Doherty Institute

Research Projects

2019

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, (Doherty Institute) 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 (in part)
- The Doherty Institute Department

The Royal Melbourne Hospital

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

Study at the Doherty Institute

Through the University of Melbourne, 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, they may be based at affiliated institutes with a co-supervisor at the Doherty Institute, including (but not limited to) the Murdoch Children's Research Institute and Sequiris. Research projects are available through several departments at the University of Melbourne including the Department of Microbiology and Immunology, the Department of Medicine and the Doherty Department.

The 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. The Department delivers specialised courses in bacteriology, virology and immunology along with more generalist infection and immunity services.

The Department of Medicine also sits within the School of Biomedical Sciences and offers projects through the Doherty Institute that focus on malaria, global and maternal and child health and infectious diseases services.

The Doherty Department sits within the Faculty of Medicine, Dentistry Institute and Health Sciences. Projects available under the Doherty Department focus on HIV and clinical and translational research in infectious diseases across Indigenous health, public health and host genomics.

To find out more, email Marie Greyer:
doherty-phdprogram@unimelb.edu.au

Honours program

Honours is a fourth year undergraduate course that involves coursework and an intensive research project. Bachelor of Biomedicine (BBiomed) and Bachelor of Science (BSc) students who obtain faculty honours in their third year will be welcome to join as BBiomed or 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

Postgraduate training at the Doherty Institute allows students to develop advanced skills in carrying out independent research on a particular topic under academic supervision. Graduate research students will learn from global leaders in infection and immunity, with access to high calibre facilities.

Doherty Institute PhD Program

This Program is available to all graduate researchers based at the Doherty Institute. The Program offers training opportunities beyond the immediate research topic, including a diverse range of workshops, seminars, and internships delivered by our partners in the biopharmaceutical industry. Students can engage with experts including patent attorney firms and large pharmaceutical companies, learn about the issues in taking discoveries to market and receive advice for research and career opportunities beyond the Institute research environment.

Program activities are designed to support students with their current research skills, as well as professional development and transferable skills.

PhD opportunities for clinicians

There are numerous opportunities for clinicians to undertake PhD training at the Doherty Institute, ranging from basic laboratory sciences, to clinical, translational, public health or health services research.

The Doherty Institute is home to a busy clinical service in infectious diseases and two large public health diagnostic laboratories. There are many clinician scientists at the Institute who head research groups focusing on antimicrobial resistance and stewardship, indigenous health, emerging infectious diseases, public health, influenza, tuberculosis, malaria, HIV and viral hepatitis.

As the world of immunotherapies expands and becomes a growing component of modern day clinical practice, there are outstanding opportunities for clinicians to train in fundamental immunology, which is now of high relevance to many medical and surgical specialties, including infectious diseases, oncology, rheumatology, gastroenterology, transplantation and dermatology. Opportunities to gain expertise in genomics, systems biology and bioinformatics as well as epidemiology and surveillance in relation to infectious disease are also available.

Our partnerships within the Melbourne Biomedical Precinct, across Australia and our many international collaborations within the Asia-Pacific region also offer opportunities for exciting, multi-site research projects. There is also the opportunity for spending some of your PhD in another laboratory or country, including low and middle income countries in the region.

Choosing a supervisor and research area

A critical element of success is choosing a research area that interests you. Departmental websites 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 as well as current or previous students. It is one thing to be interested in the project but you need to get along with your supervisor too. If possible, try to get some work experience in the lab to get an idea about the environment.

How to apply

Honours and Masters

1. For more detailed information, visit the Faculty of Medicine, Dentistry and Health Sciences Honours (MDHS) webpage: mdhs-study.unimelb.edu.au/degrees/honours/overview

   Or Masters of Biomedical Science webpage: mdhs-study.unimelb.edu.au/degrees/master-of-biomedical-science/overview
2. Visit the Department of Microbiology and Immunology webpage for further information: biomedicalsciences.unimelb.edu.au/departments/microbiology-Immunology/study/opportunities-for-honours-students
3. Review the list of prospective projects and supervisors in this handbook or online at doherty.edu.au/education/research-project
4. Identify projects of interest and contact the project supervisor to explain your research interests and provide your curriculum vitae (CV) and academic transcript. 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 the entry requirements of the University of Melbourne).
5. Lodge an online application to the University of Melbourne for admission to Honours via mdhs-study.unimelb.edu.au/degrees/honours/apply-now#apply-now
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 four project preferences. You should only preference projects after contacting the relevant supervisor(s), as supervisors are unlikely to select students without first speaking with them.

PhD and MPhil

1. Review the list of prospective projects and supervisors in this handbook or online at doherty.edu.au/education/research-project.
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: futurestudents.unimelb.edu.au/admissions/applications/research
4. More information on PhDs visit: mdhs-study.unimelb.edu.au/degrees/doctor-of-philosophy/overview
5. More information on MPhil visit: mdhs-study.unimelb.edu.au/degrees/master-of-philosophy/overview

Scholarships

Honours

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 automatically considered for a Department of Microbiology and Immunology Honours Scholarship of $5000.

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 will automatically be considered for an Frances Elizabeth Thomson Trust Scholarship. The Scholarship will award eligible students with a one-off payment of $5,000. mdhs.unimelb.edu.au/study/scholarships/n/frances-elizabeth-thomson

Graduate degrees

The Melbourne Scholarships Program is one of the most generous and comprehensive in Australia, with a wide range of scholarships available for domestic and international students. There are many different types of scholarships available, with some varying in value, duration and eligibility. Most University of Melbourne graduate students have scholarships to aid with living expenses and course fees. Some scholarships also assist with relocation fees and insurance costs whilst studying at the University of Melbourne.

Graduate Research Scholarships for domestic and international students are awarded on a competitive basis. If successful, students must also meet the entry requirements for a Doctoral degree at the University of Melbourne. More details on the different types of scholarships available, what they cover and eligibility can be found here: scholarships.unimelb.edu.au/awards/graduate-research-scholarships

Contacts:

Honours Coordinators

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Professor Katherine Kedzierska
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Postgraduate Coordinators

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Research projects

Barrow group

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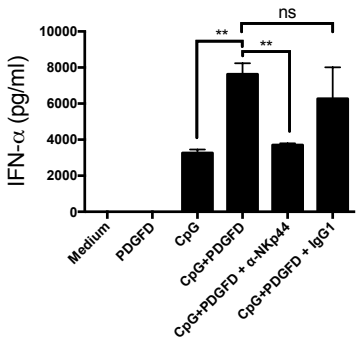
Number of vacancies available 2

Immunology **Viral Infectious Diseases** **Host-pathogen Interactions**

Discovery Research



PDGF-D binding to NKp44 costimulates CpG-DNA-induced IFN-I secretion by pDCs.

The Barrow group is interested in a new avenue of immunological research termed growth factor surveillance. Growth factors (GFs) are over-expressed by tumours to promote angiogenesis, stromal reaction and tumour growth. Moreover, many viruses encode GFs that are required for viral infectivity in vivo. The goal of our lab is to understand how GF surveillance receptors control immune responses to tumours and pathogens with the ultimate aim of identifying critical nodes in these pathways that can be exploited for cancer immunotherapy and vaccine development.

Project: Molecular basis for growth factor immune-surveillance in plasmacytoid dendritic cells

Many viruses encode GF homologues that induce proliferative lesions required for viral pathogenesis. We have recently shown the ITAM receptor NKp44 drives cancer immune-surveillance by sensing platelet-derived growth factor (PDGF)-D. Many viruses encode GF homologues and the gene for PDGF-D is associated with interferon levels, suggesting polymorphisms in GF immune-surveillance pathways are driven by selective pressure imposed by viruses. PDGF-D binding to NKp44 enhances interferon secretion by plasmacytoid dendritic cells, suggesting ITAM receptors sense GFs induced upon virus infection to enhance Toll-like receptor (TLR) signaling. The project will identify the molecules and sets of conditions that integrate ITAM and TLR signalling and constitute the basis for 'infectious GF immune-surveillance' in innate immune cells.

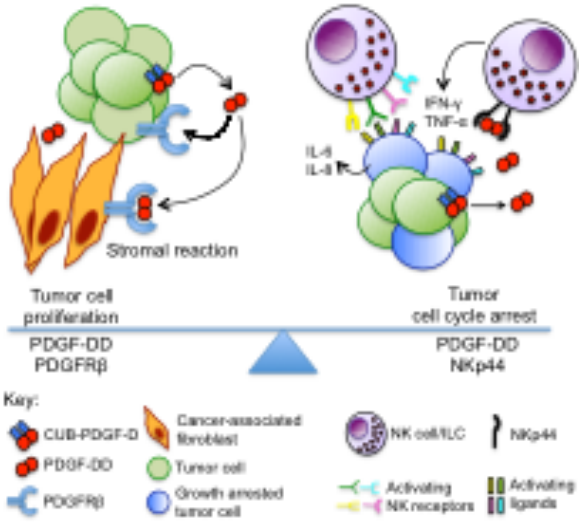
Project supervisor
Dr Alexander Barrow

Project co-supervisor
Professor Andrew Brooks

Project availability
- PhD
- MSc
- Honours

Link for further information
cell.com/cell/pdf/S0092-8674(17)31388-0.pdf

Barrow group



Many tumours secrete PDGF-DD to promote cellular proliferation, epithelial-mesenchymal transition, stromal reaction and angiogenesis through autocrine and paracrine PDGFRβ signalling. NK cells, ILC1 and ILC3 express the activating receptor NKp44 that can sense the expression of PDGF-DD by cancer cells (and potentially also infected cells). PDGF-DD triggers NK cell secretion of IFN-γ and TNF-α that induce tumour cell cycle arrest. Indeed, some pathogens can only infect proliferating cells. IFN-γ and TNF-α also induce the expression of ligands for activating NK cell receptors on growth-arrested cancer cells further enhancing NK cell immunosurveillance.

Project: Molecular basis for growth factor surveillance in natural killer and innate lymphoid cells.

We have recently shown the activating ITAM receptor NKp44 drives cancer immuno-surveillance by sensing platelet-derived growth factor (PDGF)-D. PDGF-D engagement of NKp44 triggered IFN-γ and TNF-α secretion from NK cells and ILC1 and TNF-α secretion from ILC3, which induced tumour cell growth arrest. Interestingly, several alternatively spliced NKp44 transcripts have been reported including an ITIM-encoding NKp44 isoform that is predicted to be inhibitory and is associated with poor prognosis in cancer. This project aims to determine the expression and modes of signalling of the different NKp44 isoforms in NK cells, ILC1 and ILC3 and how this impacts their effector functions in cancer models.

Project supervisor
Dr Alexander Barrow

Project co-supervisor
Professor Andrew Brooks

Project availability
- PhD
- MSc
- Honours

Link for further information
cell.com/cell/pdf/S0092-8674(17)31388-0.pdf

Bedoui group

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Number of vacancies available 2

Immunology

Host-pathogen Interactions

Discovery Research

The Bedoui group uses models of viral and bacterial infections to study how the innate and the adaptive immune systems interact. Key foci are to understand how innate cells sense pathogens and how this information is integrated into T cell responses that control infections and cancer.

Project: The role of microbiota and short chain fatty acids in improving anti-cancer potential of killer T cells

Recent studies suggest that cancer patients with reduced microbiota diversity respond poorer to T cell-based immunotherapy, but the underlying mechanisms and therapeutic consequences are largely unexplored. Ongoing work in the lab has revealed a previously unappreciated role for microbiota-derived short chain fatty acids (SCFA) in promoting anti-cancer potential in killer T cells. We are looking for highly motivated students to decipher the mechanisms that enable SCFA to support memory potential in effector CD8+ T cells and to test if SCFA can be used therapeutically to improve adoptive T cell therapy in cancer.

Project supervisor
Associate Professor Sammy Bedoui

Project co-supervisor
Dr Annabell Bachem

Project availability
- PhD

Biggs group

Contact name Dr Andre Mu
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Number of vacancies available 1

Discovery Research | Global Health | Genomics

The Biggs group are interested in the interactions between the host, the gut microbiome and the environment, the role of the microbiome in child growth and development, and the long-term effects on adult health.

Project: Understanding the impact of the gut microbiota on health outcomes in young South East Asian children.

The microbiome has been shown to play an important role in nutritional and child growth outcomes, as well as cognitive function, and social behaviours. The first two to three years of life represents a crucial period for establishing a healthy microbial community (microbiota), and microbially-derived functional genes (microbiome). This project will use methods of gDNA extraction, high throughput sequencing of the 16S rRNA gene, whole community genomic sequencing and metabolic profiling, and international databases to analyse and characterise microbial community composition, diversity, maturity and function on (already collected) stool samples from young children residing in North Vietnam. Through these methods we will aim to characterise the gut microbiome of young Vietnamese children, identify early life determinants of the gut microbiome profile, assess whether the functional gene profile in these cohorts is associated with child health outcomes and perform hypothesis-driven studies of selected samples to link populations within the microbiota to functional outcomes. There will also be scope to develop related projects that aim to advance the understanding of the role of the microbiome in health and disease.

Project supervisor

Dr Andre Mu

Project co-supervisors

Dr Sarah Hanieh, Professor Beverley Biggs

Project availability

- PhD

Davies group

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Number of vacancies available 3

Antimicrobial Resistance and Healthcare Associated Infections

Host-pathogen Interactions

Discovery Research

Global Health

Indigenous Health

Genomics

The Davies group aims to apply genome sequencing methodologies and bioinformatics approaches to understand 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 research questions such as: is there a genetic difference between strains causing different disease manifestations? What is driving the emergence and dissemination of bacterial pathogens? Do host immune factors govern disease severity? Our research closely aligns with key international collaborators including the Wellcome Trust Sanger Institute in the United Kingdom.

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 that of other geographical regions. Through linking genomics with epidemiology, we aim to examine the evolutionary relationship between disease causing Streptococcus pyogenes clones within remote communities of Australia. Furthermore, we will apply statistical genetic models to identify genetic signatures associated with different disease stats and/or 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

Davies group

Project: Application of systems genomics 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 looking at immunogenetics within a controlled human infection.

