunosuppression. There is a need to characterise the mechanisms that impair DC function following SIRS. In this project we will use mouse models of infection or trauma to investigate the mechanisms that cause DC paralysis and to develop therapies to prevent it.

#### **Project supervisor**

Prof. Jose Villadangos

#### **Project co-supervisor**

Dr. Jason White

#### **Project availability**

- PhD
- MSc
- Honours









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