Research Projects

2020

Honours, Masters, PhD and MPhil

Department of Microbiology and Immunology
Department of Medicine
Doherty Department

CELEBRATING
5 YEARS

THE UNIVERSITY OF
MELBOURNE

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 – 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 Physiology or Medicine, 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 Doherty 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
- Translational and Clinical Research
- Global 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 - Royal Melbourne Hospital (Infectious Diseases)
- Department of Medicine - Austin Health (Infectious Diseases)
- The Doherty Department

The Royal Melbourne Hospital

- Victorian Infectious Diseases Reference Laboratory (VIDRL), including the WHO Collaborating Centre for Reference and Research on Influenza
- Victorian Infectious Diseases Service (VIDS)
- 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. 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 Melbourne Medical School 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 and Health Sciences. Projects available within 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 the PhD Program Manager: doherty-phdprogram@unimelb.edu.au
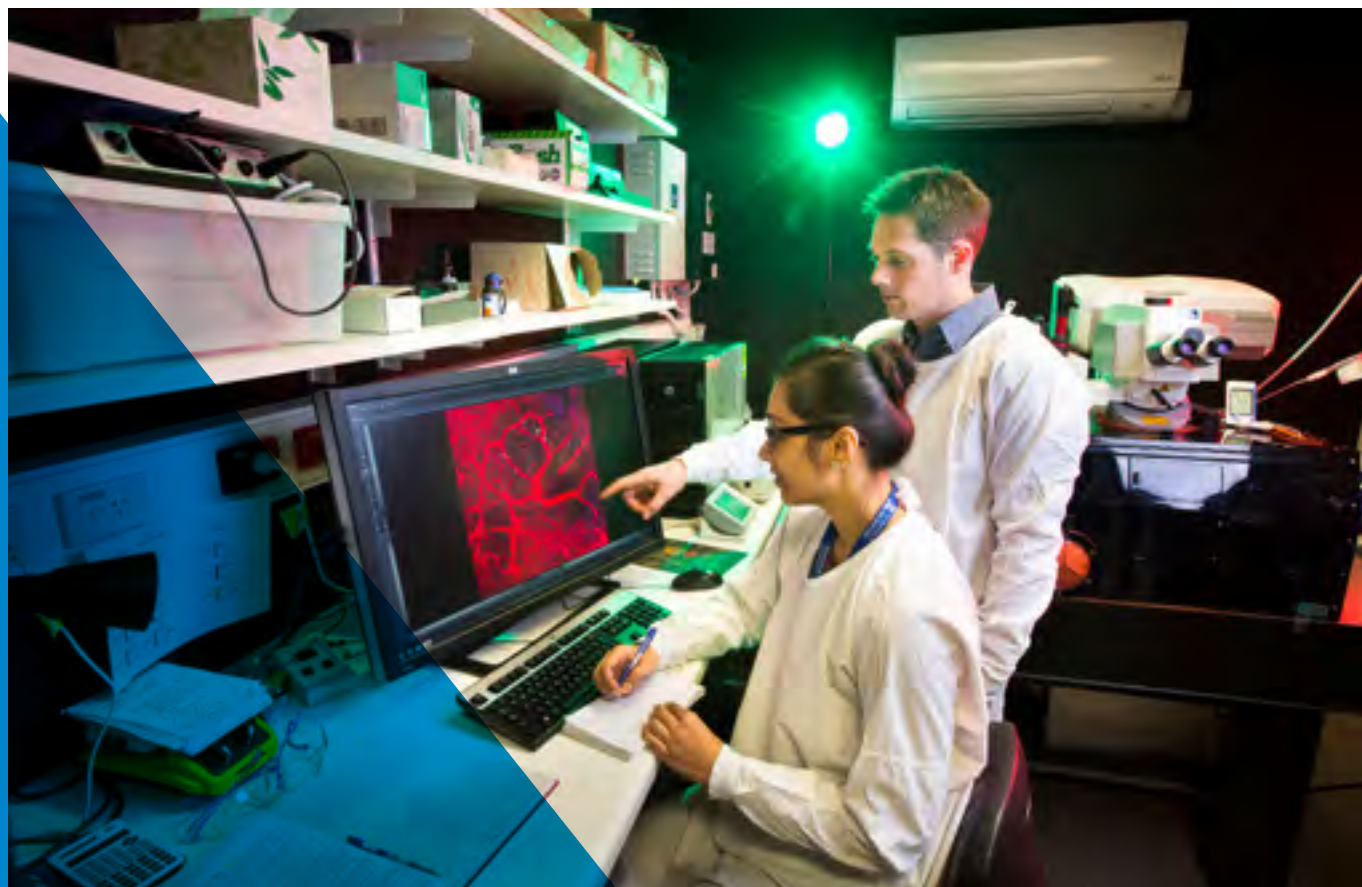
Honours

What is Honours?

Honours is a fourth-year undergraduate course that consists of a combination of a research project and coursework subjects. The course is designed to develop the student's capacity to solve problems, analyse data, read and think critically, and communicate clearly.

Honours can give you a taste of what working as a scientist would be like as a career, allows you to demonstrate academic excellence in an area of special interest to you, and provides an entry point for further research higher degree study, such as a PhD. These skills are highly sought after by employers in biological, medical and industrial areas.

What are the entry requirements?

To be considered for entry, applicants must have completed a suitable undergraduate degree (Bachelor of Biomedicine, Bachelor of Science or equivalent) with a major in a relevant discipline with a WAM (weighted average mark) of at least H3 (65%) or equivalent. However, nearly all students entering Honours in Microbiology and Immunology obtain a WAM of at least 73%.

Students who have completed or are due to complete a Bachelor of Biomedicine at the University of Melbourne should apply to complete Biomedicine Honours. Students who have completed or are due to complete a Bachelor of Science at the University of Melbourne or an equivalent course at another institution should apply to complete Science Honours. Meeting the minimum Faculty level is not a guarantee of admission and students must be accepted by a supervisor before entry into the course.

How long is Honours?

Honours is a one-year course consisting of 75 points of research and 25 points of coursework that commences mid-February and finishes in November.

How to apply

Step 1: Contact potential supervisor(s)

Decide which projects you wish to apply for and make contact with the relevant supervisor.

Applicants must contact potential supervisors either before or soon after submitting an online application for entry to a Medicine, Dentistry and Health Sciences (MDHS) Honours course.

Step 2: Online application

Lodge an online application

1. Apply online and select either the Returning Applicants, Current Students and Previous Students or First Time Applicants. Do not select the First Time Applicants option if you have previously completed study or applied to any program at the University of Melbourne.

2. Select 'MDHS Specialisations' as requirement response in the online application form.

3. Provide original or certified transcript(s) for any study not undertaken at the University of Melbourne. You are not required to provide transcripts for study already undertaken at the University of Melbourne.

Step 3: Project preference

Once you have submitted an online course application, you will receive an email within three working days with your personal login details to access the Honours Project Preference System - SONIA. Please follow the instructions in the email to set up your password and select your preferences for projects offered within MDHS departments. You may select up to four project preferences in Round 1, or three project preferences in Round 2, 3 and mid-year. You must only preference projects after making contact with the relevant supervisor(s). You are allowed to log into SONIA to change your preferences any time by the closing date.

More information including application dates and online application link: https://mdhs-study.unimelb.edu.au/degrees/honours/apply-now

Contacts

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Professor Damian Purcell

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**Melbourne Medical School
Graduate Research Coordinator**

Email: gr-parkville@unimelb.edu.au

Master of Biomedical Science

What is the Master of Biomedical Science?

The Master of Biomedical Science at the University of Melbourne is a coursework master's degree incorporating a substantial research project. This course is an alternative to the Honours as a PhD pathway. Students undertake a major research project and discipline-specific coursework subjects. In addition, a suite of professional business and communication subjects are offered to complement and enhance the research undertaken and to progress students' career opportunities.

The course encourages students to think innovatively and provides an awareness of the health and economic benefits of biomedical research. Graduates of this course gain an understanding of the research process, specialist knowledge and professional skills that are attractive to employers.

What are the entry requirements?

To be considered for entry, applicants must have completed a suitable undergraduate degree with a major in a relevant discipline with a WAM (weighted average mark) of at least H3 (65%) or equivalent. Meeting this requirement does not guarantee selection.

Note:

- Quotas may be applied to the degree as a whole, or to individual disciplines, and preference may be given to applicants with evidence of appropriate preparation or potential to undertake research.

- Entry is subject to the capacity of a participating department to provide adequate supervision in a research project appropriate to the interests and preparation of the individual student and is subject to the agreement of an academic staff member to supervise the project.

- Students entering this course are expected to organise an academic supervisor in the relevant academic unit, and select a research project as part of the application process. You will be provided with a list of current projects once your application has been assessed and deemed eligible. The theme and scope of the research project is negotiated between the student and supervisor prior to commencement of the course.

How long is the Master of Biomedical Science?

The Masters is a two-year (full time) course consisting of 125 points of research and 75 points of coursework. The course can be commenced at the start of the year or at mid-year.

How to apply

1. Apply online and select either Current Students and Previous Students or First Time Applicants. Do not select the First Time Applicants option if you have previously completed study or applied to any program at the University of Melbourne.

2. Provide original or certified transcript(s) for any study not undertaken at the University of Melbourne.

Selecting a Project

Once you have submitted an online course application, you will receive an email with your personal login details to access the Master of Biomedical Science Project Preference System - SONIA. Please follow the instruction in the email to set up your password and review projects offered within MDHS departments. You must make direct contact with the supervisor(s) and obtain permission to work on their project before submitting your project preference. Once your project has been endorsed, you will be allocated to this project in SONIA.

More information including application dates and online application link: https://study.unimelb.edu.au/find/courses/graduate/master-of-biomedical-science/how-to-apply/

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**Melbourne Medical School
Graduate Research Coordinator**

Email: gr-parkville@unimelb.edu.au

Difference between Honours and the Master of Biomedical Science

	Honours	Masters
Duration	1 year (full time)	2 years (full time), part time available
Level	Undergraduate	Graduate
CSP (commonwealth supported places) available?	Yes	Limited
PhD scholarship scoring	Considers marks from third year of Bachelor's degree and Honours marks	Only Masters marks are considered
International market recognition	Australian Honours degrees may not be recognised overseas, as many countries do not have an equivalent degree	Recognised as a graduate master's degree

Research Higher Degrees

What is a PhD?

A PhD (Doctor of Philosophy) is a three-year supervised research degree with the possibility of up to 12 months extension. A candidate may be required to supplement their research with enrolment in additional subjects if considered necessary. The research is written up as a thesis (80,000 – 100,000 words) and examined by external experts in the field.

What is a MPhil?

A MPhil (Master of Philosophy) is similar to a PhD but carried out over a shorter period of time of 18 months to two years. The research work is written up as a thesis (30,000 – 40,000 words), which demonstrates your knowledge and contribution to the field of research.

What are the entry requirements?

To be considered for entry into a PhD, applicants must have completed:

- A four-year bachelor degree (BSc Hons, BBiomed Hons) in a relevant discipline, which includes a substantial research component equivalent to at least 25% of one- year full time study and achieved a minimum WAM (weighted average mark) of 80% (University of Melbourne) or equivalent; or
- A masters degree in a relevant discipline, which includes a substantial research component equivalent to at least 25% of one-year of full time study and achieved a minimum WAM of 80% or (University of Melbourne) equivalent.

To be considered for entry into a MPhil, applicants must have completed:

- A four-year bachelor degree (BSc Hons, BBiomed Hons) in a relevant discipline, which includes a substantial research component equivalent to at least 25% of one-year full time study and achieved a minimum WAM of 75% or higher; or
- A masters degree in a relevant discipline, which includes a substantial research component equivalent to at least 25% of one-year of full-time study and achieved a minimum WAM of (University of Melbourne) 75% or higher.