Project supervisor

Dr Mark Davies

Project availability

- PhD
- Honours

Project: Unravelling the drivers of scarlet fever pandemics

Outbreaks of scarlet fever associated with multi-drug resistant Group A Streptococci (GAS) 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
- Honours

Project: Evolution of streptococcal pathovars

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
- Honours

Project: Using genomics to investigate the transmission of skin pathogens and antimicrobial resistance in a 'One Health' setting

Remote Indigenous Australian communities experience disproportionately high levels of skin disease associated with the bacterial pathogens, methicillin-resistant Staphylococcus aureus (MRSA) and Streptococcus pyogenes. Our preliminary research indicates that dogs in remote Indigenous communities also carry MRSA more commonly than dogs in urban settings. A significant knowledge gap exists as to the role of household animals in the maintenance and transmission of skin pathogens in remote Australian communities. This project aims to use bioinformatics approaches to investigate the transmission of skin pathogens between humans and animals in areas of high disease burden.

Project supervisor

Dr Mark Davies

Project co-supervisors

Dr Kate Worthing, Associate Professor Steven Tong

Project availability

- PhD
- MSc
- Honours

Fazakerley group

Contact name Dr Lukasz Kedzierski
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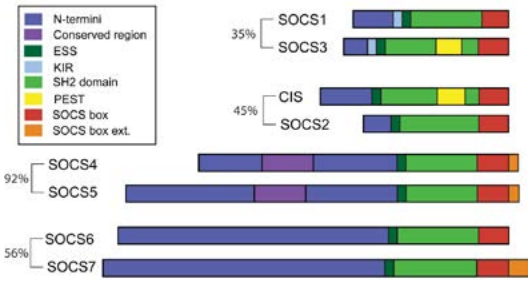
Number of vacancies available 2

Immunology **Viral Infectious Diseases** **Host-pathogen Interactions**

Discovery Research



Schematic structure of SOCS proteins. The SOCS proteins are characterised by a functional SH2 domain and C-terminal SOCS box domain.
The N-terminus is variable in length and amino acid sequence. Some members of the family share a high degree of homology (figure courtesy of Dr Ed Linossi, Walter and Eliza Hall Institute).

The Fazakerley group's main interest is in the pathogenesis of infections caused by RNA viruses, in particular vector-borne (arbovirus) alphaviruses infections of the central nervous system and insect vectors. Our main focus is to dissect the immune mechanisms during viral encephalitis and virus persistence in the central nervous system. We also investigate the arthropod responses to alphaviruses and study their transmission in mosquito vectors.

Project: Role of suppressor of cytokine signalling proteins in viral encephalitis

The suppressor of cytokine signalling (SOCS) proteins are key negative regulators of the JAK-STAT pathway and are responsible for controlling cytokine networks involved in immune response and inflammation. SOCS are expressed in the central nervous system (CNS) and by cells infiltrating the CNS during infection, and have a potential to impact the immune responses in the brain. We have recently shown that SOCS4- and SOCS5-deficient mice have different susceptibility phenotypes to Semliki Forest virus infection and that the virus RNA persists in the brain, and infectious virus can be reactivated following immunosuppression. This project aims to explore a role of SOCS4 and SOCS5 during SFV induced encephalitis in a mouse model.

Project supervisor

Dr Lukasz Kedzierski

Project co-supervisor

Professor John Fazakerley

Project availability

- Honours

Fazakerley group

Aedes aegypti mosquito, a common vector for alphaviruses including chikungunya and Semliki Forest virus.

Project: Vertical transmission of Ross River virus in mosquito vectors

Alphaviruses such as Ross River virus, chikungunya and Semliki Forest virus are transmitted by mosquito vectors between susceptible vertebrate hosts. In vertebrates, these viruses usually cause acute infections characterised by high virus production and development of disease symptoms. By contrast, when a mosquito becomes infected by an alphavirus (usually by a blood-meal), the acute infection does not show any evident disease symptoms that affect mosquito fitness. Moreover, the mosquito becomes persistently infected with virus and it is able to transmit it for the rest of its life. In addition, it has recently been suggested that vertical transmission of alphaviruses might play a role in maintaining the virus circulating within 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 alphaviruses co-infecting the same mosquito. Tools and techniques being used will include recombinant viruses, dissections, microscopy, cell culture and insectary work.

Project supervisor

Dr Julio Rodriguez-Andres

Project co-supervisor

Professor John Fazakerley

Project availability

- Honours

Godfrey group

Contact name Dr Daniel Pellicci
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Number of vacancies available 1

Immunology

Translational and Clinical Research

Discovery Research

Global Health

The Godfrey group 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.

Link for further information
ncbi.nlm.nih.gov/pubmed/26482978

Project: Understanding the role of unconventional T cells in the immune response to Mycobacterium tuberculosis

CD1-restricted T cells play a role in cancer, autoimmunity and infection. Most studies have focused on group 2 CD1d-restricted natural killer T cells, whereas much less is known about T cells restricted to group 1 CD1 molecules (CD1a, CD1b and CD1c). Group 1 CD1 molecules present lipid antigens to T cells to initiate an immune response. This project utilises novel CD1 tetramers that we have developed to characterise tuberculosis-specific T cells from Mycobacterium tuberculosis infected individuals and from BCG vaccinated donors. These studies will lay the foundation for understanding the role of CD1-restricted T cells in human disease.

Project supervisor
Dr Daniel Pellicci

Project co-supervisors
Professor Dale Godfrey, Professor Nigel Curtis, Dr Nicole Messina

Project availability
- Honours

Heath group

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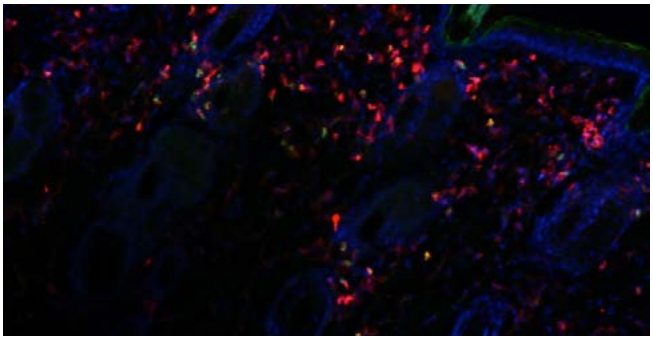
Number of vacancies available 1

Immunology

Host-pathogen Interactions

Discovery Research



Malaria-specific CD4 T cells (green) and endogenous CD4 T cells (red) in the skin with skin cell nuclei (blue) demonstrating the architecture of the hair follicles, the dermis and the epidermis of the skin

The Heath group is interested in the immune response to pathogens, particularly to malaria, which is still a major cause of mortality worldwide. We study T cell responses with the aim of improving vaccine strategies and focus on T cell responses in the skin, the liver and lymphoid organs including the spleen. Our lab recently discovered a population of resident memory T cells within the liver that are capable of protecting against malaria infection. These and other cells are currently being studied.

Project: CD4 T cells for protection against malaria infection in the skin

Plasmodium parasites are extremely complex pathogens, with a life cycle involving multiple stages within the mosquito vector and the mammalian host. An ideal vaccine for malaria would induce immunity against each of the different stages of the parasite's development within the host, including in the skin at the time of transmission. This project will determine if Plasmodium-specific CD4 T cells can protect against infection in the skin following intradermal injection or mosquito bite challenge. We will then determine the optimal Th phenotype for this protection. This project will use advanced immunological techniques including flow cytometry, and intravital imaging.

Project supervisor

Dr Lynette Beattie

Project availability

- PhD
- MSc
- Honours

Howden group

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Number of vacancies available 3

Antimicrobial Resistance and Healthcare Associated Infections

Host-pathogen Interactions

Public Health

Epidemiology

Genomics

The Howden group is embedded in the state public health laboratory - the Microbiological Diagnostic Unit Public Health Laboratory (MDU PHL) - 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 and antimicrobial resistance

The gut microbiota plays an important role in susceptibility to colonisation (and infection) with antimicrobial resistant pathogens. This study will utilise high-throughput sequencing, metagenomic analyses and culturomics to interrogate microbial population determinants of susceptibility to antimicrobial resistant pathogens (vancomycin-resistant Enterococci and carbapenem-resistant Klebsiella spp.). The study will utilise murine models of gut colonisation, complemented with samples from hospitalised patients. The expected outcomes from this study include developing skills in laboratory-based and bioinformatic techniques in microbiome and antimicrobial resistance studies.

Project supervisors

Professor Benjamin Howden, Dr Glen Carter

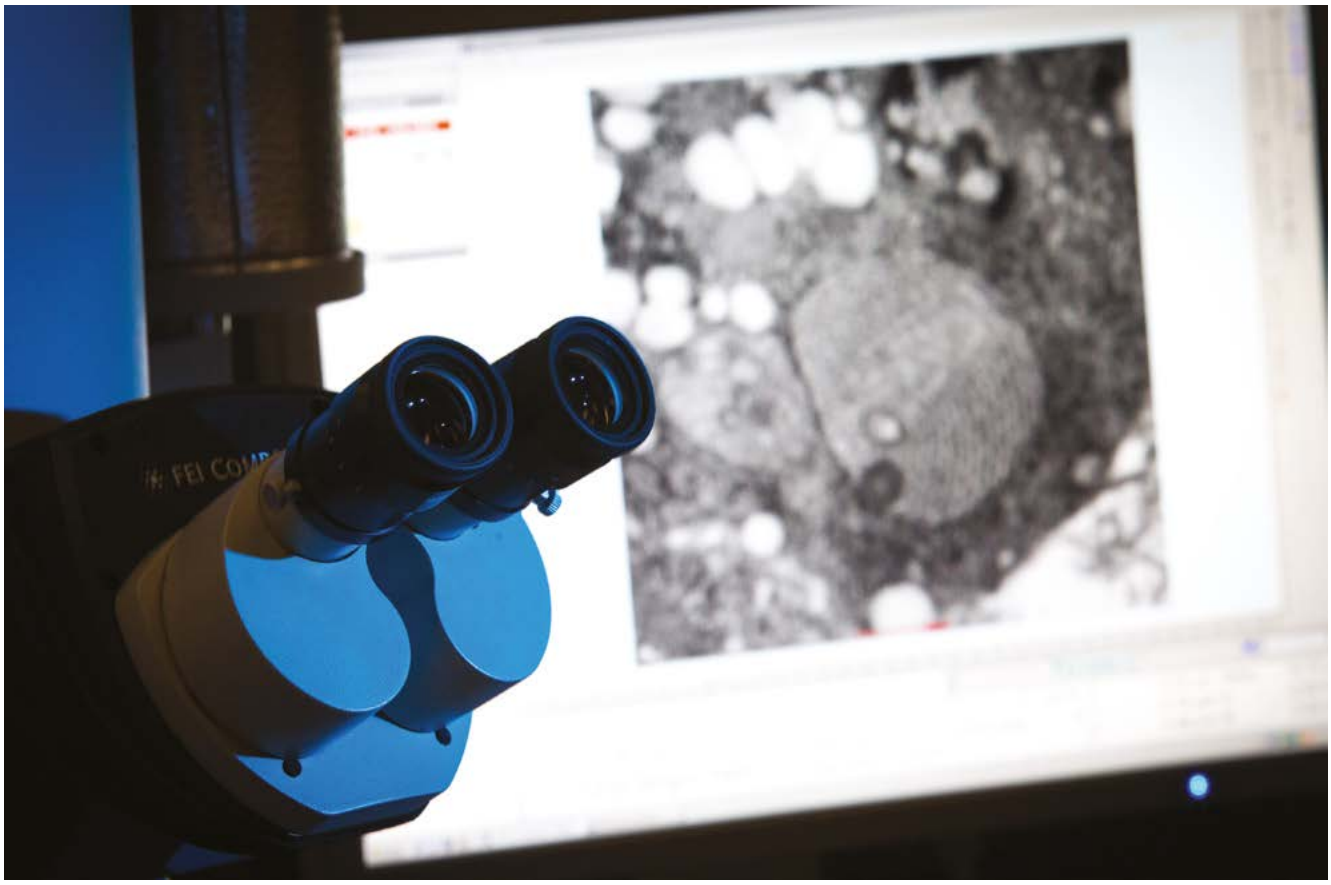
Project co-supervisors

Professor Tim Stinear, Dr Andre Mu

Project availability

- PhD
- MSc
- Honours

Howden group



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 supervisors

Professor Benjamin Howden, Professor Tim Stinear

Project co-supervisor

Dr Glen Carter

Project availability

- PhD
- MSc
- Honours

Project: Defining the impact of antibiotic resistance and convergent evolution 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, and has identified potentially important convergent mutations in Staphylococcus aureus. 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 evolution, resistance, virulence and host immunity in this important human pathogen.

Project supervisors

Professor Benjamin 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 Staphylococcus 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 Benjamin Howden

Project co-supervisor

Sarah Baines

Project availability

- PhD
- MSc
- Honours

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 Benjamin Howden

Project co-supervisor

Dr Jason Kwong

Project availability

- PhD
- MSc
- Honours

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 PHL, and with 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 supervisors

Professor Benjamin Howden, Dr Jason Kwong

Project availability

- PhD
- MSc
- Honours

Project: Application of microbial genomics in public health

Doherty Applied Microbial Genomics and the MDU PHL have recently commenced a large National Health and Medical Research Council funded Partnership Project with the Victorian Department of Health and Human Services, to investigate the role of microbial genomics in the surveillance and control of communicable diseases across four themes (antimicrobial resistance, sexually-transmitted infections, foodborne diseases and environmental pathogens). The program is underpinned by excellence in public health microbiology, and a large, well-established and internationally recognised bioinformatics team, together with a strong and productive relationship with the Health Protection Branch of the Victorian Department of Health and Human Services. The project is looking for highly motivated students with excellent track records to undertake a PhD in this area to contribute to a collaborative study, and the resulting implementation of this technology as an important tool in public health. These positions would be suitable for prospective students with experience in microbiology/molecular biology, epidemiology, bioinformatics/computer science and public health more broadly. Opportunities exist to examine the role of genomics across all themes outlined above.