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.

For future information regarding Research Higher Degrees:

https://study.unimelb.edu.au/find/courses/graduate/doctor-of-philosophy-medicine-dentistry-and-health-sciences/

https://study.unimelb.edu.au/find/courses/graduate/master-of-philosophy-mdhs-biomedical-science/

Doherty Institute PhD Program

The Doherty Institute PhD 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 Doherty Institute's 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 specialities, 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 diseases 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.

How to apply

1. Review the list of prospective projects and supervisors in this handbook or online at https://www.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 a full copy of academic transcripts.

3. Once confirmed a project and supervisor, apply online at https://study.unimelb.edu.au/how-to-apply/graduate-research.

Contacts

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PhD Program Manager

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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.

Highly ranked full time students who have enrolled in a 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 a Frances Elizabeth Thomson Trust Scholarship. The Scholarship will award eligible students with a one-off payment of $5000. mdhs.unimelb.edu.au/study/scholarships/n/frances-elizabeth-thomson.

Students with a high average WAM (weighted average mark) and a high average in their third-year marks will be considered for a Department of Microbiology and Immunology Honours Scholarship of $5000.

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 while 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

Research projects

Barrow group

Contact name Dr Alexander David Barrow
Email address alexanderdav@unimelb.edu.au

Number of vacancies available 3

Immunology

Host-pathogen Interactions

Translational and Clinical Research

Discovery Research

The Barrow group is interested in innate immune recognition programs, in particular a new immunological recognition strategy termed 'growth factor surveillance'. Growth factors (GFs) are over-expressed by cancer cells to promote tumour growth. Pathogens, especially viruses, also encode GF homologues that are required for host infectivity. We first showed how the immune system evolved activating receptors to sense aberrant GF expression by cancers and pathogens. The Barrow group's goal is to understand how the immune system recognises GF expression by tumours and infected cells with the ultimate aim of exploiting these pathways for cancer immunotherapy and the development of new vaccines.

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

Plasmacytoid dendritic cells (pDCs) are rare cells that secrete large quantities of type-I interferon (IFN-I) in response to viral infections. Some viruses encode GFs to induce proliferative lesions that are required for host infectivity. We have found that some GFs can enhance IFN-I production by pDCs. These results suggest that GFs can synergise with toll-like receptors (TLRs) to enhance IFN-I secretion by pDCs. The Barrow group is interested in identifying how the GF and TLR signalling pathways intersect to enhance IFN-I secretion by pDCs to evoke effective anti-viral immunity.
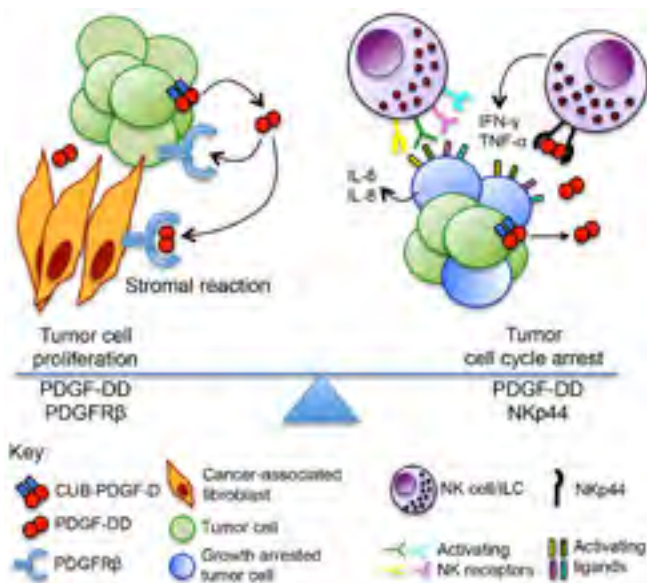
Project supervisor

Dr Alexander David Barrow

Project co-supervisor

Professor Andrew Brooks

Project availability

- PhD
- MSc
- Honours

Many tumours secrete PDGF-D to promote tumour growth (left). NK cells have evolved the activating receptor NKp44 to sense expression of PDGF-DD and trigger the secretion of cytokines that induce tumour cell cycle arrest (right) (Barrow et al Cell, 2018).

Project: Molecular basis for growth factor surveillance in natural killer cells

Many tumours secrete Platelet-derived growth factor (PDGF)-D to promote tumour growth. Natural killer (NK) cells have evolved the activating ITAM receptor NKp44 to sense the expression of PDGF-D and trigger the secretion of cytokines that halt tumour growth. An alternatively spliced NKp44 isoform encodes an 'ITIM' that is predicted to be inhibitory and is associated with poor survival in cancer. Tumours may induce this inhibitory NKp44 form to dampen NK cell function as a form of immune evasion. The Barrow group is determining the functions of the different NKp44 isoforms and how they impact NK cell surveillance of cancers expressing PDGF-D.

Project supervisor
Dr Alexander David Barrow

Project co-supervisor
Professor Andrew Brooks

Project availability
- PhD
- MSc
- Honours

Project: Immunosurveillance pathways in brain cancer

Growth factor (GF) surveillance is a new mode of cancer immunosurveillance in which the immune system responds to GFs over-expressed by cancers and infected cells. Our work has implicated natural killer (NK) cells and GF surveillance in the control of glioblastoma, a high-grade glioma with poor survival. In collaboration with the Mantamadiotis group, the Barrow group is assessing the role of NK cells and other immune cell subsets in immunosurveillance of the brain using a transgenic mouse model of glioma.

Project supervisor
Dr Alexander David Barrow

Project co-supervisor
Dr Theo Mantamadiotis

Project availability
- PhD
- MSc
- Honours

Brooks group

Contact name Professor Andrew Brooks
Email address agbrooks@unimelb.edu.au

Number of vacancies available 2

Immunology

Viral Infectious Diseases

Host-pathogen Interactions

Translational and Clinical Research

Discovery Research

The Brooks group has a diverse range of interests, largely centered on immunoreceptors that regulate natural killer cell and gamma delta T cell function. Our work focuses on how signals from these receptors are coordinated to regulate lymphocyte function in the settings of cancer, lung transplantation and viral infection. We address these questions using classical cellular immunological approaches combined with flow cytometry, immunogenetics along with an array of structural and molecular approaches.
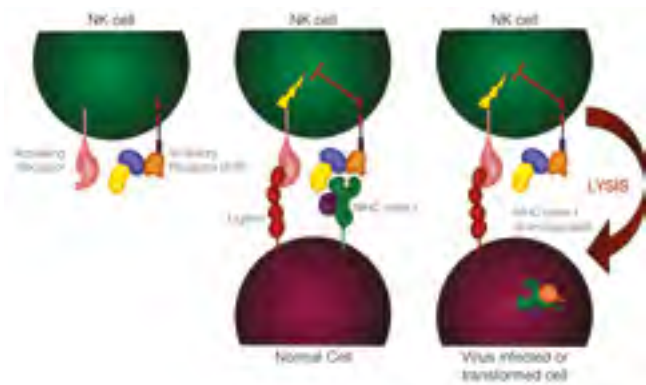
The missing-self model of NK cell activation

Project: Using transcriptional analyses to understand recognition of tumours by natural killer cells

Natural killer (NK) cells are a major component of the immune response to viral infections and cancer. As such, understanding how they are functionally regulated and the potential to manipulate their function in a clinical setting is of great importance. NK cells respond to virally infected cells or tumor modified cells through recognising down-regulation of HLA-I molecules on their cell surface. Normal cells have high levels of HLA-I on their cell surface, which following engagement of KIR receptors inhibits NK cell activation. However, in settings of virus infection and cancer, HLA-I can be down-regulated, leading to their targeting by NK cells. Detailed analyses shows genetic variability in the quality of this inhibition. Although understood at a cellular level, much less is known about underlying molecular processes that drive these distinct cellular outcomes. Understanding these intracellular pathways offers an opportunity to fine tune NK cell activity in a variety of clinical settings. This project will therefore directly investigate, (a) the strength of KIR-HLA interactions, and (b) how the types of receptors engaged regulates functional responses of primary human NK cells. This project will combine molecular and cellular immunology and offers a number of relevant immunological techniques including cell culture, functional in vitro assays with primary human cells, flow cytometric analysis, cell sorting, RNA extraction, RNASeq library preparation along downstream analysis of transcriptome and further identification of candidate genes.

Project supervisor

Professor Andrew Brooks

Project co-supervisors

Dr Sanda Stankovic, Dr Philippa Saunders

Project availability

- PhD

- MSc

- Honours

Project: Identifying novel subsets of immune cells that control cytomegalovirus following transplantation

Transplantation is a life-saving procedure for people with end-stage organ failure or malignant blood cancers. However, post-transplant immunosuppressive medications required to prevent rejection result in impaired ability to control infections. In particular, the control of cytomegalovirus (CMV) is one of the most significant hurdles to successful transplantation. Anti-viral pre-emptive therapies are routinely used, often for an uncertain duration and frequently causing bone marrow or renal toxicity. CMV-immune monitoring assays can optimise the duration of anti-viral prophylaxis by giving an indication of when the individual patient has sufficient CMV-immunity to prevent disease. However, our preliminary data indicates that several important immune cell populations are overlooked in CMV immune monitoring assays. We now wish to investigate the role of these immune cells in controlling CMV following transplantation. We anticipate our research can lead to improved diagnostic tests that provide a more accurate and comprehensive assessment of CMV immunity. Moreover, we may be able to harness novel immune cells for focused therapies with a view to reducing CMV and prolonging survival following transplantation.

Project supervisor

Dr Lucy Sullivan

Project co-supervisors

Dr Michelle Yong, Dr Sanda Stankovic

Project availability

- PhD

- MSc

- Honours

Chung group

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

Number of vacancies available 3

Immunology

Viral Infectious Diseases

Discovery Research

The Chung group has an interest in understanding how an antibody can instruct the innate immune system to attack and protect against a range of infectious diseases including HIV, *Mycobacterium tuberculosis* and malaria through engagement with their Fc regions. Ultimately, our research aims to understand the mechanisms behind these antibodies in order to guide the development of more effective antibody therapeutics and vaccines.

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

Dr Amy Chung

Project co-supervisor

Professor Stephen Kent

Project availability

- PhD
- MSc

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

Dr Amy Chung

Project co-supervisor

Professor Stephen Kent

Project availability

- PhD
- MSc

Project: How does ageing affect antibody responses?

Antibodies are a vital component of the immune response required for protection and control of infectious diseases. However, large changes can occur to the quality of an antibody response as a person grows older. One of the reasons for this change is glycosylation, where sugar structures are added to the antibody. Different glycan structures can determine how well the antibody activates surrounding innate immune cells to attack and eliminate invading pathogens. Intriguingly, within humans, large antibody glycan changes are observed within infants and elderly, which may contribute to why they are more susceptible to infection. This project aims to further understand the effect of ageing upon antibody responses using non-human primate models.

Project supervisor

Dr Amy Chung

Project co-supervisors

Dr Nichollas Scott, Professor Stephen Kent

Project availability

- MSc
- Honours

Davies group

Contact name Dr Mark Davies
Email address mark.davies1@unimelb.edu.au

Number of vacancies available 3

Antimicrobial Resistance and Healthcare Associated Infections

Host-pathogen Interactions

Global Health

Indigenous Health

Genomics

Discovery Research

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 interventions to reduce the disease burden associated with bacterial pathogens. A particular focus of our group is understanding disease processes within regions where disease burden is the highest. 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? What host immune factors govern disease outcomes? Our research benefits from key national and international collaborations.

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

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* subjected 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 model.

Project supervisor

Dr Mark Davies

Project availability

- PhD
- Honours

Project: Evolution of streptococcal pathovars

Streptococcus dysgalactiae subspecies *equisimilis* (group C and G *Streptococcus*) 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: Quantifying bacterial recombination within globally evolving streptococcal pathogens

High strain prevalence and extensive genetic diversity are key features of bacterial pathogens such as the Group A *Streptococcus* (GAS) that cause endemic disease in low-income settings throughout the world. Strain diversity and prevalence are likely associated, but the genetic mechanisms that underpin the maintenance of high strain diversity observed within streptococcal endemic settings remains poorly understood. Over the past decade, we have compiled a large database (>2000 genomes) of GAS genomes from around the world. Our preliminary investigations suggest that genomic recombination occurs much more frequently than previously appreciated, especially within disease endemic settings. By taking advantage of our unique genome databases, this project will use the latest population genomic tools and advanced Bayesian statistical (ABC) interference methods to quantify and model the role that recombination plays in maintaining GAS strain diversity within a global context.

Project supervisor

Dr Mark Davies

Project co-supervisor

Dr Nic Geard

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-supervisor

Associate Professor Steven Tong

Project availability

- PhD
- MSc
- Honours

Davies group

Project: The space of evolutionary trees in infectious disease epidemiology

Infectious disease epidemiology relies on mathematical models that describe epidemiological dynamics. These models typically consider the rate at which individuals are infected and recover from an infection. As many infectious microbes such as viruses and bacteria evolve in orders of magnitude faster than their hosts, their genomes have a signature of the transmission process. This project will pinpoint the key differences between evolutionary trees generated under different epidemiological processes. This project has three main aims: estimating evolutionary parameters for a range of pathogens, such as HIV, influenza and dengue; using these parameters to simulate evolutionary trees under different epidemiological models; and applying machine learning techniques to identify whether epidemiological processes lead to a predictable pattern of evolutionary trees. The outcome will be a framework to classify evolutionary trees from genome surveillance studies, which will contribute to current efforts to couple genomics and epidemiology.

Project supervisor

Dr Sebastián Duchêne

Project co-supervisor

Dr Mark Davies

Project availability

- MSc

- 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. This project applies genomic epidemiology approaches 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: Integrative infectious disease phylodynamics

Recent advances in sequencing technologies have increased the amount of genome data available for many organisms. As microbial pathogens evolve very rapidly, such genome data are informative about their transmission dynamics, a field known as phylodynamics. A key challenge in phylodynamics is coupling genome sequence data with other sources of information (e.g. epidemiology, drug resistance, and geographic location). This project has two broad aims: (a) to develop Bayesian hierarchical models to integrate different types of data, and (b) to leverage these models for real-time genome surveillance where computational speed is essential. This project has a strong methodological component, but it will capitalise on public health genome data. An understanding of phylogenetics, Bayesian statistics, and programming skills in one scripting language (e.g. R or Python) is essential. There are opportunities for a PhD stipend or top-up for highly motivated candidates.

Project supervisor

Dr Sebastián Duchêne

Project co-supervisor

Dr Mark Davies

Project availability

- PhD

Fazakerley group

Contact name   Dr Lukasz Kedzierski
Email address   lukaszk@unimelb.edu.au

Number of vacancies available 1

Immunology

Viral Infectious Diseases

Host-pathogen Interactions

Discovery Research

The Fazakerley group's main interest is the transmission and pathogenesis of arthropod vector-borne (arbovirus) infections of the central nervous system (CNS). The focus is on (a) dissecting immune mechanisms during acute virus encephalitis and CNS virus persistence, and (b) investigating arthropod responses to alphaviruses and transmission by 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 CNS and have the potential to modulate immune responses in the brain. We have recently shown that SOCS4- and SOCS5-deficient mice have different susceptibility phenotypes to an alphavirus infection, that virus RNA persists in the brain, and that infectious virus can be reactivated following immunosuppression. This project aims to explore the role of SOCS4 or SOCS5 during SFV induced encephalitis in a mouse model.

Project supervisor

Dr Lukasz Kedzierski

Project co-supervisor

Professor John Fazakerley

Project availability

- MSc
- Honours
- PhD

Fazakerley group

Project: Age-dependent susceptibility of neurons to RNA virus infection

Central nervous system virus infections are a significant global public health concern. Symptomatic viral encephalitis is reported in 1 in 10,000 people. Neurologic complications, particularly in children, are a major health issue. These include major brain deformities, cognitive impairment, epilepsy and Parkinsonian conditions, and are manifested in up to 50 per cent of survivors of symptomatic encephalitis. Susceptibility to these infections is age-dependent and linked to the ability of the immune system to mount an efficient antiviral response. This project aims to explore mechanisms underlying the differences between immature and mature neurons in their ability to control RNA virus encephalitis.

Project supervisor

Dr Lukasz Kedzierski

Project co-supervisor

Professor John Fazakerley

Project availability

- MSc
- Honours
- PhD

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, WEHI).

Project: Vertical transmission of Ross River virus in mosquito vectors

Alphaviruses, such as Ross River virus, chikungunya and Semliki Forest virus, are transmitted between susceptible vertebrate hosts by mosquito vectors. In vertebrates, these viruses initiate acute infections characterised by high virus production and brain or joint disease. In contrast, when a mosquito becomes infected, the virus establishes a persistent infection; there is no apparent effect on mosquito fitness and the mosquito transmits virus for the rest of its life. Using recombinant alphaviruses expressing fluorescent proteins, this project will look at aspects of the immune response in mosquitoes and the possibility that virus is transmitted vertically down the generations. Tools and techniques being used will include recombinant viruses, microscopy, cell culture and insect work.
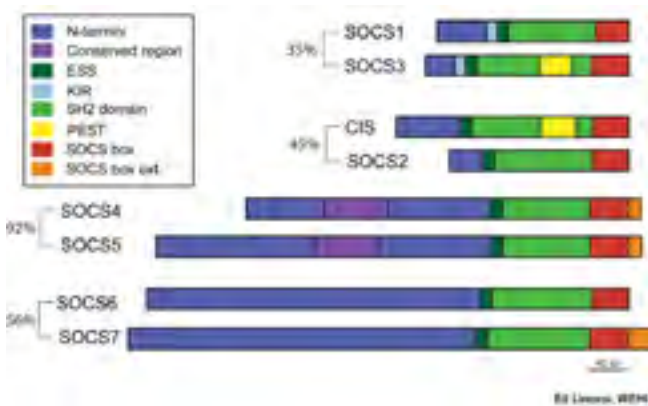
Project supervisor

Dr Julio Rodriguez-Andres

Project co-supervisor

Professor John Fazakerley

Project availability

- MSc
- Honours
- PhD

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

Heath group

Contact name Dr Lynette Beattie
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Number of vacancies available 3

Immunology

Host-pathogen Interactions

Discovery Research

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 understanding how to develop optimal immunity and focus on T cell responses in 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.
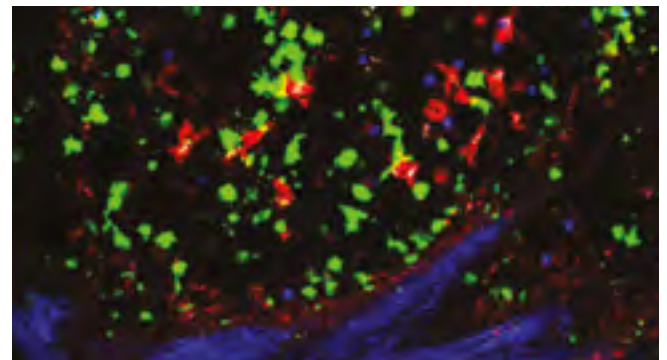
XCR1+ CD8 dendritic cells (green), T cells (blue), and macrophages in the spleen after radiation attenuated sporozoite injection.

Project: γδ T cells are important for malaria sporozoite vaccination

Plasmodium parasites which cause malaria are extremely complex pathogens, with a life cycle involving multiple stages within the mosquito vector and the human host. Sterilising immunity that can successfully protect against the liver stage of infection has many benefits, including blocking progression to clinical disease and blocking transmission back to the mosquito vector. Due to the short timeframe of liver infection prior to break out into the blood stage, it is extremely hard to generate sterilising liver stage immunity. We have recently shown that γδ T cells are crucial to the generation of immunity to liver stage infection, as without this cell population present, CD4 and CD8 T cell responses are severely impaired. We are dissecting the role that γδ T cells play in this system using a combination of cellular assays including flow cytometry, histology and live intravital imaging.

Project supervisor

Dr Lynette Beattie

Project availability

- PhD
- MSc
- Honours

Heath group

Project: Infection induced changes to splenic macrophages

There are multiple populations of macrophages in the spleen, which all have unique locations and functions. We previously showed that as a result of infection with blood stage malaria parasites, we see a CD8 T cell-mediated loss of two of the populations of macrophages, associated with a breakdown in the splenic architecture. We are now investigating this further to understand how CD8 T cells mediate this effect and determine if it has functional consequences for the development of immunity. This project will use advanced cellular immunology techniques including live imaging, immunohistology and flow cytometry.

Project supervisor

Dr Lynette Beattie

Project availability

- PhD
- MSc
- Honours
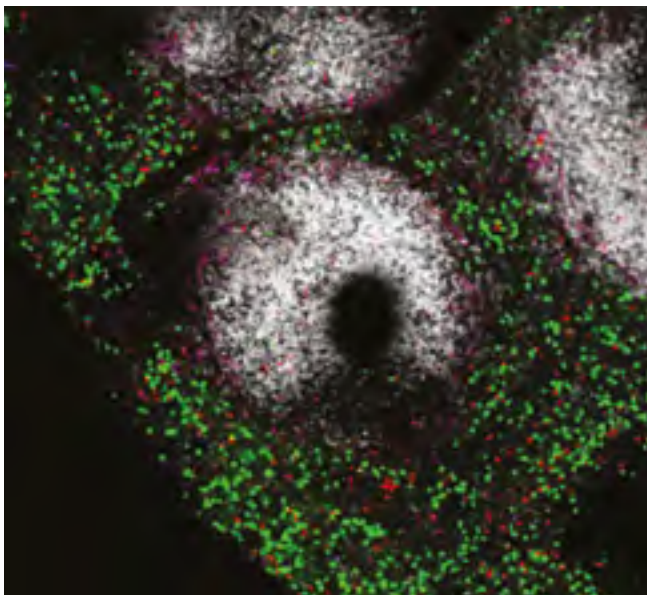
Splenic macrophages (purple) surround B cells (white) and undergo interactions with malaria-specific CD8 (green) and CD4 (red) T cells in the spleen.

Project: Protective capacity of malaria-specific liver tissue-resident memory T cells

We have developed a glycolipid-peptide conjugate vaccine that provides sterile immunity against malaria. Protection in this model is absolutely dependent on malaria-specific tissue-resident CD8 T cells, but how these cells provide protection is not clear. This project will investigate which cell population in the liver re-activates malaria-specific tissue-resident memory T cells after challenge, and how the phenotype and behaviour of these cells changes after challenge. This project will use animal models in combination with advanced immunological techniques including flow cytometry and intravital imaging.

Project supervisor

Dr Lauren Holz

Project availability

- PhD
- MSc
- Honours

Project: Discovery of malaria vaccine peptide targets

Using *Plasmodium*-specific transgenic T cells in a mouse model we demonstrated that tissue-resident memory T cells can fight malaria parasites in the liver with great efficacy. We then developed novel malaria vaccines aimed at the generation of these cells and achieved high levels of protection against infection. However, the lack of known parasite-derived protective epitopes that can be included as antigens in these vaccines is an important limitation for their future development and hinders translation into humans. We have recently defined multiple candidate parasite epitopes with high potential as vaccine antigens. This project will develop an innovative method to test the immunogenicity of these epitopes and to assess the protective capacity of specific liver tissue-resident memory T cells against parasite infection in the mouse model. Promising epitopes will be included in our tissue-resident memory-based malaria vaccines and the immunogenicity of ortholog antigens in human parasites will be tested. This project will involve several advanced immunological techniques with a strong focus on flow cytometry.