Project supervisor

Professor Benjamin Howden

Project availability

- PhD

Kallies group

Contact name Professor Axel Kallies
Email address axel.kallies@unimelb.edu.au

Number of vacancies available 2

Immunology **Viral Infectious Diseases** **Host-pathogen Interactions**

Translational and Clinical Research

The work of the Kallies group 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 antigens, leading to impaired T cell responses. Thus, improving T cell functionality using immunotherapy 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 to 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-supervisors

Dr Sarah Gabriel, Dr Daniel Utzschneider

Project availability

- PhD
- Honours

Kedzierska group

Contact name Professor Katherine Kedzierska
Email address kkedz@unimelb.edu.au

Number of vacancies available 2

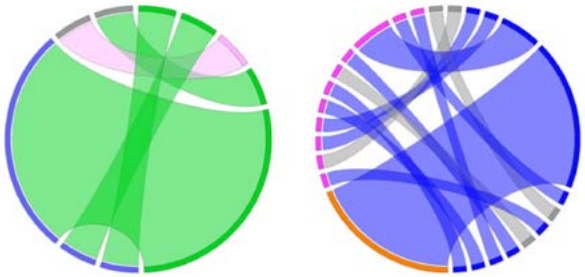
Immunology

Viral Infectious Diseases

Discovery Research

Indigenous Health

Translational and Clinical Research



Tcell receptor repertoires towards novel influenza epitopes.

The Kedzierska group has a strong international profile in human immunology, with a major focus on universal broadly-protective T cell immunity to seasonal, pandemic and avian influenza viruses. The main goals are to identify key correlates of severe and fatal influenza disease in high-risk groups, and to understand mechanisms underlying generation of optimal immunity to influenza viruses in young children, adults, the elderly, pregnant women, hospitalised patients and Indigenous Australians. Our studies intend to improve vaccine and therapeutic designs to protect against severe influenza, with possible applications to other infectious diseases and tumours.

Project: Generation of protective immunity against severe influenza disease in Indigenous populations

Hospitalisation rates and mortality from influenza are increased in Indigenous populations, especially when new viruses emerge. There is a need for vaccines which generate immunity across distinct influenza strains and protect vulnerable populations. Long-lasting immunity can be elicited by killer T cells recognising conserved viral regions. However, T cell responses are restricted by an individual's human leukocyte antigen (HLA) and specific HLA variants vary across ethnicities. Here, novel influenza T cell targets will be identified for HLA-A*1101, one of the most common HLAs in Indigenous and Asian populations. This project forms a part of a large-scale study aimed at designing and assembling a universal T cell-based influenza vaccine.

Project supervisor

Professor Katherine Kedzierska

Project co-supervisors

Dr Bridie Clemens, Luca Hensen

Project availability

- MSc
- Honours

Kedzierska group

Project: Understanding immunity towards seasonal influenza vaccines

Annual influenza vaccinations provide the most effective strategy to blunt the impact of seasonal influenza infections and protect from severe disease. However, the efficacy of influenza vaccines varies from year to year and between individuals. Our recent study (Koutsakos M et al, Science Translational Medicine, 2018) dissected immunity towards seasonal influenza vaccine in healthy adults and identified that T follicular helper cells, antibody-secreting cells and memory B cells are associated with successful influenza vaccination. The current project provides exciting opportunities to understand immunity to seasonal influenza vaccines in individuals at high risk of severe disease, specifically the elderly and immunosuppressed patients.

Project supervisor

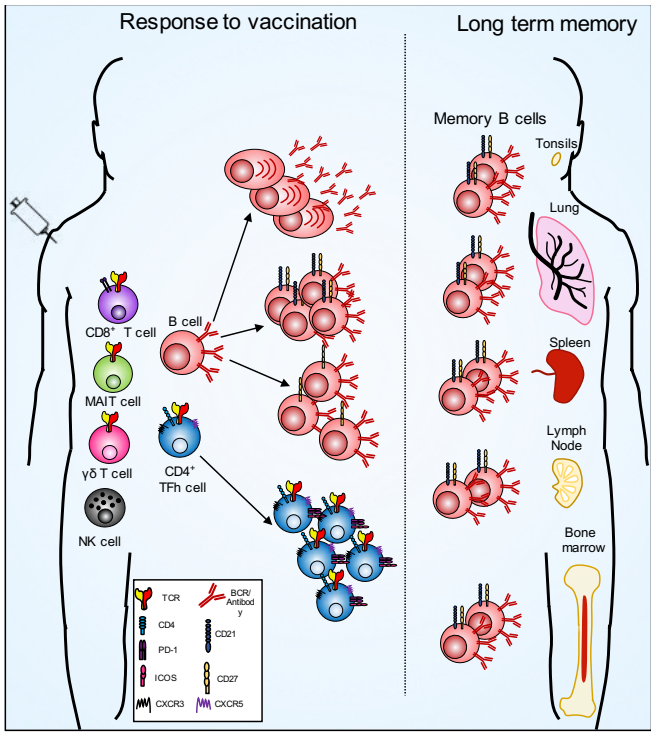
Professor Katherine Kedzierska

Project co-supervisor

Dr Oanh Nguyen

Project availability

- PhD
- MSc
- Honours



Human immune responses to the current influenza vaccine.

Project: Defining the reactogenic properties of influenza vaccines

Vaccination walks a fine line between potency and reactogenicity. We recently identified that influenza B viruses within the current influenza vaccines have the potential to trigger cytokine production contributing to the adverse events that occur post vaccination. This project provides the opportunity to conduct bioinformatics analysis of influenza genes, create influenza viruses by molecular rescue that comprise genes from different subtypes, culture, purify and test these viruses for their reactogenic potential. The information will be used to help develop less reactogenic influenza vaccines. Work will be conducted at both the Doherty Institute and Seqirus.

Project supervisor

Professor Katherine Kedzierska

Project co-supervisors

Associate Professor Steven Rockman, Marios Koutsakos

Project availability

- MSc
- Honours

Project: Understanding the evolution of influenza viruses by herd and host immunity

Influenza viruses evolve to escape herd immunity. For over four decades we have been developing monoclonal antibodies to influenza viruses. Examination of these antibodies with drifted H3N2 strains demonstrated, for the first time, the recurrence of specific epitopes. The project will provide the opportunity to conduct experiments to determine whether individuals pre and post infection have developed antibodies to these recurrent epitopes. With the use of human purified immunoglobulin, viruses will be stressed to escape and these escape mutants will be mapped and compared to natural viral evolution. Work will be conducted at both the Doherty Institute and Seqirus.

Project supervisor

Professor Katherine Kedzierska

Project co-supervisors

Associate Professor Steven Rockman, Marios Koutsakos

Project availability

- MSc
- Honours

Kent group

Contact name Dr Amy Chung
Email address awchung@unimelb.edu.au

Number of vacancies available 3

Immunology

The Kent group has an interest in understanding how the immune response can be harnessed in the control of infectious pathogens including HIV, Mycobacterium tuberculosis and influenza. This includes understanding non-conventional T cells and how they are impacted by HIV infection despite the fact that they are not target cells for HIV replication. We use animal models to investigate ways to manipulate these cells and to understand how they are regulated during viral infection. We also examine how antibodies can instruct the innate immune system to attack invading pathogens through their Fc regions. Our research aims to understand the mechanisms behind these antibodies in order to guide the development of more effective antibody therapeutics and vaccines.

Project: Identifying macaque MAIT cells using MR1 tetramers

This project will make use of a newly developed macaque MR1 tetramer to characterise MR1-restricted mucosal-associated invariant T (MAIT) cells in pigtail macaques. It will involve defining surface phenotype, co-receptor expression and antigen-reactivity of tetramer-reactive cells in peripheral blood and tissue samples, and will use a variety of molecular and flow cytometry-based techniques.

Project supervisor

Professor Stephen Kent

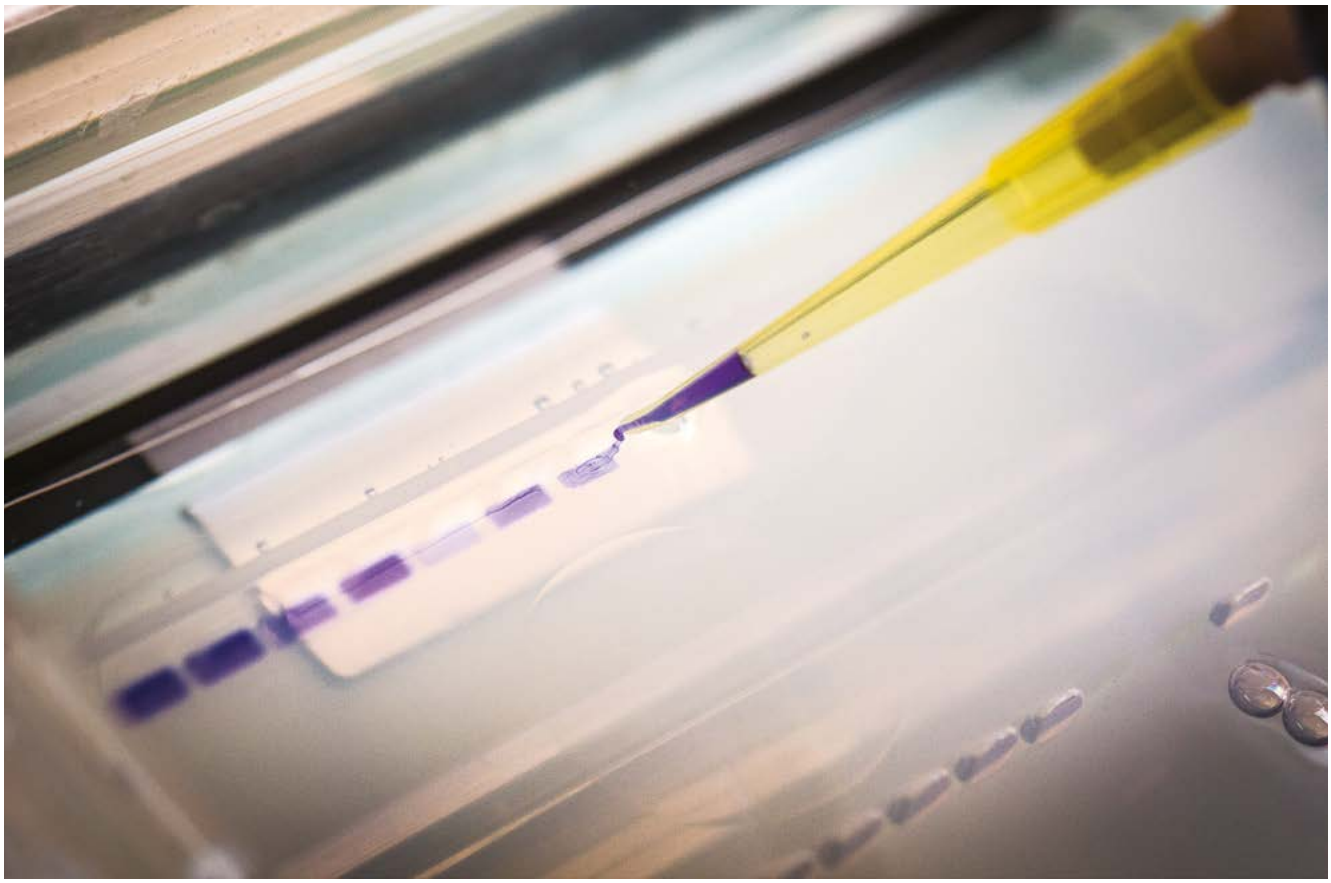
Project co-supervisors

Jennifer Juno, Dr Sidonia Eckle

Project availability

- Honours

Kent group



Project: Investigating the role of functional antibodies against Mycobacterium tuberculosis

Mycobacterium tuberculosis (Mtb) infects approximately one third of the world's population and is currently one of the major causes of morbidity and death worldwide. The role of antibodies in Mtb is underexplored, although rare studies suggest that antibodies may contribute to Mtb control. Preliminary studies by our lab suggest that patients that can control Mtb (latently infected) have improved functional antibody responses compared to symptomatic (active) Mtb patients. Therefore, we are interested in characterising the antibodies from patients with different clinical Mtb disease outcomes in order to further understand the importance of these potentially protective antibodies.

Project supervisor
Professor Stephen Kent

Project co-supervisor
Dr Amy Chung

Project availability
- PhD
- MSc
- Honours

Project: The importance of IgA in the protection and control of infectious diseases

The human body produces more IgA than any other immunoglobulin, especially in mucosal secretions. However, the importance of IgA in both protection from HIV-1 and control of HIV-1 disease progression is highly controversial. Results from the only protective human HIV vaccine trial associated plasma IgA with reduced vaccine efficacy. In contrast, recent studies suggest that mucosal HIV-specific IgA may be protective. This project aims to further explore the mechanisms behind both the protective and immunomodulatory role of IgA in the control of HIV-1 and other infectious diseases.

Project supervisor
Professor Stephen Kent

Project co-supervisor
Dr Amy Chung

Project availability
- PhD
- MSc

Lawson group

Contact name Associate Professor Vicki Lawson
Email address vlawson@unimelb.edu.au

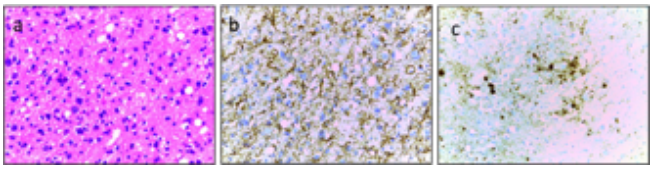
Number of vacancies available 3

Host-pathogen Interactions

Public Health

Discovery Research

Translational and Clinical Research



Prion diseases share common pathologies of vacuolation (a), a reactive gliosis (b) and deposition of a misfolded form of the prion protein (c). It is the shape of the misfolded protein that is believed to encode strain variation. (From Whitechurch, Welton, Collins, Lawson (2017). Prion Diseases in Adv. Neurobiology, Vol. 15, Philip Beart et al. (Eds): Neurodegenerative Diseases, Springer Nature).

The Lawson group is focused on understanding how protein misfolding in the central and enteric nervous system gives rise to diseases such as prion and Parkinson's diseases, with a focus on diagnosis, treatment and prevention, as well as understanding how the normal function of these proteins may contribute to diseases such as cancer.

Project: Diagnosis, treatment and prevention of medically-relevant prion diseases

Prion diseases are invariably fatal neurodegenerative disorders that affect both humans and animals. Prion diseases are caused by the propagation of a misfolded form of the normal cellular prion protein. Despite advances in our understanding of the nature of the transmissible agent of prion diseases there is still no treatment that has been shown to be effective in slowing or preventing progression of disease in humans. Furthermore, there is currently no pre-symptomatic diagnostic method that can identify patients with early disease who might respond to therapeutic intervention should it become available or identify individuals who are at risk of transmitting disease. A further challenge to the diagnosis, treatment and prevention of prion diseases is the existence of prion strains that reflect different conformations of the misfolded prion protein. The existence of these strains, which manifest in different disease phenotypes, can affect treatment and diagnosis of disease and effect decontamination of surgical equipment. Projects are available that use mouse adapted human prion strains in cell-free, in vitro and in vivo assays using a range of techniques to investigate the effect of prion strain variation on diagnosis, treatment and prevention of prion disease (Brazier et al 2006, Lawson et al 2007, Lawson et al 2008, Klemm et al 2012).

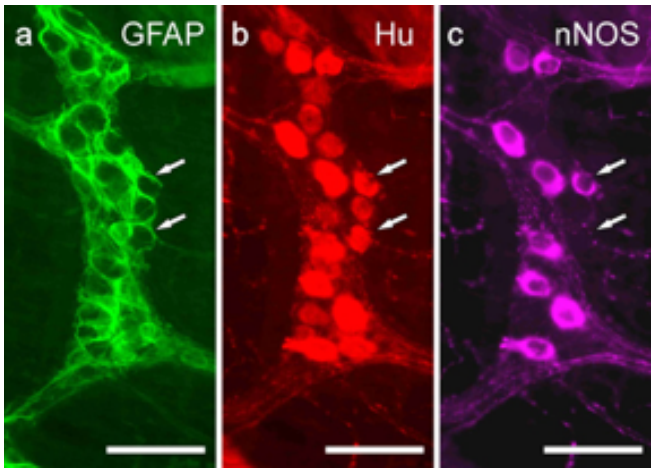
Project supervisor

Associate Professor Vicki Lawson

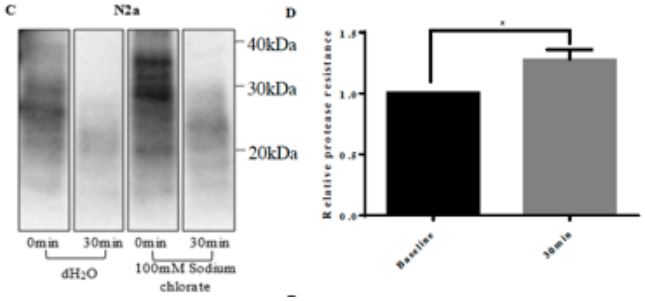
Project availability

- PhD
- MSc
- Honours

Lawson group



Neuronal populations in the enteric nervous system. Chemical markers of enteric glial cells (GFAP, a) neurons (Hu, b) and inhibitory motor neurons (nNOS, c) can be used to identify cell populations affected by protein misfolding and neurodegeneration in the enteric nervous system (from Lawson et al 2010)



Preventing sulfation of glycosaminoglycans (sodium chlorate treatment) increases the protease resistance of the prion protein in neuronal cells (N2a). Protease resistance is a feature of the transmissible form of the prion protein (Whitechurch and Lawson, unpublished).

Project: Neurodegeneration in the enteric nervous system

The enteric nervous system controls the function of the gastrointestinal tract and depends on extrinsic innervation arising from the brain and spinal cord and intrinsic innervation derived from neurons within the neuronal plexus of the gastrointestinal tract. Recent studies suggest that neurons and glial cells of the enteric nervous system are vulnerable to the degeneration that is observed in the neurons and glial cells of the central nervous system (Albanese et al 2008, Lawson et al 2010, Ellet et al 2016). We are interested in parallels in disease (pathology and pathogenesis) observed in the enteric and central nervous system in neurodegeneration and the potential for neurodegeneration to originate in the enteric nervous system. This project investigates the consequences of the loss of neuronal populations and neuroinflammation in the enteric nervous system from mouse models of neurodegeneration (prion disease, Parkinson's disease, Amyotrophic lateral sclerosis) and exploring diagnostic paradigms utilising tissues from the gastrointestinal tract.

Project supervisor

Associate Professor Vicki Lawson

Project availability

- MSc
- Honours

Project: A cell-based model of sporadic prion disease

Prion diseases are invariably fatal neurodegenerative disorders caused by the misfolding of the normal cellular prion protein. Although the prion protein is required for the development of prion disease, it is thought that additional factors (cofactors) may contribute to prion protein misfolding and the development of sporadic prion disease. Several polyanions (macromolecules with negative charges at several sites) have been implicated as cofactors in prion propagation, including nucleic acids and glycosaminoglycans. We have shown that nucleic acids and the glycosaminoglycan heparan sulfate are required for prion protein misfolding in cell free assays (Lawson et al 2010). We have further shown that altering the charge on glycosaminoglycan changes prion protein localisation, and susceptibility to misfolding (Ellett et al, 2015). We hypothesise that changes in the expression of the sulfotransferase enzymes that add negatively charged sulfates to glycosaminoglycans contribute to the development of sporadic prion disease. In this project, exogenous protein expression and RNA silencing paradigms will be used to alter the expression of various sulfotransferease enzymes in an established cell culture system. The properties of PrP expressed in this system will be evaluated using immunofluorescence and biochemical analysis. Identification of enzymes that affect the properties of the prion protein will then be evaluated in a prion infected cell culture model.

Project supervisor

Associate Professor Vicki Lawson

Project availability

- MSc
- Honours

Lewin group

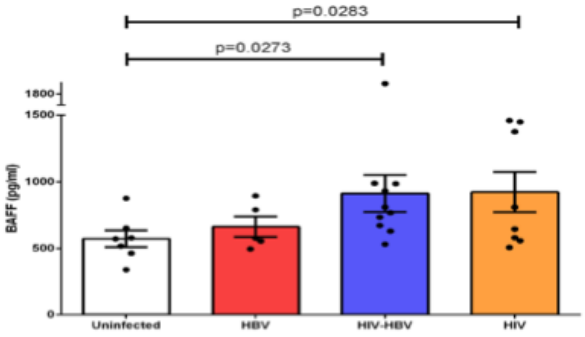
Contact name Professor Sharon Lewin
Email address sharon.lewin@unimelb.edu.au

Number of vacancies available 2

Immunology

Viral Infectious Diseases

Translational and Clinical Research



Circulating BAFF is significantly elevated in HIV-HBV co-infection and HIV mono-infection compared to uninfected controls.

Co-infections with viral or bacterial pathogens cause significant morbidity in people with HIV. In the case of HIV and hepatitis B virus (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 HIV and HBV. The HBV Immunology group investigates the mechanism of how HIV can accelerate liver disease in patients co-infected with HBV. We 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 is observed following antiviral treatment of individuals with HIV-HBV co-infection. We hypothesise 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 also be examined and the effect of a BAFF-HBV fusion protein on production of antibodies to HBsAg determined.

Project supervisor

Professor Sharon Lewin

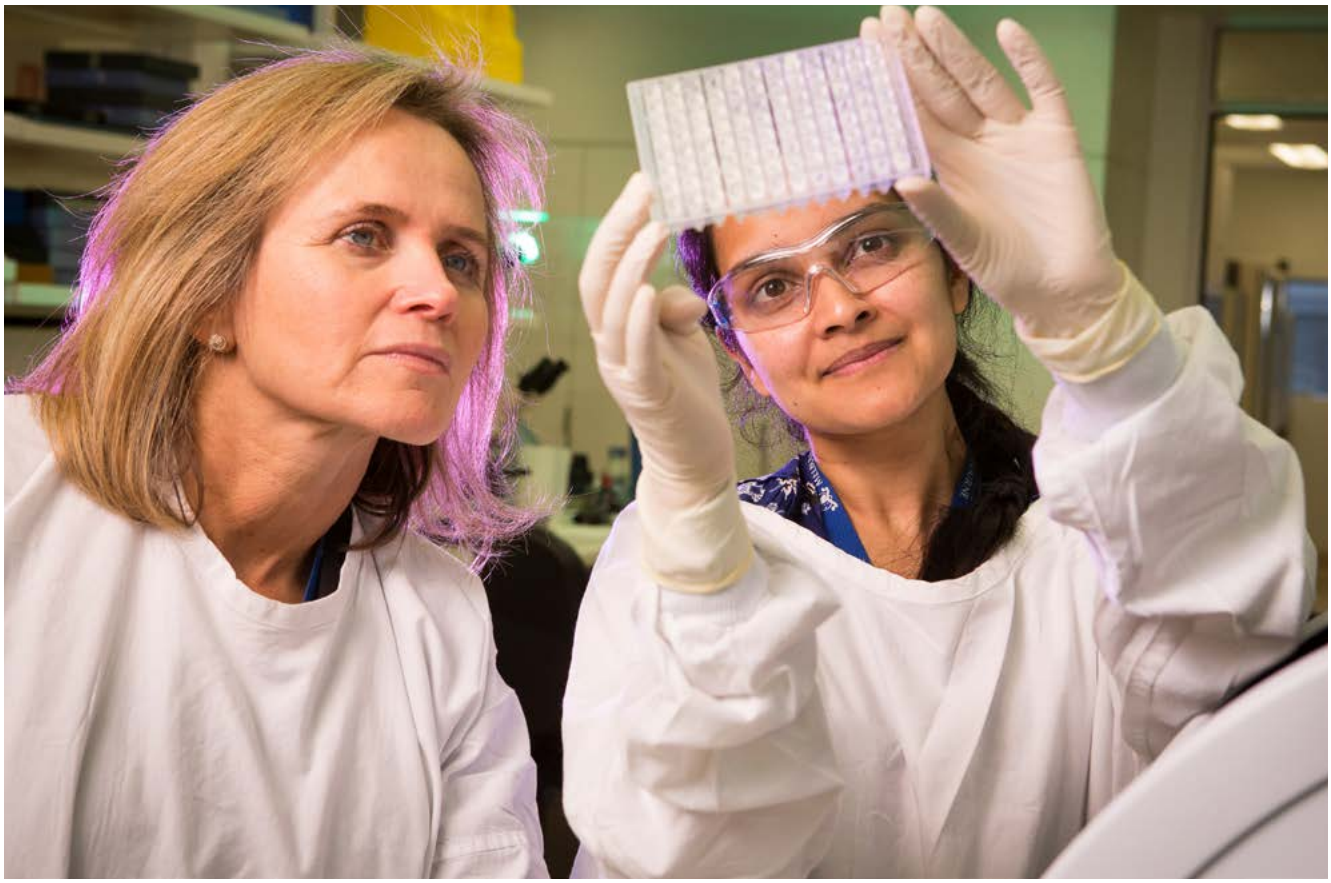
Project co-supervisors

Professor Fabienne Mackay, Dr Jennifer Audsley

Project availability

- PhD
- Honours

Lewin group



Project: Putting the kill into shock and kill

HIV persists in individuals on antiretroviral therapy (ART) primarily due to long lived memory CD4+ T cells latently infected by HIV. A popular strategy to purge these latently infected cells in individuals on ART to try achieve remission or a cure is termed “shock and kill”. This involves treatment with drugs termed latency reversing agents (LRAs) that “shock” or reactivate the latent virus to express viral RNA and proteins. This was originally proposed to “kill” these reactivated cells through viral protein-mediated cytotoxicity or immune mediated clearance. However, while clinical trials testing promising single LRAs demonstrate that viral RNA is reactivated, these drugs alone have not led to a decline in latently infected cells. Therefore, new strategies are required to drive the death of reactivated, latently infected cells. HIV proteins expressed late in the viral replication cycle can induce cell death via triggering apoptosis. This project aims to combine potent LRAs to reactivate the efficient expression of pro-apoptotic viral proteins, together with pro-apoptotic drugs to lower the threshold of cells for apoptosis, to drive the selective death of latently infected cells. Various combinations of clinically relevant LRAs and pro-apoptotic compounds will be tested in established HIV latency models to identify combination/s that could potentially advance to future clinical testing.

The project will involve a variety of techniques including primary T cell isolation, culture of primary T cells and cell lines, virus production, infections, cell staining, flow cytometry, and qPCR-based methods in PC2 and PC3 laboratories.

Project supervisor

Dr Jenny Anderson

Project co-supervisor

Professor Sharon Lewin

Project availability

- PhD
- Honours

Link for further information:

doherty.edu.au/our-work/institute-themes/viral-infectious-diseases/hiv/research?lab=lewin-lab

ncbi.nlm.nih.gov/pubmed/29324227

Mackay, Fabienne group

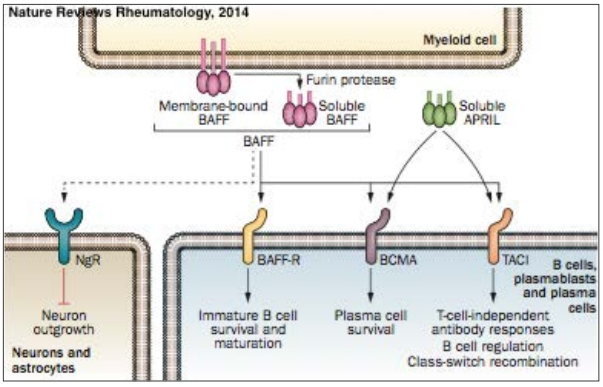
Contact name Professor Fabienne Mackay
Email address fabienne.mackay@unimelb.edu.au

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 group 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 tumour necrosis factor superfamily named BAFF/BLyS and demonstrated the role of this factor in B cell survival. Excess B cell activating factor (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 Professor Mackay's work on BAFF.

Link for further information

biomedicalsciences.unimelb.edu.au/sbs-research-groups/microbiology-and-immunology-research/b-lymphocytes,-baff-and-autoimmunity/developing-new-therapies-for-systemic-lupus-erythematosus

doherty.edu.au/people/professor-fabienne-mackay

Project: Restoring B cell tolerance in Systemic Lupus Erythematosus

Normally, the immune system effectively fights infections and eliminates 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 signalling 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

Mackay, Fabienne group

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

Link for further information
biomedicalsciences.unimelb.edu.au/sbs-research-groups/microbiology-and-immunology-research/b-lymphocytes,-baff-and-autoimmunity/chronic-lymphocytic-leukemia

Dissecting new functions of post-translational modifications in B lymphocytes

B lymphocytes are immune cells essential for the life of mammals, producing protective antibodies, designed to recognise and neutralise pathogens. Signalling via the B cell receptor (BCR) leads to protein methylation. In support of a fundamental role for protein arginine methyltransferase 1 (PRMT1) in B cells, our work has demonstrated that many aspects of B cell biology are defective in PRMT1-deficient mice. This project aims to dissect the role of PRMT1 in B cell activation with the hypothesis that PRMT1 is a central arginine methyltransferase required for modifying key proteins of unappreciated functional importance in B cells, as part of an additional dimension of B cell regulation.