Project supervisor

Dr Daniel Fernandez-Ruiz

Project availability

- PhD
- MSc
- Honours

Kent group

Contact name Professor Stephen Kent
Email address skent@unimelb.edu.au

Number of vacancies available 3

Immunology

Discovery Research

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: Interrogating B cell immunity to influenza vaccines

Influenza remains a persistent threat to human health, with current vaccines eliciting sub-optimal and transient protection from infection. Mechanistically, vaccine protection is afforded by antibodies targeting a cluster of highly variable sites in the viral entry protein hemagglutinin (HA). However, next-generation vaccines seek to expand immune recognition to alternative sites within HA, or alternative viral proteins, in order to increase protective breadth. This project will utilise advanced microscopy and flow cytometry-based techniques to interrogate influenza-specific B cell responses (memory B cells, antibodies) to infection and immunisation in both relevant animal models of human influenza, and human clinical samples. Insights will be used to guide the design and testing of novel influenza vaccine concepts in animal models.
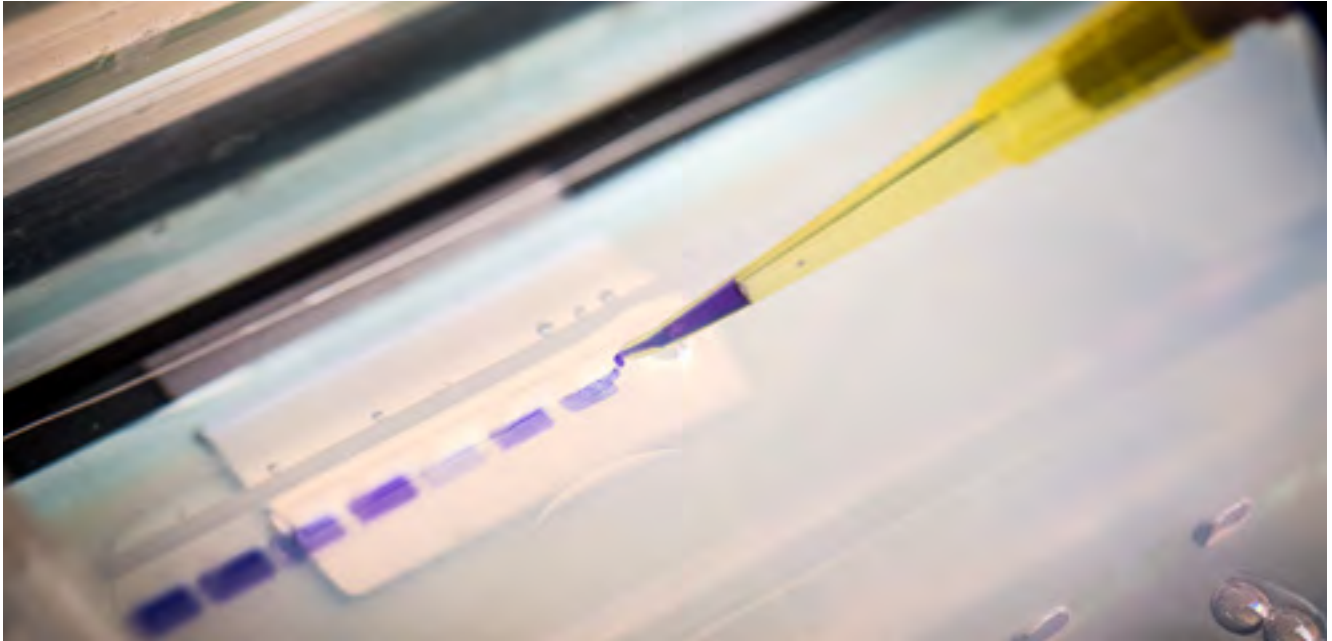
Project supervisor

Professor Stephen Kent

Project co-supervisors

Dr Adam Wheatley, Dr Hyon-Xhi Tan

Project availability

-   PhD
-   MSc

Kent group

Project: Can resident memory B cells in the lung protect against respiratory syncytial virus?

A protective role for memory T lymphocytes localised outside of traditional immune sites has been comprehensively established. However, recent studies have shown memory B cells can similarly take up tissue residence, although the immune benefit for doing so remains unclear. Respiratory syncytial virus (RSV) causes acute respiratory infections in paediatric and geriatric populations associated with significant morbidity, and effective vaccines are currently lacking. This project will assess if immunisation to establish antiviral memory B cells in the lung can combat RSV infection. It will involve: engineering novel influenza-based viral vectors to deliver RSV vaccine antigens, testing in animal models and characterising B cell immunity using a variety of advanced microscopy and flow cytometry-based techniques.

Project supervisor

Professor Stephen Kent

Project co-supervisors

Dr Adam Wheatley, Dr Hyon-Xhi Tan

Project availability

- PhD
- MSc

Project: Programming gamma delta T cells for HIV immunotherapy

Gamma delta T cells are an unconventional T cell subset with cytotoxic activity. These cells are currently being tested in human clinical trials for their ability to kill cancer cells, but less is known about their utility in treating infectious diseases. Preliminary studies from our lab have identified gamma delta T cell subsets with different cytotoxic potential. This project will focus on identifying methods to expand gamma delta T cell populations that can kill HIV-infected T cells in vitro.

Project supervisor

Professor Stephen Kent

Project co-supervisor

Dr Jennifer Juno

Project availability

- MSc
- Honours

Lawson group

Contact name Associate Professor Vicki Lawson
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Number of vacancies available 3

Host-pathogen Interactions

Public Health

Translational and Clinical Research

Discovery Research

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.

Neural spheres growing in vitro from neural stem cells isolated from prion protein knockout mice. Adult neural stem cells will be isolated from mice to enable in vitro (cell culture) characterisation of the contribution of prion protein expression to the hallmarks of cancer in glioblastoma.

Project: The role of the prion protein in brain cancer

Recent studies have reported that the cellular form of the prion protein is upregulated in several cancer types and has been associated with disease progression and poor treatment response. This project will investigate the role of the prion protein in cancer using a mouse model of glioblastoma in which PrPC expression has been ablated. This project will involve breeding and selection (genotyping) of mice, induction of glioblastoma, monitoring of mice for signs of disease and analysis of tissue for evidence of disease. Adult neural stem cells will be derived from this mouse model to enable in vitro (cell culture) characterisation of the cells that give rise to glioblastoma and the contribution of PrPC expression on cancer specific processes.

Project supervisor

Associate Professor Vicki Lawson

Project availability

- MSc
- Honours

Lawson group

Project: The role of co-pathologies in the clinical presentation of prion disease

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. A unique feature of prion diseases is their range of clinical presentations, which affect memory and movement. While these features can be attributed to differences in the shape of the misfolded prion protein, we do not understand how or why prions with different shapes (prion strains) have different clinical presentations. Another recent observation is the presence of co-pathologies, or misfolded proteins associated with other neurodegenerative disorders that have either the clinical presentation of deteriorating movement (alpha-synuclein in Parkinson's disease and TDP-43 in Motor Neuron Disease) or deteriorating memory (amyloid-beta and tau in Alzheimer's disease). We propose that some of the clinical variation in prion disease is due to these co-pathologies and that the presence of co-pathologies is dependent on the shape (or strain) of the misfolded prion protein. We will investigate the role of co-pathologies in prion disease by assessing the behaviour (gait and memory), pathology (histology and western immunoblot analysis) and propagation of prions using our unique panel of mouse adapted human prion strains.

Project supervisor

Associate Professor Vicki Lawson

Project availability

- PhD
- MSc
- Honours

Paw print analysis can be used to identify variation in stride, stance, paw print length and proportion of full paw print. In the paw prints of a mouse with clinical prion disease it can be observed that full paw prints were observed for the left paw, but only partial paw prints were observed for the right paw. An observation that is consistent with a gait abnormality.

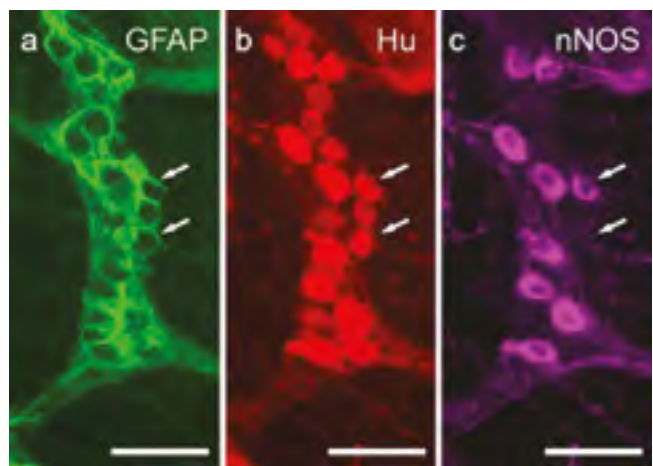## Project: Neurodegeneration in the enteric nervous system

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 systems 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

- PhD
- MSc
- Honours

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).

Lawson group

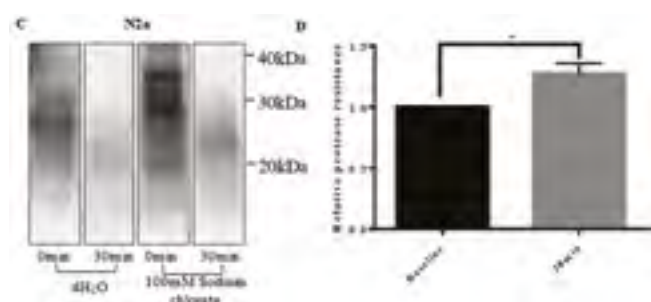## Project: A cell-based model of sporadic prion disease

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 (co-factors) 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 co-factors 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. We have further shown that altering the charge on glycosaminoglycan changes prion protein localisation and susceptibility to misfolding. 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

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: 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.

Project supervisor

Associate Professor Vicki Lawson

Project availability

- MSc

- Honours

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).

Lewin group

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Number of vacancies available 1

Viral Infectious Diseases

Host-pathogen Interactions

Translational and Clinical Research

Discovery Research

The main focuses of the Lewin group is to understand why HIV infection persists on antiretroviral therapy, to develop new strategies to eliminate latency and to define the biological determinants of immune reconstitution and factors that drive liver disease in HIV-hepatitis B virus co-infection.

Project: Harnessing the molecular clock to activate diverse strains of latent HIV

HIV cannot be eradicated from infected individuals by combination antiretroviral therapy (cART), and treatment must continue lifelong. This is due to the presence of silently or 'latently' infected cells, which harbour HIV that is not active. One strategy to eliminate these long-lived latently infected cells is to turn on the virus inside the cell. Recently we have discovered that latent HIV can be activated by modulating one of the transcription factors that drive the circadian rhythm, brain and muscle ARNT-Like 1, or bmal-1. In this project, we aim to determine if this activation potential by BMAL-1 is consistent across the many diverse strains and subtypes of HIV. This information will tell us whether modulating circadian rhythms can be a viable approach to eliminating latently infected cells in regions where the HIV burden is highest, such as sub-Saharan Africa. During this project, the student will learn and apply a range of molecular techniques including transfection, RNA interference, western blotting and real time PCR.