Project supervisor
Professor Fabienne Mackay

Project co-supervisor
Dr Simona Infantino

Project availability
- PhD
- MSc
- Honours

Mackay, Laura group

Contact name Dr Laura Mackay
Email address lkmackay@unimelb.edu.au

Number of vacancies available 1

Immunology

Viral Infectious Diseases

Discovery Research

Research in the Mackay group has shown that specialised immune cells, called resident memory T cells, are critically important for protection against infection. These immune cells live in body tissues, where they stand guard at sites of pathogen invasion to directly combat infection. Within the Mackay lab, we aim to greatly enhance our fundamental understanding of resident memory T cell biology, and how these cells protect against disease. By learning to control these immune cells we can harness their protective function, with the ultimate goal of translating our basic discovery research into novel treatments for infectious disease, cancer and autoimmune disease.

Link for further information
doherty.edu.au/people/dr-laura-mackay

Project: Discovery of novel targets to enhance tissue resident immunity

Generation of optimal immunotherapies requires the generation of effective T cell responses. A unique subset of T cells called tissue-resident memory T (TRM) cells permanently exists within tissues of the body where they form a front-line defence against pathogens, as well as immune defence against various cancers. However, targeting TRM cells is currently difficult, as their developmental requirements are only partially understood. Using sophisticated genetic approaches, this project will investigate novel gene targets and molecular pathways that may be harnessed therapeutically, and this knowledge will be applied to TRM cell vaccine design to enhance protection against infectious disease and cancer.

Project supervisor
Dr Laura Mackay

Project co-supervisor
Dr Maximillien Evrard

Project availability
- PhD
- MSc
- Honours

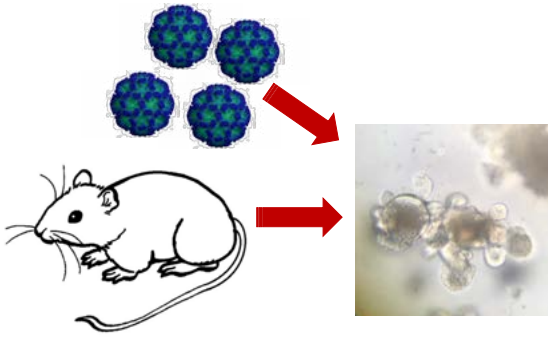
Mackenzie group

Contact name Professor Jason Mackenzie
Email address jason.mackenzie@unimelb.edu.au

Number of vacancies available 1

Immunology **Viral Infectious Diseases** **Host-pathogen Interactions**

Discovery Research



Isolation of intestinal tissue from mice and subsequent infection with MNV.

The Mackenzie group investigates how viruses interact with the cells they infect. In particular the molecular and cellular processes that are manipulated by flaviviruses (dengue, Zika and West Nile viruses) and noroviruses for their own gain. We aim to understand how the intracellular events of virus replication result in innate immune evasion and ultimately how the consequences of infection result in a diseased state. Answering these questions will guide and inform us of areas for antiviral therapeutic development.

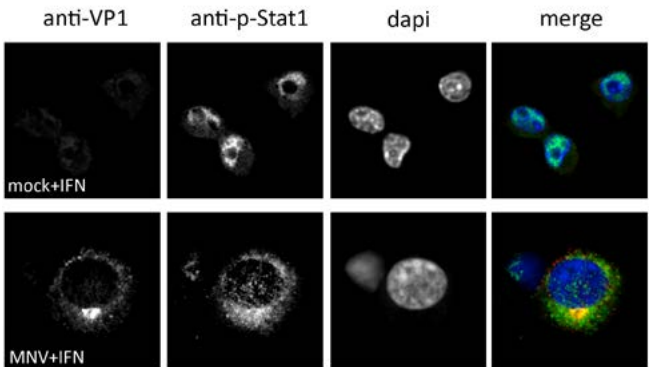
Project: The guts of norovirus infection

The aim of the project is to culture and infect isolated intestine explants with norovirus. Intestine will be isolated from mice, sectioned and placed in a dish for culture before infection with murine norovirus (MNV). This approach will enable us to investigate how MNV infects enteric tissues, interacts with the microbiota and immune cells in the gut. We will visualise these interactions by immunofluorescence and determine the activation of the immune response via qRT-PCR for transcription of immune genes and the production of cytokines by ELISA. This approach is completely novel and will advance our research significantly.

Project supervisor
Professor Jason Mackenzie

Project co-supervisor
Turget Aktepe

Project availability
- Honours



MNV infection of macrophages induces phosphorylation of the immune transcription factor Stat-1, but prevents its nuclear translocation thus impeding its function.

Project: Evading the innate immune response; the norovirus way

The innate immune response is our greatest controlling factor against norovirus infection, yet 700 million infections still occur annually. In this project we will investigate how noroviruses can evade our innate immune response, particularly the induction of interferon and the downstream signalling events. We aim to identify the mechanism(s) noroviruses employ to manipulate the host and identify the viral protein(s) responsible for these actions. These findings will reveal targets that can be later pursued for the development of antiviral therapies.

Project supervisor

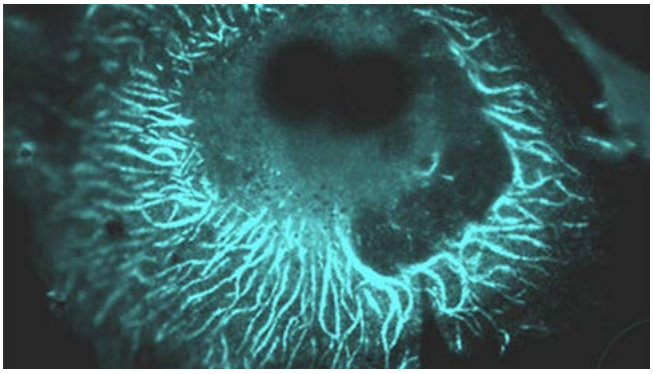
Professor Jason Mackenzie

Project co-supervisor

Turgut Aktepe

Project availability

- Honours



Infection of cells with the flavivirus, West Nile virus, drastically alters the intracellular architecture providing an efficient environment for virus replication.

Project: Reno rumble: how flaviviruses remodel the intracellular architecture of infected cells

Infection with flaviviruses (dengue, Zika and West Nile viruses) results in an amazing remodelling of the cytoplasmic membrane architecture. This 'reno rumble' indices the formation of virus organelles that comprise the virus replication complex that facilitates efficient virus replication and innate immune evasion. We aim to understand how this remodelling occurs and utilising green fluorescent protein-tagged viruses we will visualise membrane remodelling over real time, with epi-fluorescent video capture. This will enable us to understand how this process occurs, and utilising specific virus mutants we can determine the viral factors that contribute to this process.

Project supervisor

Professor Jason Mackenzie

Project co-supervisor

Turgut Aktepe

Project availability

- Honours

McDevitt group

Contact name Associate Professor Christopher McDevitt
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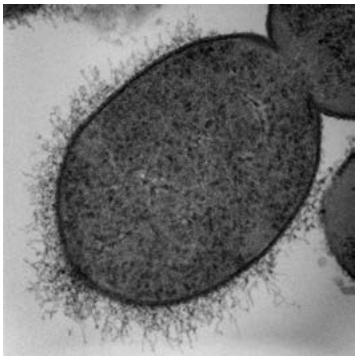
Number of vacancies available 2

Antimicrobial Resistance and Healthcare Associated Infections

Host-pathogen Interactions

Discovery Research



Transmission electron micrograph of S. pneumoniae.

Metal ions are essential for cellular chemistry in every cell in all forms of life. Research in the McDevitt group seeks to understand the role of metal ions in bacteria and how they influence host-pathogen interactions. Our specific research interests are: to understand how bacteria acquire essential metal ions from the environment; characterise the cellular roles of metal ions in bacteria; and elucidate the role of metal ions at host-pathogen interface. By understanding the chemical biology of bacteria, our work opens the way to developing novel antimicrobials to starve invading pathogens of crucial trace elements.

Project: Understanding the biological chemistry of pneumococcal disease

All pathogenic organisms, whether bacterial, viral or parasitic, require metal ions (e.g. manganese, iron and zinc) to mediate disease. These metals are stolen directly from the host and so the pathways that pathogens use to scavenge these essential ions are ideal targets for novel antimicrobials. Streptococcus pneumoniae is the world's foremost human bacterial pathogen responsible for more than 1 million deaths every year. Building on our expertise in bacterial chemical biology, this project will investigate the pathways involved in Streptococcus pneumoniae metal ion homeostasis, elucidate their function, and reveal their roles in the host-pathogen interaction.

Project supervisor

Associate Professor Christopher McDevitt

Project co-supervisor

Dr Stephanie Begg

Project availability

- PhD
- Honours

Project: Metal ion homeostasis in Pseudomonas aeruginosa

Pseudomonas aeruginosa is a major opportunistic human pathogen and the leading cause of death in cystic fibrosis. Our recent studies investigating the chemical biology of this pathogen have identified novel pathways involved in the acquisition of essential metal ion nutrients, such as zinc and molybdenum, from the lung environment. This project will build on our detailed insights to assess the roles of these major, yet uncharacterised, pathways and how they influence the growth and behaviour of Pseudomonas aeruginosa. This study will define new pathways involved in metal ion homeostasis in Pseudomonas aeruginosa and other gram-negative bacteria.

Project supervisor

Associate Professor Christopher McDevitt

Project co-supervisor

Dr Stephanie Begg

Project availability

- PhD
- Honours

Project: How is selective metal ion transport achieved at the host-pathogen interface?

Biological discrimination between metal ions remains poorly understood, yet essential to their function in the chemically complex environment of the host-pathogen interface. Recent studies from our group have shown that many bacterial metal ion transporters are not restricted to solely interacting with the ion(s) that they import. These observations have challenged the prevailing dogma for how biological selectivity of metals is achieved. To resolve this question, this project will use state-of-the-art methods, including single molecule FRET, electron paramagnetic resonance spectroscopy and reconstituted proteoliposomes, to reveal how bacterial metal ion transporters achieve selectivity for their physiological substrates.

Project supervisor

Associate Professor Christopher McDevitt

Project co-supervisors

Dr Alex Carey Hulyer, Dr Stephanie Begg

Project availability

- PhD
- Honours

Project: Mapping elemental fluxes during host-pathogen interaction

During infection, the host modulates tissue concentrations of key metal ions (e.g. iron, copper and zinc) to either starve or intoxicate invading bacteria. This project will investigate the temporal and spatial interplay between pathogenic bacteria and the flux of inorganic chemical components at the host-pathogen interface. This will be achieved using an innovative new approach called elemental bio-imaging that allows us to quantitatively map the distribution of metal ions within host organs. This study will provide new insights into how the host manipulates metal ion concentrations to resist bacterial infection.

Project supervisor

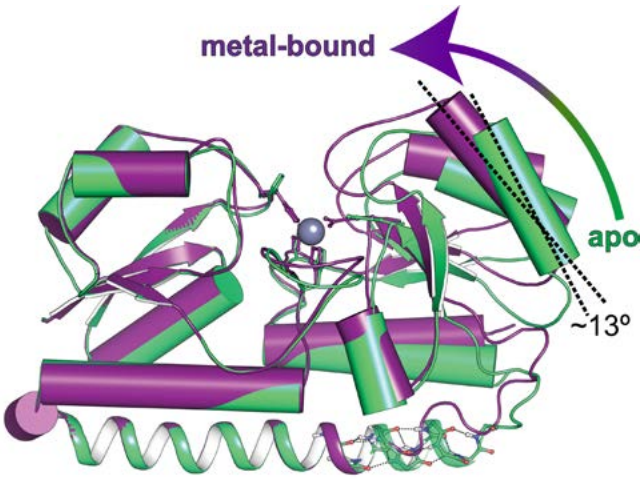
Associate Professor Christopher McDevitt

Project co-supervisor

Professor Philip Doble

Project availability

- PhD
- Honours



Cartoon representation of the structural changes induced by metal binding in the Streptococcus pneumoniae PsaA protein.

Mueller group

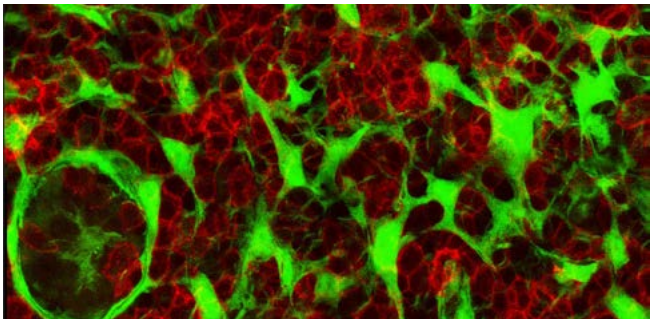
Contact name Associate Professor Scott Mueller
Email address smue@unimelb.edu.au

Number of vacancies available 2

Immunology

Viral Infectious Diseases

Discovery Research



High resolution confocal microscopy image of the organised stromal cell network in the T cell zone of a lymph node. Shown are T cells (red) and fibroblasts (green).

Research in the Mueller group is focused on examining immune responses to acute and chronic viral infections and to tumours. We are 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 nerves in tissues for the design of new vaccines and therapeutics.

Project: How do tumours impact normal tissue functions?

Cancer cells hijack local tissue environments to support their growth, survival and metastasis. Stromal cells such as fibroblasts form critical supportive networks in tissues and express key molecules that influence tumour growth. The overall impact of tumours on the functions of stromal cells within tissues is poorly understood. This project will examine the bi-directional interactions between tumour cells and stromal cells in the lymphoid organs in order to define how cancer impacts tissue functions, and identify mechanisms to restrict tumour growth and improve disease outcomes. Advanced multi-colour imaging, flow cytometry and molecular techniques will be used in this project.