Project supervisor

Professor Sharon Lewin

Project co-supervisor

Dr Michael Roche

Project availability

- Honours

Mackay, Fabienne group

Contact name Dr Catherine Kennedy
Email address catherinek@unimelb.edu.au

Number of vacancies available 2

Immunology

Translational and Clinical Research

Discovery Research

Professor Fabienne Mackay's group has a keen interest in B cell biology and pathology, with research projects that focus B cell development and homeostasis as well as B cell driven diseases such as systemic lupus erythematosus and chronic lymphocytic leukemia. A focal point of this research is the cytokine BAFF; a TNF-like ligand, which signals through three receptors BAFF-R, TACI and BCMA. BAFF is a key survival signal for B cells, however excessive BAFF production drives autoimmunity and is also a driver of chronic lymphocytic leukemia.

Project: Novel master-regulators of B cell biology

We generated CRISPR knock-out mouse lines in which putative B cell regulating genes are specifically deleted. Changes in the B cell repertoire are detectable using flow cytometry and immunofluorescence techniques. This project aims to understand more about the function and mechanism of these novel proteins and determine how they control fundamental B cell biology.

Project supervisor

Professor Fabienne Mackay

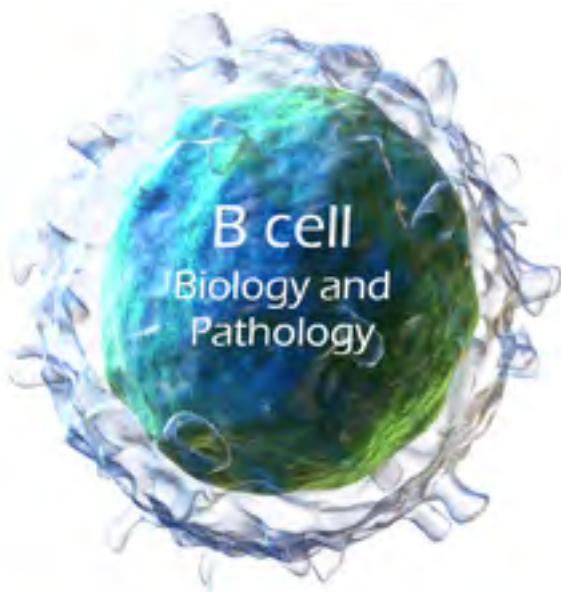**Project co-supervisors**

Dr Catherine Kennedy, Dr William Figgett

Project availability

- MSc
- Honours

Mackay, Fabienne group

The Mackay group studies B cell biology and pathology using a variety of mouse models and immunological techniques with a strong translation angle. (Image from Blausen.com staff (2014) DOI:10.15347/wjm/2014.010).

Project: Testing a novel strategy to target chronic lymphocytic leukemia

Chronic Lymphocytic Leukemia (CLL) is a B cell malignancy that is the most common cause of leukemia in adults aged over 65. Recent studies have shown that CLL cells produce IL-10, an immunosuppressive cytokine that helps the cancer cells evade the immune system by shutting down anti-tumor immunity. New exciting data from our lab shows that IL-10 production by CLL cells is triggered by BAFF, a TNF-like cytokine critical for B cell maturation and survival that is implicated in the development and progression of CLL. Preliminary data show that BAFF-driven IL-10 production by CLL cells is mediated via the receptor TACI, as TACI inhibition resulted in attenuated IL-10 secretion. This project aims to test whether targeting TACI in a model of CLL will be effective at restoring immunocompetency. Flow cytometry, ELISA, in vitro assays and others will be used throughout the project.

Project supervisor

Professor Fabienne Mackay

Project co-supervisor

Dr Simona Infantino

Project availability

- PhD
- MSc
- Honours

Project: Validating human transgenic mouse models for lupus therapeutics development

BAFF is a key survival factor for B cells yet excess BAFF can lead to autoimmune manifestations such as systemic lupus erythematosus (SLE), a disease with limited treatment options. We generated mice where the murine version of a new therapeutic target is replaced by a human version of the molecule. This project aims to evaluate the expression and activity levels of the humanised protein in these mice to validate the mice for preclinical therapeutics testing. Experimental treatments targeting the humanised protein will be tested for therapeutic effect. The project will utilise FACS, ELISA, microscopy, and ex vivo culture of B cell activation to assess experimental therapy in the humanised and conventional mouse models of lupus.

Project supervisor

Professor Fabienne Mackay

Project co-supervisor

Dr William Figgett

Project availability

- PhD
- MSc
- Honours

Project: Determining the role of diet and microbiota in the progression of lupus

Systemic Lupus Erythematosus (SLE) is a debilitating autoimmune disease driven by aberrant B cells producing antibodies against self. This leads to inflammation and ultimately tissue destruction. Today we have no cure for SLE and the current treatments are symptom-focused. Recent advancements in the understanding of the importance of diet and gut microbiota point to a potential role for dietary intervention in the treatment of various auto-inflammatory diseases. The role of the gut microbiome and the potential for diet-based therapies in SLE and their mechanisms of protection will be studied in this project using SLE-prone mouse models, incorporating advanced methods of metabolomics and microbial metagenomics profiling.

Project supervisor

Professor Fabienne Mackay

Project co-supervisors

Dr Catherine Kennedy, Dr William Figgett

Project availability

- PhD
- MSc
- Honours

Mackay, Laura group

Contact name Dr Claire Gordon
Email address claire.gordon@unimelb.edu.au

Number of vacancies available 1

Immunology

Translational and Clinical Research

Discovery Research

The Laura Mackay group studies memory T cell responses, with a focus on the signals that control tissue-resident memory T cell differentiation, with a view to harness these cells to develop new treatments against infection and cancer.

Project: Whole body analysis of human tissue-resident memory T cells

The majority of T cell responses occur in tissues, however, our knowledge of human T cells is largely derived from blood. In collaboration with surgeons from Austin Health and DonateLife, we have access to samples from multiple lymphoid, visceral and barrier sites from research-consented organ donors. Using our unique resource, this project will investigate the pathways that guide tissue-resident memory T cells (TRM) differentiation and maintenance in diverse tissue sites, with the overall goal of developing therapies and vaccines that manipulate TRM.

Project supervisor

Dr Claire Gordon

Project co-supervisor

Associate Professor Laura Mackay

Project availability

- PhD

Mackenzie group

Contact name   Professor Jason Mackenzie
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Number of vacancies available 1

Immunology

Viral Infectious Diseases

Host-pathogen Interactions

Public Health

Global Health

The Mackenzie group investigates the intracellular replication of flaviviruses and noroviruses to understand how replication influences cellular functions and immune dysfunction. In particular, the influences viral replication imparts on metabolic and stress pathways that ultimately lead to immune regulation and dysfunction. We aim to use this knowledge to develop prevention and treatment options against these highly pathogenic viruses.
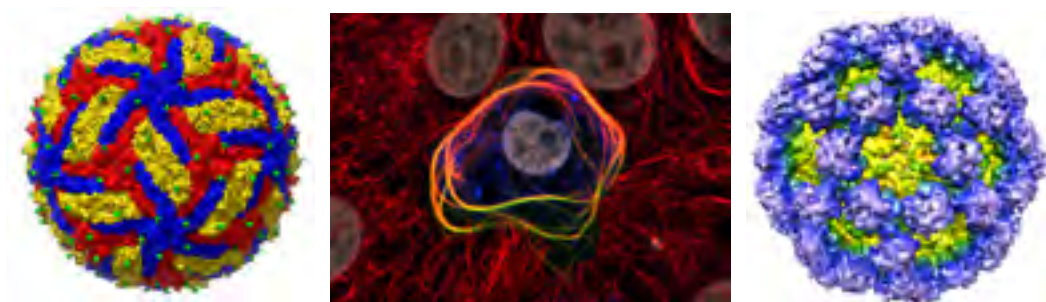
Left hand side: The flavivirus virus particle; Middle: Norovirus infection of mouse macrophages altering the cytoskeleton to look like Australia; Right hand side: The norovirus virus particle

Project: Why is the flavivirus RdRp in the nucleus?

Arguably all (+)RNA viruses replicate in the cytoplasm and the flaviviruses, such as dengue, West Nile and Zika viruses are no exception. Yet surprisingly the viral encoded RNA polymerase (i.e. RdRp) NS5 protein localises to the nucleus. Intriguingly, NS5 does have a nuclear localisation signal and mutation of this motif significantly impairs virus replication. So what is this protein doing in the nucleus? Is it affecting the innate immune response, cell transcription, metabolism or some other modification of host/viral RNA or proteins? During this project you will hopefully figure this out. We have a range of wild-type and mutant NS5 proteins that will be utilised to explore and decipher why the nucleus is involved in flavivirus replication. You will utilise high-end imaging and visualisation approaches to assess nuclear trafficking and also state-of-the-art biochemical approaches to elucidate binding partners of NS5 in the nucleus. You will combine these studies with proteins suppression via RNAi or CRISPR and assess the impact of NS5 on many of the host cellular pathways. Of particular importance will be to assess the immune competency of cells that contain wild-type and mutated NS5. Ultimately, the aim is to identify compounds that can impede the transport of NS5 into the nucleus or attenuate the activity of NS5 in the nucleus to prevent and treat flavivirus infections.

Project supervisor

Professor Jason Mackenzie

Project availability

- PhD
- MSc
- Honours

Project: Preventing infections of the highly puke-ogenic virus - norovirus

Norovirus infections result in a highly acute disease with symptoms that include explosive diarrhea and projectile vomiting. It is an infection that affects 700 million people each year and you are likely to get four to five infections over your lifetime. Yet there is no treatment or prevention options against this significant pathogen, as efforts have been hampered by the inability to effectively cultivate the virus in laboratory conditions. In this project we aim to utilise a vaccine development platform to generate virus-like particles of norovirus and determine their effectiveness in priming and providing a protective immune response to infection. The project will involve the design and production of the virus-like particles to be used in vaccination regimes. Subsequently, the immune response generated to these particles will be assessed. We will also generate virus-like particles to the related mouse norovirus, providing us with an effective model to assess neutralisation and immune correlates, and a tool for us to isolate reactive memory B cells for antibody isolation.

Project supervisor

Professor Jason Mackenzie

Project co-supervisor

Professor Joe Torresi

Project availability

- PhD
- MSc
- Honours

Mantamadiotis group

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Number of vacancies available 1

Immunology

Translational and Clinical Research

Discovery Research

The Mantamadiotis group's research aims to understand how the tumor microenvironment, including immune cells, contribute to oncogenesis and how to modulate the immune system to improve current brain cancer therapy.

Project: Understanding the immune microenvironment in brain tumours

Understanding the best immunotherapy which could be applied to a specific cancer type requires a deep understanding of the immunobiology of the tumour tissue. This project aims to understand the types and distribution of immune cells in brain tumour tissue and how the tumour microenvironment, including immune cells, contribute to oncogenesis. Unique brain cancer cell lines and brain tumour tissue from animal models and patients will be used to investigate the tumour microenvironment using state-of-the-art multiplex immunohistochemistry and computational analysis.

Project supervisor

Dr Theo Mantamadiotis

Project co-supervisor

Dr Stanley Stylli

Project availability

- PhD
- MSc
- Honours

McCluskey group

Contact name Dr Alexandra Corbett
Email address corbetta@unimelb.edu.au

Number of vacancies available 4

Immunology

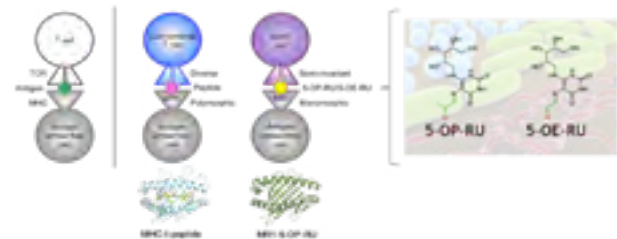**Antimicrobial Resistance and Healthcare Associated Infections**

Host-pathogen Interactions

Translational and Clinical Research

Discovery Research

MAIT cells recognise metabolite antigens, metabolic by-products from vitamin B2 (riboflavin) biosynthesis.