Project supervisor

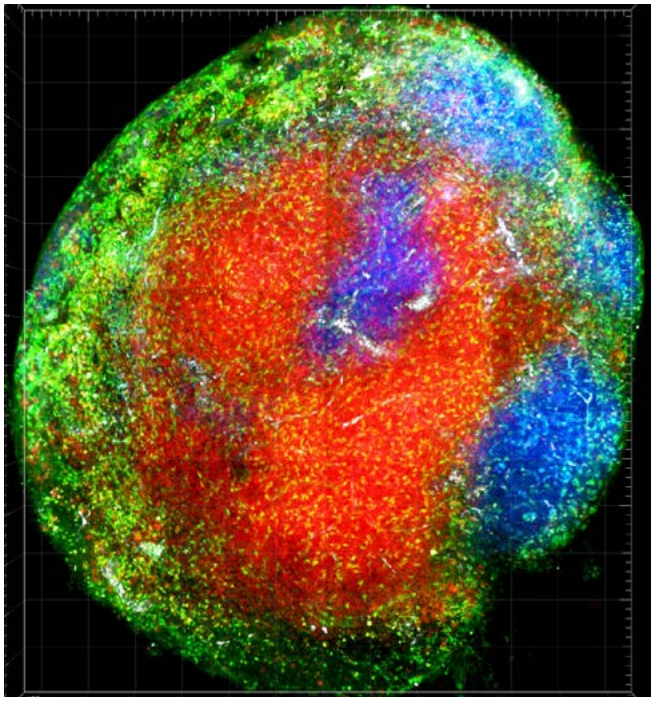
Associate Professor Scott Mueller

Project co-supervisor

Dr Yannick Alexandre

Project availability

- PhD
- MSc
- Honours



Confocal microscopy image of the organised architecture of a lymph node stained to show T cells (red), B cells (blue), blood vessels (white) and stromal cells (green).

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
- MSc
- Honours

Newton group

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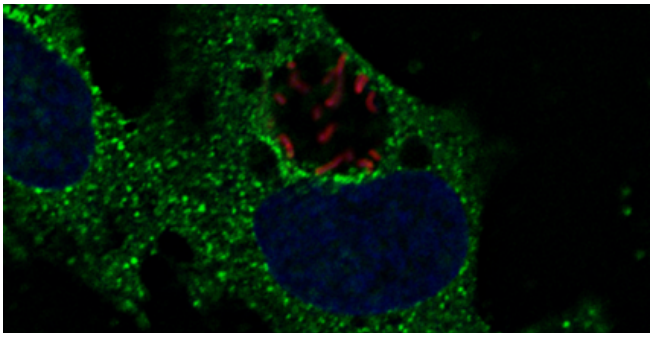
Number of vacancies available 2

Host-pathogen Interactions

Discovery Research

The Newton group uses a range of molecular and cell biology approaches to investigate the host-pathogen interactions that occur during infection with intracellular bacterial pathogens. Studies are particularly focused on the causative agent of Q fever, Coxiella burnetii, which uses a large cohort of novel effector proteins to convert the normally bactericidal lysosome into an efficient replicative niche. Understanding the function of these important effector proteins will shed light on both the pathogenesis of Coxiella and important human cellular processes.



A clathrin heavy chain (green) surrounding the Coxiella-containing vacuole (red).

Project: CCVs: Clathrin-coated vesicles and Coxiella containing vacuoles

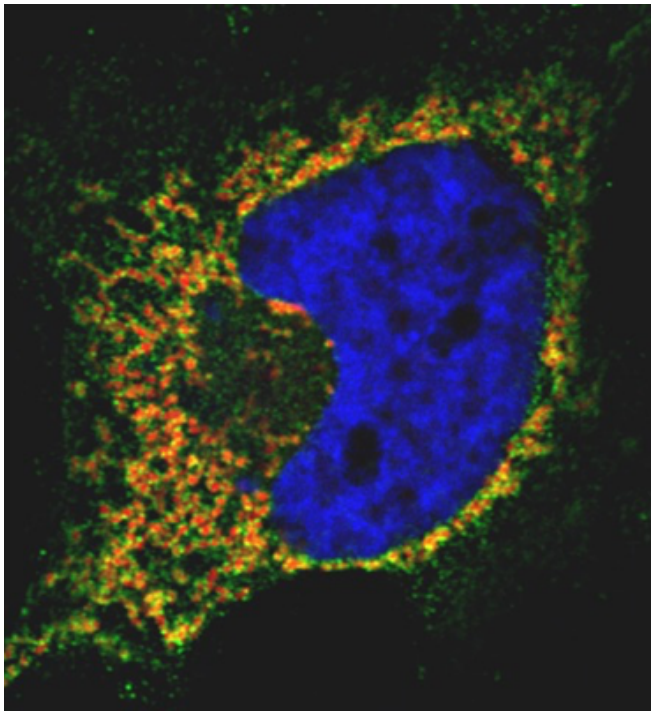
Coxiella burnetii, the causative agent of Q fever, creates a unique replicative niche by modifying the human lysosome. One key feature of this vacuole is the recruitment of clathrin heavy chain to the vacuole membrane. Recruitment of this protein is important for intracellular success of Coxiella and vacuole expansion, through facilitation of autophagosome-vacuole fusion. We have identified several bacterial virulence factors that are involved in commandeering clathrin machinery. This project will address whether this process also involves clathrin light chain and other key components of classical clathrin-mediated trafficking. Key methodologies will include microscopy, tissue culture and protein biochemistry.

Project supervisor

Dr Hayley Newton

Project availability

- PhD
- Honours



A bacterial effector protein (green) localising to mitochondria (red).

Project: Mitochondria and intracellular bacterial pathogens

Intracellular bacterial pathogens employ specialised secretion systems that transport virulence proteins, termed effectors, into the host cytosol. These effectors can subvert normal eukaryotic functions allowing the pathogen to create a replicative niche and evade killing. Some effector proteins target the host cell mitochondria where their functions remain largely unknown. This project will use cutting edge biochemistry, microscopy, microbiology and eukaryotic cell biology to explore the impact of intracellular bacterial pathogens on mitochondrial function.

Project supervisor
Dr Hayley Newton

Project co-supervisor
Diana Stojanovski

Project availability
- PhD
- MSc
- Honours

Purcell group

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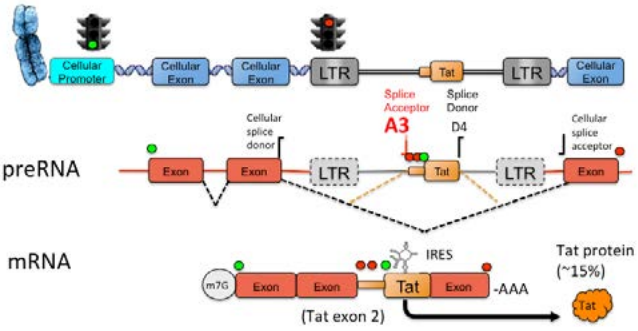
Number of vacancies available 3

Immunology | **Viral Infectious Diseases** | **Host-pathogen Interactions**

Discovery Research | **Global Health** | **Genomics** | **Indigenous Health**



Structured RNA controls Tat protein expression to regulate HIV latency

Professor Damian Purcell's group investigates the HIV-1 and HTLV-1 human retroviruses that cause AIDS, leukaemia and inflammatory pathogenesis respectively. We study their genetic structure and gene expression with a focus on defining the mechanisms that control viral persistence and pathogenesis. We examine the molecular interplay of viral and host factors during viral infection and the innate and adaptive immune responses to viral infection. We use these molecular insights 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 give the finger to HIV transmission

Prophylactic HIV vaccines aim to elicit broad neutralising antibody (bNAb) at the sexual mucosa to block virus transmission. We were 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 the bovine plasmablasts producing bNAbs for production of monoclonal antibodies that define the responses needed for an effective protective antibody response.

Project supervisor
Professor Damian Purcell

Project co-supervisor
Dr Behnaz Heydarchi

Project availability
- PhD
- MSc
- Honours

Link for further information
dx.doi.org/10.1080/19420862.2016.1270491

Revill group

Contact name Associate Professor Peter Revill
Email address peter.revill@mh.org.au

Number of vacancies available 1

Viral Infectious Diseases

Public Health

Translational and Clinical Research

International Health

The Revill group's work is focused on the molecular virology 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 HBV are associated with liver cancer, the fifth most prevalent cancer worldwide (Bayliss et al, J. Hepatol, 2013), and that splice variants are more diverse than previously appreciated (Betz-Stablein et al., 2016). Yet the complexity of splice variants associated with advanced liver disease and liver cancer is unknown. This project will utilise next generation sequencing, cloning, and in vitro cell culture studies to identify and characterise novel splice variants associated with advanced liver disease and liver cancer across different HBV genotypes, and determine their replication phenotype. Techniques utilised will include cell culture; real time PCR/digital PCR; next generation sequencing; Southern, Northern and Western blotting; and quantitative serology. This project will make a major contribution to our understanding of the role of HBV splice variants in liver disease progression.

Project supervisor

Associate Professor Peter Revill

Project co-supervisor

Dr Margaret Littlejohn

Project availability

- Honours

Rogerson group

Contact name Professor Stephen Rogerson
Email address sroger@unimelb.edu.au

Number of vacancies available 2

Immunology

Host-pathogen Interactions

Translational and Clinical Research

International Health

Discovery Research

The Rogerson group 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 are taking novel approaches to identifying antibody responses that protect pregnant women and young children from malaria, and block malaria transmission to mosquitoes.

Project: What do antibodies need to do to protect a woman against pregnancy-malaria?

Pregnant women are susceptible to malaria and though we know which antigen women's antibodies need to recognise, we don't know the most efficient way for these antibodies to protect women. Antibodies may confer protection by interacting with complement. This project would involve measuring complement binding antibodies towards placental malaria antigen using plate-based immunoassays in samples from pregnant women and/or individuals from Phase I vaccine trials, and analysing if they are protective or if they are generated. This will help us identify the role of complement binding antibodies in protection, information needed to effectively design and evaluate a pregnancy-malaria vaccine.

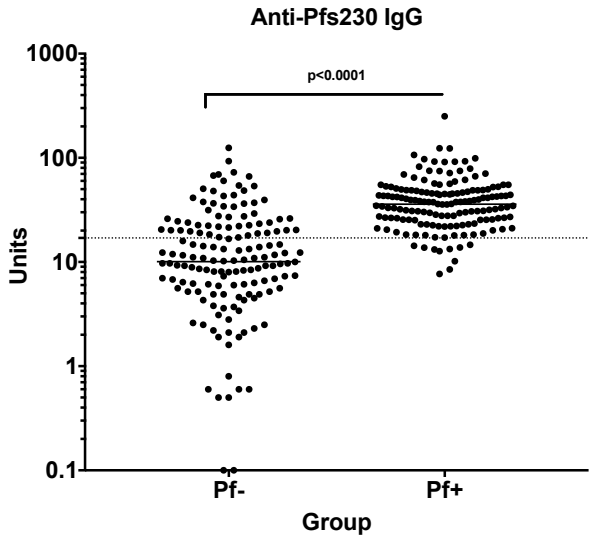
Project supervisor

Dr Elizabeth Aitken

Project availability

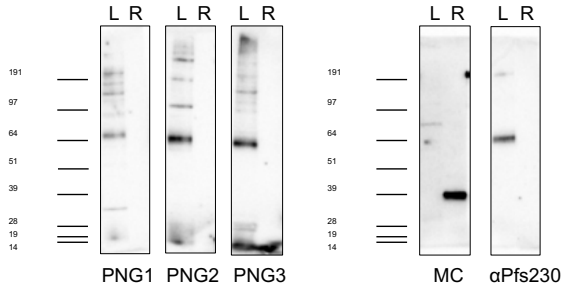
- Honours

Rogerson group



IgG antibody levels specific for the gametocyte stage antigen, Pfs230, can be detected in sesra from malaria-infected individuals with and without parasitaemia. A higher proportion of parasitaemic individuals are seropositive.

Figure 5. Gametocyte antigens targeted by IgG Abs in serum samples from a malaria-endemic population



Western blot was performed with SDS gel-resolved gametocyte/trophozoite cell lysate (L) or recombinant truncated Pfs230 (23kDa) (R) incubated with sera from 3 study subjects (PNG 1-3), non-endemic uninfected control (MC) or Pfs230 reactive rabbit serum (αPfs230)

Western blot analysis demonstrates that sera from malaria-infected individuals have antibodies targeting multiple proteins expressed by in vitro cultured P. falciparum gametocytes.

Project: Characterisation of antibodies against Plasmodium falciparum gametocytes to elucidate mechanisms of transmission blocking immunity

Immunity against sexual stage that underpin transmission blocking vaccines directed at parasite molecules expressed in the gametocyte through to ookinete stages are not well-understood. Antibodies (Ab) directed against these molecules are likely be crucial for transmission blocking immunity (TBI). We propose to characterise the sexual stage Ab targets in Plasmodium falciparum, the cause of the most severe form of malaria, and to better understand the properties of Abs that confer TBI. The goals of this project are to functionally characterise anti-gametocyte antibodies in sera from malaria-infected individuals that mediate TBI using biochemical and immunological techniques.

Project supervisor

Associate Professor Siddhartha Mahanty

Project co-supervisor

Professor Stephen Rogerson

Project availability

- Honours

Project: Micro-RNA and severity of clinical malaria

Infection with Plasmodium falciparum ranges in severity from asymptomatic parasitaemia to severe or fatal disease. Host and parasite-derived factors are involved in determining severity of illness. Plasmodium falciparum-infected red blood cells release small membrane particles, called extracellular vesicles (EV), into the circulation that directly interact with, and influence, host cells through the proteins and nucleic acids (RNA/DNA). EV are capable of transporting functional micro-RNA (miRNA). The goal of this project is to determine if EV in circulation and/or extracellular miRNA associated with vesicles contribute to the regulation of the clinical severity of falciparum malaria.

Project supervisor

Associate Professor Siddhartha Mahanty

Project co-supervisor

Professor Stephen Rogerson

Project availability

- Honours

Satzke group

Contact name Catherine Satzke
Email address catherine.satzke@mcri.edu.au

Number of vacancies available 4

Viral Infectious Diseases | Host-pathogen Interactions | Public Health | Translational and Clinical Research | Discovery Research | International Health | Genomics

The Satzke group conducts discovery research in a clinically-relevant context. We focus on two pathogens of major global health importance (pneumococcus and group A streptococcus) to understand their pathogenesis, interaction with viruses, and how infections can be best prevented with vaccines. We collaborate closely with immunologists, clinicians and epidemiologists, including in more than ten countries in the Asia-Pacific region.

Project: Streptococcal transmission and disease

The bacterium Streptococcus pyogenes (group A streptococcus, Strep A) causes a range of mild to severe infections, ranging from sore throat to streptococcal toxic shock syndrome. Importantly, Streptococcus pyogenes infections can lead to serious sequelae such as rheumatic fever and rheumatic heart disease. Streptococcus pyogenes can also colonise a variety of human tissues including the upper respiratory tract and skin in healthy people. In a related bacterial species, Streptococcus pneumoniae, we have shown that viral co-infection can enhance bacterial virulence by increasing bacterial density and inflammation in the host, and by driving changes in expression of bacterial virulence genes. There is recent clinical epidemiologic evidence that viruses are also important in Streptococcus pyogenes pathogenesis, but little is known about this process. In this project, the student will use a murine model of Streptococcus pyogenes colonisation to examine the effect of viruses on Streptococcus pyogenes colonisation, transmission (spread to co-housed littermates) and disease, and the mechanisms involved. To achieve these aims, a range of methods will be employed including animal and tissue handling, immunological assays, traditional microbiology and molecular approaches such as qPCR, and gene expression analyses. This project will provide important novel data on key components of Streptococcus pyogenes pathogenesis, and inform a pathway towards improving strategies for preventing Streptococcus pyogenes infections.

Project supervisor

Associate Professor Catherine Satzke

Project co-supervisors

Dr Eileen Dunne, Professor Andrew Steer

Project availability

- PhD
- MSc
- Honours

Satzke group

Project: Characterisation of a putative phage-inducible chromosomal island in Streptococcus pneumoniae

Phage-inducible chromosomal islands (PICIs) are genetic elements that benefit bacteria by restricting bacteriophage replication in favour of their own survival. Upon induction by bacteriophage infection, PICIs block bacteriophage reproduction and preferentially package their own DNA into the bacteriophage-encoded capsid, forming transducing particles that contain PICI DNA that can be horizontally transferred to a new host. Most research involving functional characterisation of PICIs have been conducted in Staphylococcus aureus; our knowledge of PICIs in other bacteria is limited. We have identified a putative PICI in a Streptococcus pneumoniae (the pneumococcus) strain isolated from the nasopharynx of a healthy child. In this project, you will investigate the functional significance of this mobile genetic element in pneumococci. You will isolate and characterise pneumococcal bacteriophages and determine whether pneumococci carrying the PICI are protected against bacteriophage infection, as well as investigate other phenotypes the PICI may confer to its bacterial host. You will also conduct molecular screening using clinical samples to determine the prevalence of the PICI. This project will involve a range of skills including traditional microbiological culture and molecular biology techniques.

Project supervisor

Associate Professor Catherine Satzke

Project co-supervisors

Dr Steve Petrovski, Dr Sam Manna

Project availability

- MSc
- Honours

Project: Transcriptional regulation in Streptococcus pneumoniae

Streptococcus pneumoniae (the pneumococcus) is a leading cause of pneumonia in children world-wide. This bacterium asymptomatically colonises the upper respiratory tract, but can transition to a pathogenic state to cause disease in the lower respiratory tract. We are interested in identifying the genetic factors that trigger this transition and have identified a putative transcriptional regulator we hypothesise may play a role in this process. In this molecular microbiology project, you will use pneumococcal strains in which the gene encoding the regulator has been deleted or overexpressed to identify which virulence and non-virulence genes are under the control of this regulator, as well as the associated phenotypes. Key approaches include: genetic manipulation of pneumococcal strains, experiments with DNA and RNA, as well as conducting functional assays in vitro and/or in vivo. Your work in helping us elucidate the function of this regulator will make a substantial contribution to our understanding of how pneumococcal gene expression is regulated and how this is coupled with its pathogenesis.

Project supervisor

Associate Professor Catherine Satzke

Project co-supervisor

Dr Sam Manna

Project availability

- MSc
- Honours

Project: Pathogenesis of pneumococcal pneumonia

Streptococcus pneumoniae (the pneumococcus) is the most common cause of community-acquired pneumonia and a leading killer of children world-wide. However, it is also commonly found as an asymptomatic coloniser of the upper respiratory tract, particularly in children. We are interested in elucidating the molecular processes by which the pneumococcus can transition from the carriage to infection state, and identifying signals of pneumococcal pneumonia. Previous work in our laboratory using clinical samples collected from children in The Gambia, West Africa, hospitalised with pneumonia has identified several pneumococcal genes that were upregulated in the lung. The project will have two main aims: to elucidate the role of these genes in pneumococcal pneumonia, and to examine pneumococcal gene expression in samples collected from pneumonia patients at the Royal Children's Hospital. You will use a variety of approaches to identify and characterise pneumococcal genes and proteins involved in pneumococcal pneumonia. This includes genetic manipulation of pneumococci, functional assays to characterise bacterial mutants, and measurement of gene and protein expression using methods such as qRT-PCR, RNA-seq, western blotting, and ELISA. Access to clinical samples such as pleural fluid provides the unique opportunity to examine pneumococcal gene expression during pneumonia. This project will provide exciting new data on the pathogenesis of pneumococcal pneumonia.

Project supervisor

Associate Professor Catherine Satzke

Project co-supervisors

Dr Eileen Dunne, Professor Sarath Ranganathan

Project availability

- PhD
- MSc
- Honours

Scott group

Contact name Dr Nichollas Scott
Email address nichollas.scott@unimelb.edu.au

Number of vacancies available 2

Antimicrobial Resistance and Healthcare Associated Infections

Host-pathogen Interactions

Discovery Research

The Scott group focuses on the identification and characterisation microbial mediate protein glycosylation. This post translational modification allows pathogens to radically alter the function of proteins both within them, and their hosts. Within a range of pathogens such as malaria and Burkholderia, microbial protein glycosylation is used for both defensive and offensive processes, enabling pathogens to fortify themselves against the host immune response or to disarm the host's ability to resist infection. Using mass spectrometry-based approaches, the Scott group seeks to develop methodologies to identify and track microbial glycosylation events to understand how microbes remodel their proteome and that of the hosts.

Project: Role of O-linked glycosylation system across the Burkholderia genus

Protein glycosylation, the chemical addition of sugars to proteins, is an important but poorly understood aspect of bacterial physiology. Within the Burkholderia genus, we have discovered a highly conserved O-linked glycosylation system. The conservation of this system across pathogenic and non-pathogenic species suggests that glycosylation plays a far more fundamental role in the physiology of Bukholderia than previously thought. The goal of this project is to understand the role and diversity of glycosylation in Bukholderia. By studying glycosylation within Burkholderia we aim to gain a fundamental understanding of this biological processes and how it contributes to bacterial survival.

Project supervisor

Dr Nichollas Scott

Project availability

- PhD
- MSc
- Honours

Project: Development of novel proteomic tools to explore Burkholderia glycosylation dependent pathogenesis

Bacterial protein glycosylation, once thought to be a rare event, has now been shown to be widespread. To date, multiple general glycosylation systems have been identified yet the precise role in bacterial physiology are still unknown. A common theme is the requirement of glycosylation for persistence and virulence in mammalian hosts. Within this project, we aim to explore the role of glycosylation in Burkholderia species virulence in the mammalian host. By coupling recent innovations in metabolic labelling, redox probes and mass spectrometry workflows we seek to explore how glycosylation influence intracellular survival to increase our understanding of the molecular pathogenesis of Burkholderia.

Project supervisor

Dr Nichollas Scott

Project availability

- PhD
- MSc
- Honours

Stinear group

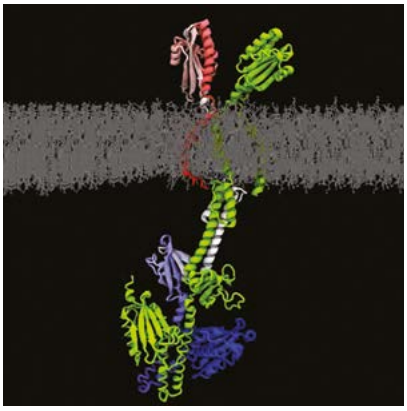
Contact name Professor Tim Stinear
Email address tstinear@unimelb.edu.au

Number of vacancies available 2

Antimicrobial Resistance and Healthcare Associated Infections

Host-pathogen Interactions

Genomics



Model of the essential Staphylococcus aureus two-component regulator, WalKR

The Stinear group 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.

Project: Understanding essential gene regulation in Staphylococcus aureus

Two component systems (TCS) enable bacteria to respond rapidly to the host environment. Among the 16 TCS 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 of WalKR essentiality.

Project supervisor

Professor Tim Stinear

Project co-supervisor

Dr Ian Monk

Project availability

- PhD
- MSc
- Honours

Project: New antibiotics from old bacteria

Development of new antibiotics is key to addressing the crisis in human health caused by the rise of multi-drug resistant superbugs. Traditionally, soil-derived Actinobacteria, particularly the genus Streptomyces, are the most prolific antibiotic producers, however, high re-discovery rates of known compounds demand the testing of new reservoirs of biodiversity and bioactive molecules. Human-associated bacteria, including pathogenic bacteria, are a previously untapped source of antimicrobial diversity. This project will investigate the antibacterial activity of a diverse collection of 700 human pathogenic Actinobacteria held by our state microbiology reference laboratory, with the ultimate aim to identify new antimicrobials that can inhibit hospital superbugs, such as methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci. A combination of techniques will be used in this project, including genomics, molecular biology, biochemistry and mass spectrometry, to identify new antibiotics produced by this collection of bacteria. Students will develop a broad range of skills in each of these areas and will use these to increase the antimicrobial drug discovery pipeline.

Further reading

Pidot, et al., 2014, Int J Med Microbiol, 304(1), 14-22.

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 tuberculosis. In this project you 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-supervisors

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 supervisors

Professor Tim Stinear, Professor Ben Howden

Project co-supervisor

Dr Glen Carter

Project availability

- PhD
- MSc
- Honours

Stinear group

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 Staphylococcus 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 and 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 supervisors

Professor Tim Stinear, Professor Ben Howden

Project co-supervisor

Dr Ian Monk

Project availability

- PhD
- MSc

Tong group

Contact name Associate Professor Steven Tong
Email address steven.tong@mh.org.au

Number of vacancies available 2

Antimicrobial Resistance and Healthcare Associated Infections

Indigenous Health

Translational and Clinical Research

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 mathemetical modelling groups, and the Doherty Applied Microbial Genomics team.

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 that of other geographical regions. Through linking genomics with epidemiology, we aim to examine the evolutionary relationship between disease causing Streptococcus pyogenes clones within remote communities of Australia. Furthermore, we will apply statistical genetic models to identify genetic signatures associated with different disease stats and/or 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

Associate Professor Steven Tong

Project co-supervisor

Dr Mark Davies

Project availability

- PhD
- MSc
- Honours

Tong group

Project: Characterisation of antimicrobial resistance and virulence of novel staphylococcal lineages

We have recently described emerging lineages of Staphylococcus aureus and Staphylococcus argenteus in northern Australia. The ST5 Staphylococcus aureus lineage has acquired resistance to trimethoprim and appears to have a clinically virulent phenotype. The project will determine the likelihood and mechanism of generation of resistance to co-trimoxazole (a commonly used antibiotic) and the virulence of this ST5 clone in relation to other Staphylococcus aureus clones. For Staphylococcus argenteus, we have identified a lineage associated with invasive infections and seek to identify genomic elements that confer this phenotype.

Project supervisor

Associate Professor Steven Tong

Project co-supervisor

Professor Benjamin Howden

Project availability

- PhD
- Honours

Link for further information

ijs.microbiologyresearch.org/content/journal/ijsem/10.1099/ijs.0.062752-0#tab2

linkinghub.elsevier.com/retrieve/pii/S1198-743X(18)30360-4

Project: SNAP - Staphylococcus aureus Network Adaptive Platform Trial

We are developing a novel adaptive platform trial to optimise management of Staphylococcus aureus bacteraemia. There are many elements involved in setting up such a platform trial, ranging from Bayesian statistical modelling, protocol development, streamlined consent processes and ethical considerations. We are looking for motivated individuals keen to learn about applying these novel methodologies to a key clinical infectious diseases syndrome.

Project supervisor

Associate Professor Steven Tong

Project availability

- PhD
- MSc
- Honours

Project: Evolution of streptococcal pathovars

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

Associate Professor Steven Tong

Project co-supervisor

Dr Mark Davies

Project availability as follows

- PhD
- Honours

Project: Using genomics to investigate the transmission of skin pathogens and antimicrobial resistance in a 'One Health' setting

Remote Indigenous Australian communities experience disproportionately high levels of skin disease associated with the bacterial pathogens, methicillin-resistant Staphylococcus aureus (MRSA) and Streptococcus pyogenes. Our preliminary research indicates that dogs in remote indigenous communities also carry MRSA more commonly than dogs in urban settings. A significant knowledge gap exists as to the role of household animals in the maintenance and transmission of skin pathogens in remote Australian communities. This project aims to use bioinformatics approaches to investigate the transmission of skin pathogens between humans and animals in areas of high disease burden.

Project supervisor

Associate Professor Steven Tong

Project co-supervisors

Dr Kate Worthing, Dr Mark Davies

Project availability

- PhD
- MSc
- Honours

Villadangos group

Contact name Professor Jose Villadangos
Email address j.villadangos@unimelb.edu.au

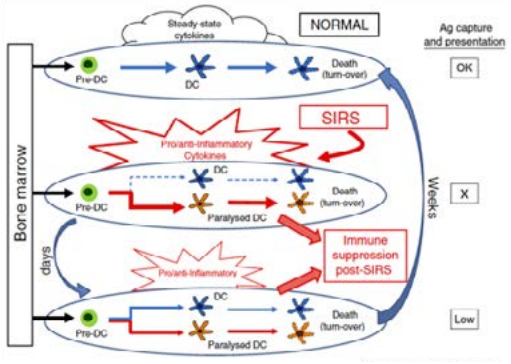
Number of vacancies available 3

Immunology

Host-pathogen Interactions

Discovery Research

Translational and Clinical Research



Induction of DC paralysis following SIRS.