The McCluskey group is an internationally-leading laboratory in mucosal-associated invariant T (MAIT) cell research, having made significant breakthrough discoveries in MAIT cell immunity. These include identifying the antigens recognised by MAIT cells and the associated development of tetramers to characterise MAIT cells (patented). The McCluskey group has also developed human in vitro and in vivo models to understand MAIT cell function and the role of MAIT cells as part of the immune system. In addition, the group has deep expertise in biochemistry, including MAIT cell ligand discovery by mass spectrometry and cellular immunology, allowing to comprehensively address big picture research questions.

Project: Are there additional MAIT cell antigens?

Our team identified the known natural MAIT cell antigens, small molecule antigens which derive from microbial riboflavin biosynthesis. We seek to further understand how these antigens are produced and whether other antigens exist. We have preliminary data for three projects on MAIT cell antigen discovery that we are happy to discuss in detail in person. Broadly speaking, MAIT cell antigen discovery involves in vitro cell line model systems, human blood cell assays, flow cytometry, microbial culture and our proven protein-folding/mass-spectrometry approach.

Further reading

Kjer-Nielsen *et al.* Nature 491(7426):717-23 (2012)

Corbett, Eckle, Birkinshaw, Liu *et al.* Nature 509(7500):361-5 (2014)

Project supervisors

Dr Sidonia Eckle, Dr Lars Kjer-Nielsen, Dr Alexandra Corbett

Project availability

- PhD
- MSc
- Honours

McCluskey group

Project: Understanding the role of MAIT cells in protection from microbial infections

There are very few studies that have investigated the role of MAIT cells in protection to microbial infections. In collaboration with microbiologists and clinicians, we have set up a number of infection models in mice relevant to human diseases. By comparing the pathogen burden in MAIT cell deficient versus competent mice, we determine in each model whether MAIT cells are protective. Using MAIT cell specific tetramers, developed originally in our laboratory, we characterise the frequency and function of MAIT cells by a range of flow cytometry-based techniques. Pathogenesis is assessed by histology. Such analysis provides an insight in the underlying mechanisms of protection, which are also determined in protection experiments with mice knocked-out for specific immune mediators. Microbial infection models include viral, bacterial and fungal pathogens. They are also complemented with human in vitro models of infection and where possible, with experiments on samples from patients. As part of this project it is possible to focus only on human in vitro models of infection (and patient samples) or mouse work.

Further reading

Wang *et al.* Nature Communications 22;9(1):3350 (2018)

Chen, Wang *et al.* Mucosal Immunology 10(1):58-68

Project supervisors

Dr Sidonia Eckle, Dr Zhenjun Chen, Dr Alexandra Corbett

Project availability

- PhD
- MSc
- Honours

Project: Manipulating MAIT cells for increased protection by vaccination and therapy

We, and others, have demonstrated that MAIT cells, unlike other innate like T (NKT or γδ T) cells, are capable of forming memory after priming or primary infection, which provides the foundation for MAIT cell-based vaccination. Since MAIT cells are donor-unrestricted (identical between individuals), and MAIT cell immunity is highly conserved between species, with regards to both the MAIT cell antigen and the immune receptors involved, future MAIT-cell based interventions, including vaccination and therapies, will be universally applicable among all human individuals (not restricted by MHC polymorphism) and farm animals (pigs, sheep and cattle) as relevant to the food industry. We have developed methods to 'boost' MAIT cells in vivo by primary bacterial infection or synthetic antigen and toll-like receptor agonists. In collaboration with microbiologists and clinicians, we have set up a number of infection models in mice to evaluate the efficacy of MAIT cell-based therapies. We also seek to understand MAIT cell fate after 'boosting', and the best methods to drive MAIT cell numbers and function towards better protection. Analysis includes examination of both the quantity and quality of boosted MAIT cells with various combinations of vaccination components, following the fate of animals and determining pathogen burden in vaccinated versus non-vaccinated mice. Using MAIT cell specific tetramers, generated originally in our laboratory, we characterise the frequency and function of MAIT cells by flow cytometry after various manipulations.

Further reading

Wang *et al.* Nature Communications 22;9(1):3350 (2018)

Chen, Wang *et al.* Mucosal Immunology 10(1):58-68

Project supervisors

Dr Alexandra Corbett, Dr Zhenjun Chen, Dr Sidonia Eckle

Project availability

- PhD
- MSc
- Honours

Project: Understanding the role of MAIT cells in immune-mediated pathology

There are very few studies that have definitively determined a role for MAIT cells in immune pathologies, such as allergies and inflammatory diseases. We have previously identified drug metabolites that stimulate MAIT cells and now want to understand if drug and other metabolites cause hypersensitivities, allergies or inflammatory conditions. In collaboration with clinicians, we have access to samples from several cohorts of patients. Based on in vitro stimulation assays with the relevant metabolites in healthy donors and patient samples, we seek to establish if MAIT cells can mediate allergic reactions. This also builds on the group's previous work in drug hypersensitivities mediated by conventional T cells. Human clinical data will be complemented with in vitro human cell line model systems and potentially characterisation of the TCR recognition event at a molecular level using surface plasmon resonance and X-ray crystallography, together with collaborators.

Further reading

Keller, Eckle *et al.* Nature Immunology 18(4):402-411 (2017)

Illing *et al.* Nature 486(7404):554-8 (2012)

Project supervisors

Dr Sidonia Eckle, Dr Lars Kjer-Nielsen, Dr Alexandra Corbett

Project availability

- PhD
- MSc
- Honours

McDevitt group

Contact name Associate Professor Christopher McDevitt
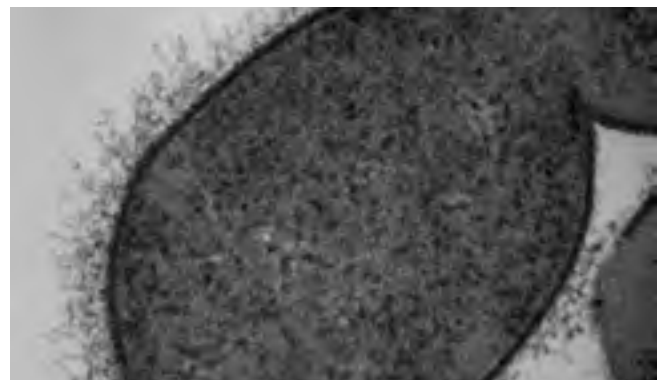**Email address** christopher.mcdevitt@unimelb.edu.au

Number of vacancies available 2

Antimicrobial Resistance and Healthcare Associated Infections

Host-pathogen Interactions

Discovery Research

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 to elucidate the role of metal ions at the 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.

Transmission electron micrograph of *Streptococcus pneumoniae*

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 one 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 Neville

Project availability

- PhD
- Honours

McDevitt group

Project: Metal ion homeostasis in *Klebsiella pneumoniae*

Klebsiella pneumoniae is a globally significant multi-drug resistant pathogen. Our recent studies investigating the chemical biology of this bacterium have identified numerous uncharacterised pathways involved in the acquisition of essential metal ion nutrients, such as zinc and molybdenum, from the host. This project will provide the first descriptions of these pathways and how they contribute to the growth, virulence and antibiotic resistance of *Klebsiella pneumoniae*. The outcomes of this study will provide information essential to exploiting nutrient dependency in breaking multi-drug resistance in *Klebsiella pneumoniae* and other Gram-negative bacteria.

Project supervisor

Associate Professor Christopher McDevitt

Project co-supervisor

Dr Aimee Tan

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 poison 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 during infection. 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

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) 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.
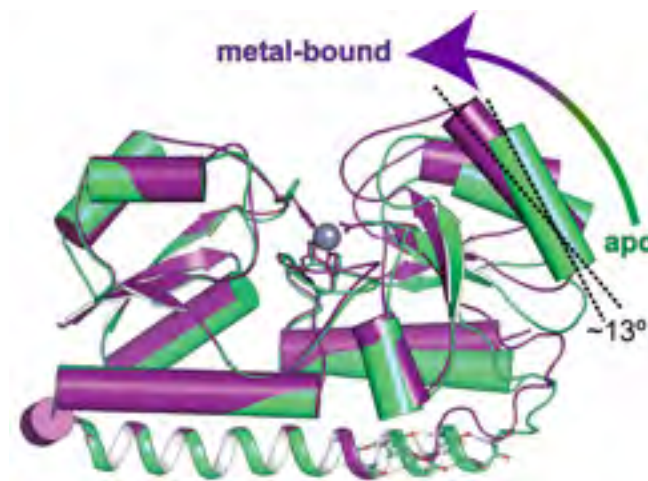
Project supervisor

Associate Professor Christopher McDevitt

Project co-supervisor

Dr Alex Carey Hulyer

Project availability

- PhD
- Honours

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

McVernon group

Contact name   Professor Jodie McVernon
Email address   j.mcvernon@unimelb.edu.au

Number of vacancies available 9

Immunology

Viral Infectious Diseases

Antimicrobial Resistance and Healthcare Associated Infections

Public Health

Indigenous Health

Jodie McVernon's group uses established and emerging biostatistical, epidemiologic and modelling methods to address infectious diseases questions of public health relevance. We bring a suite of collaborators from animal health and ecology to provide a 'One Health' perspective on emerging human pathogens.

Project: Investigating the determinants of persistent or recurrent infections with group A *Streptococcus*

Severe diseases arising as sequelae of superficial skin and throat infections with group A *Streptococcus* (GAS) are important causes of morbidity and mortality worldwide, with the burden of GAS disease overwhelmingly borne by people living in settings of poverty. This project will examine the epidemiology of skin sores, throat infections and throat carriage in a Fijian cohort study. To investigate factors contributing to the persistence or recurrence of GAS infection in individuals, we will analyse data on the presence and characteristics of skin sores, scabies and throat infections, together with demographic and household information. Project findings will inform the development of transmission models for GAS infections, with the ultimate aim of designing sustainable intervention strategies. This project would suit students with analytical skills, familiarity with statistical software such as Stata or R, and an interest in understanding the drivers of infectious disease transmission.

Project supervisor

Dr Patricia Campbell

Project availability

- MSc

Project: Acute respiratory infection presentations and prescribing in primary care

Epidemiologists at The Doherty Institute undertakes surveillance for influenza-like illness (ILI) from a network of sentinel general practices from May to October each year. ILI data are used to epidemiologically characterise influenza seasons in Victoria, and provide a practical alternative measure of influenza activity in the community to notifiable laboratory confirmed influenza. They have also recently established a collaboration with the Health and Biomedical Informatics Centre at the University of Melbourne, in which data on patients presenting with upper respiratory tract infections to ten general practices over a five-year period will be extracted from general practice software. The aim of this project is to assess whether the epidemiological information provided by automated data extraction is supplementary or redundant to that provided from sentinel general practices network. This project would suit students with analytical skills, familiarity with statistical software such as Stata or R, and an interest in understanding how infectious data are used, understood and reported.

Project supervisor

Dr James Campbell

Project co-supervisor

Kylie Carville

Project availability

- MSc

Project: Establishing the determinants of fluctuating incidence of exotic arboviruses in Victoria

Arboviral diseases are notifiable in Victoria, even if they are acquired overseas. This project will examine the epidemiology of exotic (overseas acquired) arboviral diseases in Victoria, such as dengue, chikungunya and/or Zika viruses. To establish the determinants of changes in notification incidence, we will analyse data relating to arboviral disease surveillance (Department of Health and Human Services), travel patterns (Australian Bureau of Statistics) and disease incidence (various sources) for countries where these diseases are acquired. Findings will allow us to understand when and where exotic arboviral diseases are likely to be acquired, and to develop appropriately timed public health warnings for clinicians and travellers. This project would suit a student with analytic skills, familiarity with a statistical program (e.g. Stata), and an interest in infectious disease epidemiology and public health.

Project supervisor

Dr Katherine Gibney

Project availability

- MSc

Project: Analysis of screening and management of viral hepatitis in primary care

Viral hepatitis affects at least half a million Australians, however the existing evidence indicates that many people living with infection are not engaged in care and continue to experience preventable outcomes such as liver failure and viral hepatitis-related death. This project aims to understand the current patterns of care, uptake of prevention and testing, and gaps in engagement for people living with viral hepatitis in primary care in Victoria, which has previously not been systematically assessed. Project findings will guide the implementation of a comprehensive intervention to improve awareness of and clinical practice in relation to viral hepatitis in primary care. This project would particularly suit a student with interest in analysis of longitudinal clinical data and in chronic infectious disease prevention and care.

Project supervisor

Dr Nicole Allard

Project co-supervisor

Jennifer MacLachlan

Project availability

- MSc

Project: Optimal design of competitive mixture experiments

Competitive mixture experiments consist of infecting a host (in this case, a ferret), with different proportions of virus subtypes with nominally differing fitness levels. The ferret is then co-housed with a susceptible (uninfected) ferret, and the abundance of the viral-subtypes is quantified in each host over time. The aim of these experiments is to determine the absolute and relative fitness levels of the subtypes, both in terms of their ability to replicate within the host, and transmit to a new host. To date, the proportions of competing-strains has been chosen uniformly, with equal numbers of ferrets infected with mixtures of 0:100, 20:80, 50:50, 80:20 and 100:0 percent. Virus-dynamics models (coupled systems of differential equations) are used to capture the within- and between-host dynamics observed in the data. In this project, we will investigate models of the viral dynamics, and use these in conjunction with optimal design tools to establish the optimal setup for experiments of this type (with respect to, e.g., proportions of strains, time to introduce the susceptible host, etc.), for strains with different levels of fitness, and for differing experimental aims. This project will be best suited to someone with strong coding skills, and studying a degree in mathematics or statistics e.g. MSc (Mathematics and Statistics) in applied mathematics, stochastic processes or statistics.

Project supervisors

- Dr David Price, Professor James McCaw

Project availability

- PhD
- MSc

Project: Understanding the impact of new testing for infectious diseases

Infectious diseases epidemiology is undergoing a paradigm shift, mainly due to the implementation of new technologies such as whole genome sequencing (WGS) of pathogens. WGS is being introduced into public health settings in Australia and globally, however, there is currently no standard framework for assessing and quantifying the impact on public health outcomes (e.g. reduction in time to diagnosis; change in number of disease clusters, costs associated with diagnosis). This project aims to establish an initial framework based on available data for assessing the impact of WGS on pre-specified public health outcomes, using tuberculosis as an exemplar. The project will involve interaction with epidemiologists, laboratory staff and policy makers. Project findings will guide best practice for translating genomic analyses into public health action. This project would suit a student with analytic skills, familiarity with a statistical program (e.g. Stata), and an interest in infectious disease epidemiology and public health.

Project supervisor

Associate Professor Deborah Williamson

Project availability

- PhD
- MSc

Project: Sample size determination for within-host animal studies of infection

Within-host animal studies are routinely used to determine the efficacy of a treatment for clearing a bacterial infection in a host. Determining adequate sample sizes for powering these studies is often complicated, given the various dynamics at play which are often not well understood. Instead, in designing an experiment, we are typically limited by the amount of resources we have available, and attempt to allocate these resources in the "best" way, to "learn" the most about the within-host dynamics. In this project, we will explore the use of an approximate, likelihood-free inference method with simulations from the model to evaluate the optimal experimental designs. These tools will subsequently be applied to these within-host experimental studies, to derive the optimal allocation of resources based on different experimental aims. This project will be best suited to someone with strong coding skills, and studying a degree in mathematics or statistics e.g. MSc (Mathematics and Statistics), in applied mathematics, stochastic processes or statistics.

Project supervisor

Dr David Price

Project availability

- PhD
- MSc

Project: Bias in vaccine effectiveness studies

Vaccine effectiveness data are routinely used to inform updates to the influenza vaccine. However, the validity of these studies has not been fully explored. This project will use re-analysis of existing data, systematic review and simulations to understand the circumstances under which influenza vaccine effectiveness estimates can reliably inform influenza vaccine strain selection. This project would suit a student with analytic skills, familiarity with a statistical program (e.g. Stata), and an interest in biostatistical and epidemiological methods.

Project supervisor

Dr Sheena Sullivan

Project availability

- PhD
- MSc

Project: Buruli Ulcers' Most Wanted – Understanding the mosquito associated with the flesh-eating bacteria, *Mycobacterium ulcerans.*

Aedes notoscriptus has been identified in association with the emerging bacterial pathogen *Mycobacterium ulcerans,* as well as being a vector of Ross River virus. Key ecological features such as bloodmeal feeding patterns and movement dynamics of individuals, are, however, not clearly defined. This project will involve both laboratory and field-based components. Firstly, field collections will be conducted on instead of in the Mornington Peninsula using a combination of trapping techniques, with the aim of obtaining haematophagous 'blood feeding' insects including *Ae. notoscriptus*. A range of entomological and molecular techniques will be used for insect identification, with *Ae. notoscriptus* screened for a series of genetic markers to understand movement estimates. Additionally, insects identified to contain a bloodmeal will be screened for host DNA using a high-throughput metabarcoding DNA sequencing pipeline. Both aims of this project will feed into a larger project, which is attempting to control *Mycobacterium ulcerans* in Victoria. This project would suit students with skills in molecular biology and a keen interest in field work, most likely coming from undergraduate studies in Science (Biochemistry and Molecular Biology, Computational Biology, Ecology, and Evolutionary Biology, Environmental Science and Microbiology). During this project the potential candidate will obtain experience in planning field work, setting insect traps, some basic insect identification, next-generation library preparation, sequencing and bioinformatic analysis of sequencing data. This project is a collaboration between Agriculture Victoria in Bundoora and Bio21 in Parkville, with the successful candidate spending time in both institutes.

Project supervisors

Dr Stacey Lynch, Dr Peter Mee, Professor Ary Hoffmann, Dr Tom Schmidt

Project availability

- MSc

Mueller group

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

Number of vacancies available 2
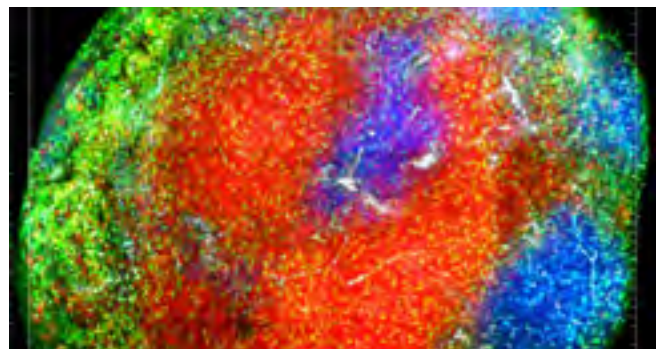
Immunology

Viral Infectious Diseases

Discovery Research

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).

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. We are also defining the role of the tissue microenvironment in immune responses, including how stromal cells guide immunity and neuroimmune interactions that shape responses for the design of new vaccines and therapeutics.

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

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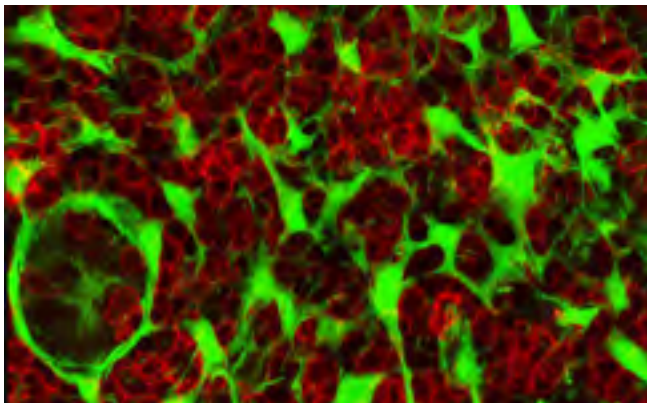
High resolution confocal microscopy image of the organised stromal cell network in the T cell zone of a lymph node. Shown are T cells (red) and fibroblasts (green).

Project: Neural regulation of anti-cancer immunity

Tissues are innervated by fibres of the sympathetic nervous system (SNS), which release SNS neurotransmitters during stress. SNS neurotransmitters bind to adrenoceptors (ARs) on multiple cell types to induce genomic and functional changes. Studies have shown that immunity is compromised during times of stress, raising the possibility that SNS signalling impairs immune cell functions. However, little is known about the mechanisms of SNS neurotransmitter signalling on the cells of the immune system. We have discovered that adrenergic receptor signalling inhibits the migration of immune cells within tissues, and impacts protective immunity against infections and cancer. This project will investigate sympathetic innervation of tumours and how neural signals impact immune responses in the tumour microenvironment in order to design new therapies to treat cancer.
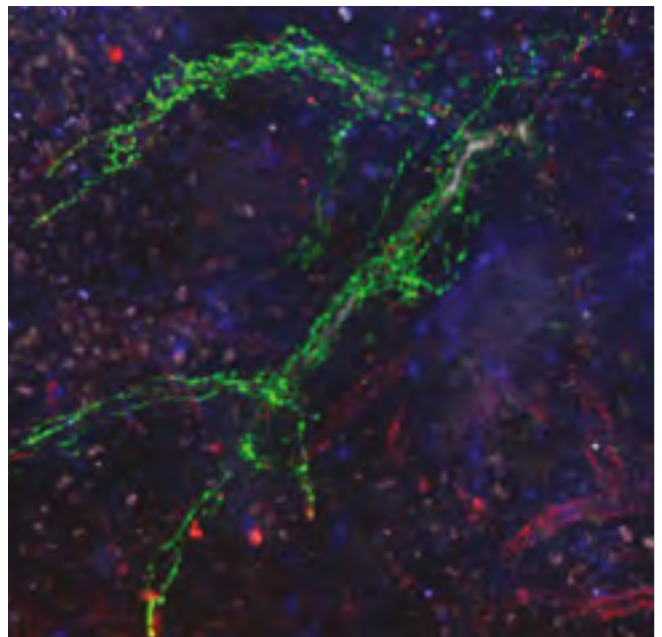
Project supervisor

Associate Professor Scott Mueller

Project co-supervisor

Dr Sapna Devi

Project availability

- PhD
- MSc
- Honours

High resolution confocal microscopy image of sympathetic nerves (Tyrosine hydroxylase, green) in the spleen.

Newton group

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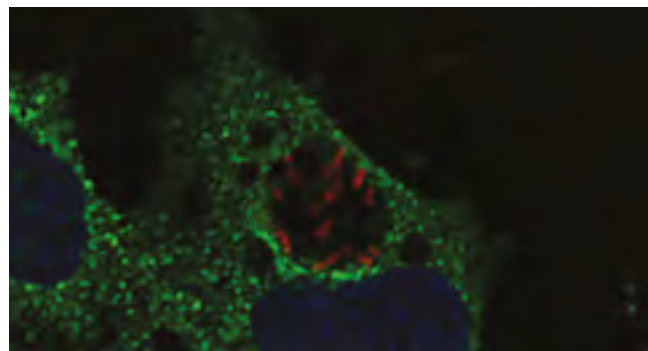**Email address** hnewton@unimelb.edu.au

Number of vacancies available 2

Host-pathogen Interactions

Discovery Research

Clathrin heavy chain (green) surrounding the *Coxiella*-containing vacuole (red).