The Villadangos group studies the first event that triggers adaptive immune responses: the presentation of pathogen or tumour antigens to T cells by dendritic cells, B cells and macrophages. We are characterising the development, regulation and impairment of antigen presenting cells by pathogens, inflammatory mediators and tumours. We are also dissecting the biochemical machinery involved in antigen capture, processing and presentation. We use this knowledge to understand how T cell-dependent immunity is initiated and maintained, and apply it to design better vaccines and immunotherapies against infectious agents and cancer.

Project: Immuno-paralysis following severe infections or trauma

Systemic Inflammatory Response Syndrome (SIRS) is a common condition associated with severe infections and trauma. It is characterised by inflammation followed by a period of immunosuppression that can last for several weeks. Immunosuppressed patients are at risk of suffering secondary or opportunistic infections, a major cause of death in intensive care units. Impairment of dendritic cells (DC), the primary initiators of T cell immunity, plays a prominent role in this immunosuppression post-SIRS. In this project we will use models of infection and trauma to characterise the mechanisms that cause DC paralysis and to develop therapies to prevent immunosuppression.

Project supervisor

Professor Jose Villadangos

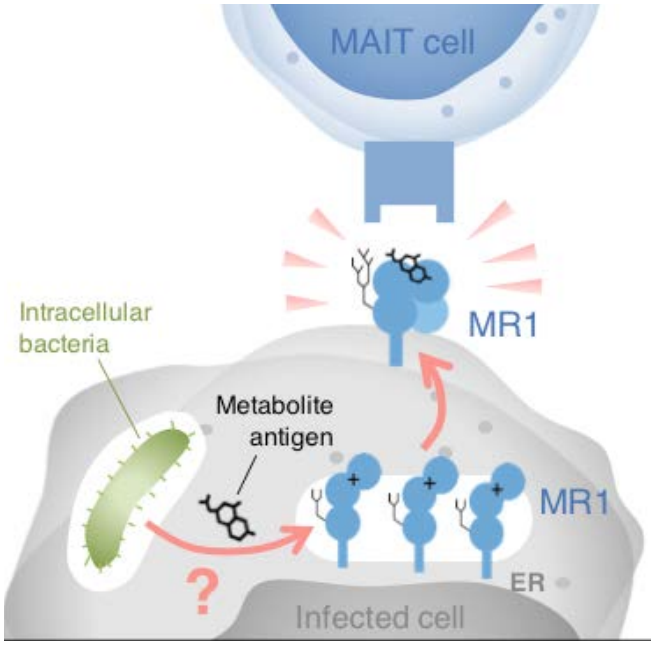
Project co-supervisor

Dr Jason White

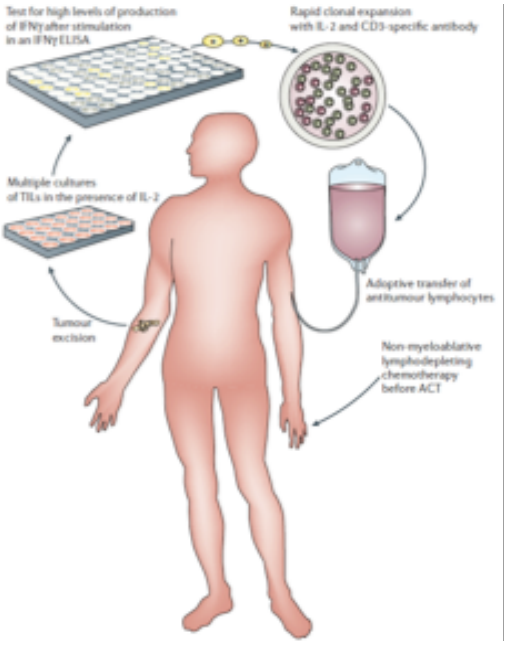
Project availability

- PhD
- MSc
- Honours

Villadangos group



Pathogens (in this case an intracellular bacterium, green) produce unique metabolic products (antigens) that bind to MR1 molecules (blue) expressed by host cells. The MR1 molecules are displayed on the cell surface, enabling Mucosal Associated Invariant T (MAIT) cells specialised in fighting bacterial infections to detect the bacterial antigen. Detection triggers an immune response.



Overview of Adoptive Cell Therapy against cancer (Gattinoni L. et al., Nat Rev Immunol, 2006).

Project: MR1 – a molecular alarm system for bacterial infection

MR1 functions as a molecular alarm system to alert the immune system that a bacterial infection is taking place. It does this by capturing metabolite by-products from bacteria and presenting them at the cell surface to activate a highly abundant T cell subset, called mucosal-associated invariant T (MAIT) cells. MR1 is a highly conserved piece of the mammalian immune repertoire to detect bacterial pathogens, yet basic aspects of its cell biology are not well understood. This project will investigate the molecular machinery underpinning the biology of MR1 molecules, using CRISPR/Cas9 gene editing and cutting-edge cell biology and biochemistry techniques.

Project supervisor
Dr Hamish McWilliam

Project co-supervisor
Professor Jose Villadangos

Project availability
- PhD
- MSc
- Honours

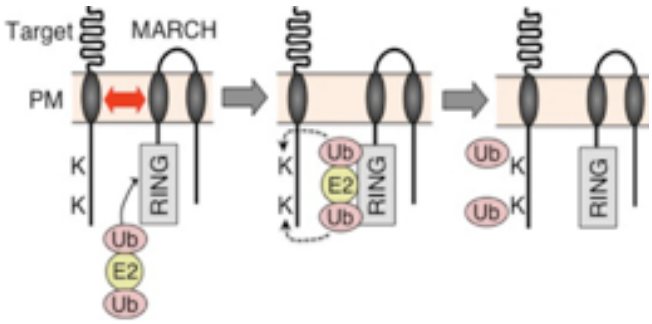
Project: Understanding the mechanisms that impair anti-tumour adoptive cell therapy

Tumour cells express neo-antigens that can be recognised by cytotoxic T lymphocytes (CTL). These tumour-specific CTL can be isolated, expanded and inoculated to kill cancer. Unfortunately, in many individuals the tumour 'fights back' and inactivates the infused CTL, compromising the therapy. Using a mouse model of lymphoma, we are performing studies to improve outcomes. Our goal is to apply our findings to the clinic and improve the efficacy of adoptive cell therapy. The aims of this project will be to identify genes that control the outcome of adoptive cell therapy, and characterise the interactions between T cells and the tumour.

Project supervisor
Professor Jose Villadangos

Project co-supervisor
Dr Sathishkumar Selvaraj

Project availability
- PhD
- MSc
- Honours



Ubiquitination of membrane proteins by MARCHs. The MARCHs recognise their substrates via transmembrane region interactions (left); the RING-CH domain of the MARCH binds an E2 ligase, which then transfers ubiquitin (Ub) to receptor sites in the cytoplasmic tail of the target (centre), leaving a ubiquitinated substrate (right).

Project: Immunoregulatory functions of the MARCH family of ubiquitin ligases

Protein localisation and abundance (proteostasis) are controlled in eukaryotic cells by regulatory pathways, which remain poorly understood. These pathways regulate changes in protein expression or localisation, in response to environmental cues such as the presence of pathogens. Addition of the small protein ubiquitin (Ub) to membrane proteins by the membrane-associated RING-CH (MARCH) family of ligases is an important mechanism of control of membrane immunoreceptors. This project will employ biochemical techniques, microscopy, proteomics, and CRISPR-Cas9 technology to characterise the function of the MARCH family; identify novel MARCH substrates; and characterise the machinery involved in ubiquitination by MARCHs. The MARCHs have also been shown to play an important role in control of infection by HIV and other enveloped viruses. Our goal is to develop novel therapeutic approaches to fight infection based on manipulation of membrane protein ubiquitination.

Project supervisor

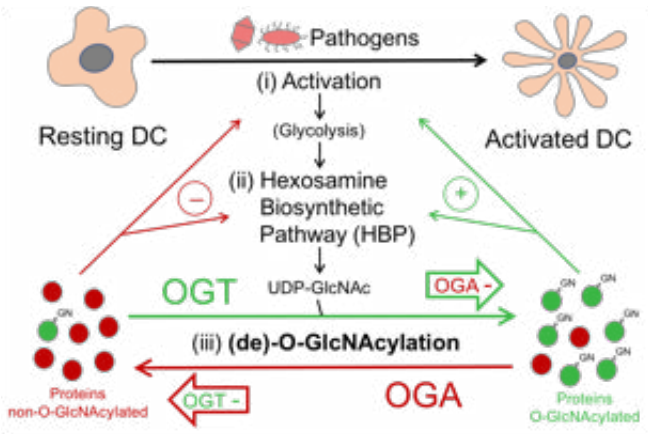
Professor Jose Villadangos

Project co-supervisor

Dr Justine Mintern

Project availability

- PhD
- MSc
- Honours



Reciprocal regulation of immunity and metabolism via O-GlcNAcylation.

Project: The role of glucose metabolism in the regulation of immunity

O-GlcNAc glycosylation involves addition of a single sugar, β-N-acetylglucosamine, to serine or threonine residues of proteins. It is a unique type of glycosylation found on nuclear and cytoplasmic proteins. The addition and removal of O-GlcNAc is catalysed by O-GlcNAc transferase (OGT) and O-GlcNAse (OGA) respectively. It is a reversible modification akin to phosphorylation. Indeed, O-GlcNAc glycosylation occurs in dynamic interplay with phosphorylation, either on the same or adjacent residues. The cross-talk between these two modifications in turn regulates various cellular processes. We are characterising the function of O-GlcNAc glycosylation in immune cells by identifying changes in patterns of glycosylation in different metabolic states and upon encounter of pathogens. The function of glycosylated proteins will be further studied to understand the relevance of their O-GlcNAc status in various immune cell activities.

Project supervisor

Professor Jose Villadangos

Project co-supervisor

Dr Nishma Gupta

Project availability

- PhD
- MSc
- Honours

Wakim group

Contact name Dr Linda Wakim
Email address wakiml@unimelb.edu.au

Number of vacancies available 2

Immunology

Viral Infectious Diseases

Discovery Research

Translational and Clinical Research

The Wakim group research focus is understanding how T cells resident along the respiratory tract can be utilised to protect against influenza virus infection. Our main focus is to characterise the influenza virus fighting T cells in the lung and nasal tissue, identify factors important in their differentiation and longevity, and optimise approaches to lodge these highly protective T cells along the respiratory tract with the intent to improve influenza vaccine design and efficacy.

Project: Blocking the development of secondary bacterial pneumonia

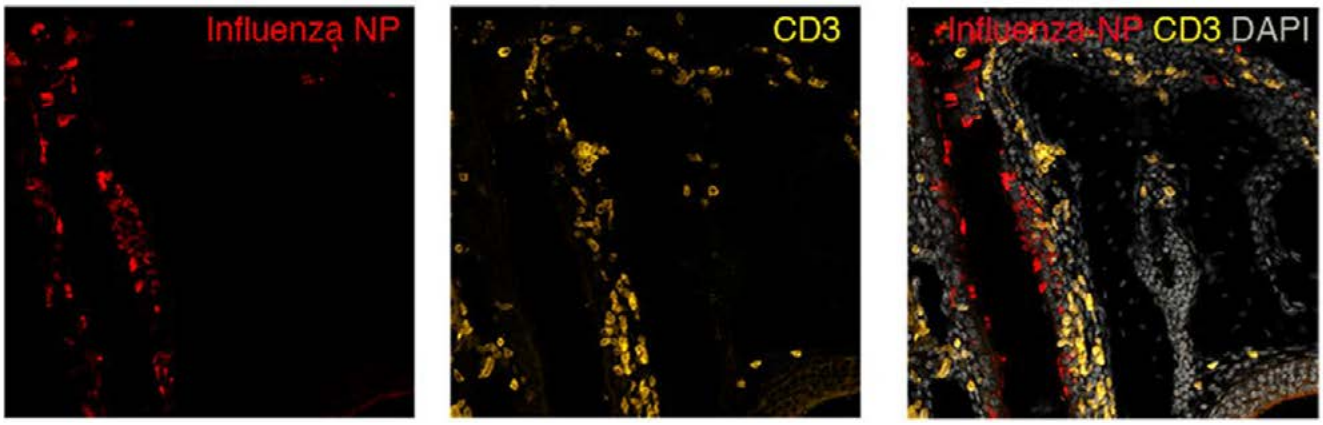
A complication associated with influenza virus infection is the development of a secondary bacterial pneumonia. Staphylococcus aureus is a frequent perpetrator of secondary bacterial pneumonia following influenza A virus (IAV) infection. These bacteria are a commensal organism found in the nasal passage of 20% of humans, and persistent nasal carriage of Staphylococcus aureus is a significant risk factor for secondary staphylococcal pneumonia in IAV infected patients. We are looking for highly motivated students to determine why influenza infection causes Staphylococcus aureus to transition from the upper to the lower respiratory tract resulting in the development of bacterial pneumonia.

Project supervisor

Dr Linda Wakim

Project availability

- PhD
- MSc



T cells (CD3+) along the respiratory tract surrounding influenza virus (NP+) infected cells.

Project: Location, location, location – lodging virus specific T cells in the lung as an approach to protect against influenza virus infection

This research project will characterise the influenza virus fighting T cells in the lung and nasal tissue, identify factors important in their differentiation and longevity, and optimise approaches to lodge these highly protective T cells along the respiratory tract, with the intent to improve influenza vaccine design and efficacy.

Project supervisor

Dr Linda Wakim

Project availability

- PhD
- MSc

Project: Exosomes – a role in influenza virus defence

Exosomes (EV) are extracellular vesicles secreted by cells that have an important biological function in intercellular communication. A role for EV in antimicrobial defence has recently emerged, however little is known regarding the nature of EV, particularly during an active viral infection. We found that during an influenza virus infection, the body releases EV into the airways which changed their protein composition over the course of the infection. The functional relevance of these vesicles and whether they have antiviral actions that can modulate the course of the infection is not known and will be explored in this research project.

Project supervisor

Dr Linda Wakim

Project co-supervisor

Professor Patrick Reading

Project availability as follows

- PhD
- MSc

Doherty Institute

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