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.

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

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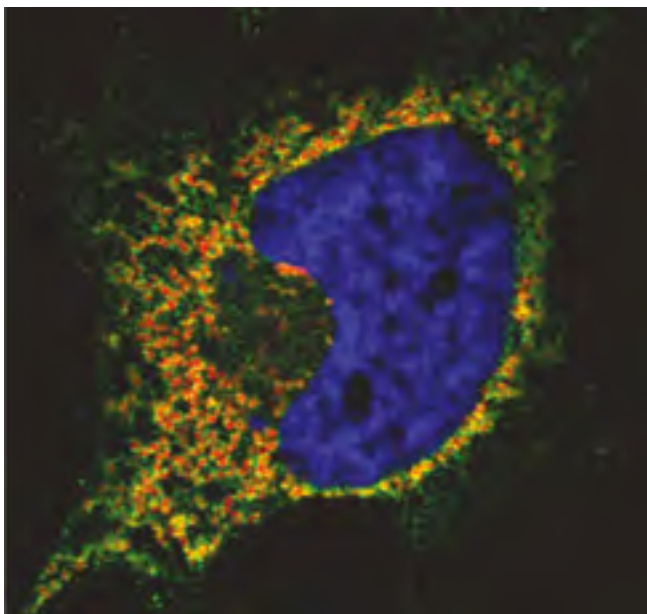
A bacterial effector protein (green) localising to mitochondria (red).

Project: Using genomics to track transmission of *Chlamydia trachomatis*

Chlamydia trachomatis is an obligate intracellular bacterial pathogen that causes one of the most common sexually transmitted infections in Australia. Due to the inability to culture *C. trachomatis* in vitro there are limited studies on the utility of employing genomics as a tool to explore transmission of this important pathogen. This research will combine the expertise in the Williamson group in using genomics as a tool to track pathogens of public health importance with expertise in the Newton group in culturing intracellular bacterial pathogens to explore genomic stability and transmission of *C. trachomatis*.

Project supervisors

Associate Professor Deborah Williamson, Dr Hayley Newton

Project availability

- Honours

Purcell group

Contact name   Professor Damian Purcell
Email address   dfjp@unimelb.edu.au

Number of vacancies available 3

- Immunology
- Viral Infectious Diseases
- Host-pathogen Interactions
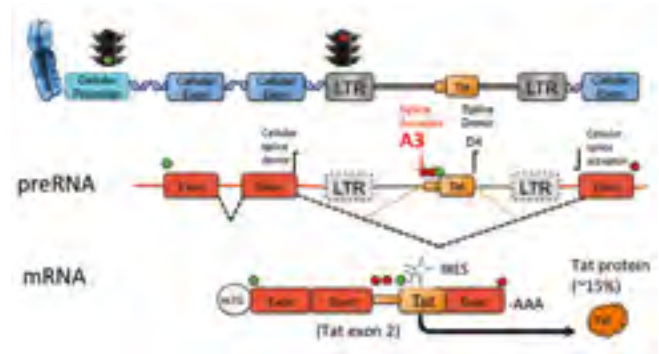- Translational and Clinical Research
- Global Health
- Indigenous Health
- Genomics

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 availability

- PhD
- MSc

Further reading

Khoury G, et al. 2018. Retrovirology 15:36

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 availability

- PhD
- MSc

Further reading

Nguyen W; Jacobson J, et al. 2019. J Med Chem 62:5148-5175

Project: Pathogenesis of HTLV-1c infecting remote Indigenous Australians

The HTLV-1 subtype-C (HTLV-1c) is endemic in remote central Australian Indigenous communities with prevalence greater than 50 per cent. 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 is 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 Paula Ellenberg

Project availability

- PhD
- MSc
- Honours

Further reading

Yurick D, et al. 2019. J Clin Microbiol 57.

Project: Antibodies preventing HTLV-1c infection

The HTLV-1c virus is mostly spread by cell-cell contact with infected T-lymphocytes at the sexual mucosa or following blood exposure. Nevertheless, neutralising antibodies have been reported to block virus transmission. We have engineered and expressed soluble HTLV-1c Env trimers and with these, have developed assays that measure the potency and breadth of HTLV-1c neutralising antibody in patient serum. This project will seek to produce monoclonal antibody NAbs against HTLV-1c Env trimers for development of a passive immunotherapy strategy to prevent HTLV transmission. We will also examine the potential of HTLV-1c Env trimers as a candidate preventive vaccine in mice vaccinated with them.

Project supervisor

Professor Damian Purcell

Project co-supervisor

Samantha Grimley

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 the 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 will further characterise monoclonal antibody bNAbs we have isolated from vaccinated cows, and define the genetic evolution of the immunoglobulin genes during the immune response needed to form an effective protective antibody.

Project supervisor

Professor Damian Purcell

Project co-supervisor

Dr Behnaz Heydarchi

Project availability

- PhD
- MSc
- Honours

Link for further information

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

Revill group

Contact name Associate Professor Peter Revill
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Number of vacancies available 1

Viral Infectious Diseases

Public Health

Translational and Clinical Research

Global Health

The Revill group's work is focused on the molecular virology of the hepatitis B virus (HBV), which is one of the most important human pathogens, infecting 257 million people worldwide, including 239,000 Australians. The group 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: Investigating the effect of hepatitis B virus splice variants in liver cells and disease progression

Hepatitis B virus (HBV) is one of the most important human pathogens, infecting 257 million people worldwide, including 239,000 Australians. We have previously shown that naturally occurring splice variants of HBV are associated with liver cancer, the fifth most prevalent cancer worldwide, and that splice variants are more diverse than previously appreciated. Although the biological impact(s) of splice variants on liver cells is unclear, we have shown that while splice variants production can be abolished by gene mutations, their replication and infection competence are conserved. Building on these observations, this Honours project will

investigate how splice variants affect liver cells following infection of primary and transformed hepatocytes. Techniques utilised will include cell culture; real time PCR/digital PCR; southern, northern and western blotting; quantitative serology; RNA sequencing; and basic bioinformatics analysis. This project will make a major contribution to our understanding of the role of HBV splice variants in liver cells and disease progression.

Project supervisor

Professor Peter Revill

Project co-supervisors

Dr Margaret Littlejohn, Dr Kai Yan Mak

Project availability

- Honours

Rogerson group

Contact name   Dr Elizabeth Aitken
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Number of vacancies available 2

Immunology

Host-pathogen Interactions

Translational and Clinical Research

Global 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 will 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

Project: Identification and characterisation of novel malarial transmission-blocking antigens

How do antibodies against *Plasmodium falciparum* gametocytes induce transmission-blocking immunity? Immunity against the sexual stage that underpins transmission-blocking vaccines (TBV) directed at parasite molecules expressed in the gametocyte through to ookinete stages are not well understood. Antibodies directed against these molecules are likely to be crucial for transmission blocking immunity. We propose to characterise the sexual stage antibody targets in *Plasmodium falciparum*, the cause of the most severe form of malaria, and to better understand the properties of antibodies that confer transmission blocking immunity.

The goals of this project are to identify previously unidentified antigens and functionally characterise anti-gametocyte antibodies in sera from malaria-infected individuals that mediate transmission-blocking immunity using biochemical and immunological techniques.

Project supervisor

Associate Professor Siddhartha Mahanty

Project co-supervisor

Professor Stephen Rogerson

Project availability

- MSc
- Honours

Satzke group

Contact name   Catherine Satzke
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Number of vacancies available 4

Immunology

Viral Infectious Diseases

Antimicrobial Resistance and Healthcare Associated Infections

Host-pathogen Interactions

Public Health

Translational and Clinical Research

Global Health

Genomics

Discovery Research

The Satzke group conducts research in a clinically-relevant context. We focus on the microbiology of 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 countries in the Asia-Pacific region, to facilitate translation and global impact.

Project: Streptococcal transmission and disease

The bacterium *Streptococcus pyogenes* (Group A *Streptococcus*) 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, you will use a murine model of *Streptococcus pyogenes* colonisation to examine the effect of respiratory viruses (e.g. influenza) on *Streptococcus pyogenes* colonisation, including for 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. Your 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 Jonathan Jacobson, Professor Andrew Steer

Project availability

- PhD
- MSc
- Honours

Satzke group

Project: Understanding the importance of variation in the capsular polysaccharide of *Streptococcus pneumoniae*

Streptococcus pneumoniae (the pneumococcus) is a leading cause of morbidity and mortality worldwide. Over 90 immunologically distinct serotypes are known, defined by their unique capsular polysaccharide. Decisions around which serotypes are included in licensed vaccines have largely been based on data from high-income countries. These vaccines have subsequently been introduced into low and middle-income countries (LMICs), where limited local information on serotype prevalence and diversity is often available. Using DNA microarray, we have identified pneumococci from LMICs with significant genetic variation in the capsule locus. Some of this variation is predicted to change the capsule structure, indicating there is potential for undiscovered serotypes and/or the misidentification of existing serotypes. This project will focus on the identification and characterisation of these variants. This includes the molecular basis of the variation and potential for mistyping, and also the relevance of such changes to the capsule on pneumococcal pathogenesis. Key approaches to this project include genetic manipulation of pneumococcal isolates, experiments with DNA and RNA, capsular typing of pneumococcal isolates as well as conducting functional assays in vitro. Your work in helping us uncover these novel variants (and potentially new serotypes) will allow us to improve serological and molecular tools for their detection, which will be vital for accurately assessing vaccine impact and serotype replacement globally.

Project supervisor

Associate Professor Catherine Satzke

Project co-supervisor

Dr Sam Manna

Project availability

- MSc
- Honours

Project: Synergistic and antagonistic interplay between *Streptococcus pneumoniae* and respiratory viruses

The contribution of bacterial-viral co-infections to the onset and severity of disease is increasingly attracting interest from researchers globally. Specifically, it is well established that co-infections of *Streptococcus pneumoniae* with respiratory viruses (e.g. influenza or respiratory syncytial virus) impact the severity of acute respiratory infections. This is because viral replication creates a more hospitable environment for pathogenic bacteria of the respiratory tract to flourish, predisposing individuals to a bacterial super infection. However, recent research has found that the interplay between pneumococci and viruses is more complex than previously anticipated. We, and others, have shown that some aspects of co-infection are synergistic (resulting in greater disease severity), while others are antagonistic, where the presence of one pathogen negatively impacts the other. In this project, you will elucidate the underlying microbiological and/or immunological mechanisms that govern the synergistic and antagonistic aspects of the interplay between pneumococci and respiratory viruses. Key approaches to this project include working with in vivo models as well as microbiological and immunological analysis of tissues from the respiratory tract. Your work will help us understand the complexities of pneumococcal-viral co-infection, including their implications for the effectiveness of vaccines targeting these pathogens.

Project supervisor

Associate Professor Catherine Satzke

Project co-supervisor

Dr Sam Manna

Project availability

- PhD
- MSc
- Honours

Satzke group

Project: Pathogenesis of pneumococcal pneumonia

Streptococcus pneumoniae is the most common cause of community-acquired pneumonia and a leading killer of children worldwide. 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. Recently, we have collected clinical samples from children with severe pneumonia at the Royal Children's Hospital. The project aims will be to examine pneumococcal gene expression in samples collected from pneumonia patients at the Royal Children's Hospital, and elucidate the role of several candidate genes in pneumococcal pneumonia. To do this, you will use a variety of approaches including measurement of gene and/or protein expression (using methods such as qRT-PCR, RNA-seq, western blotting, and ELISA) and analysing their importance through genetic manipulation of pneumococci and functional assays. 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.
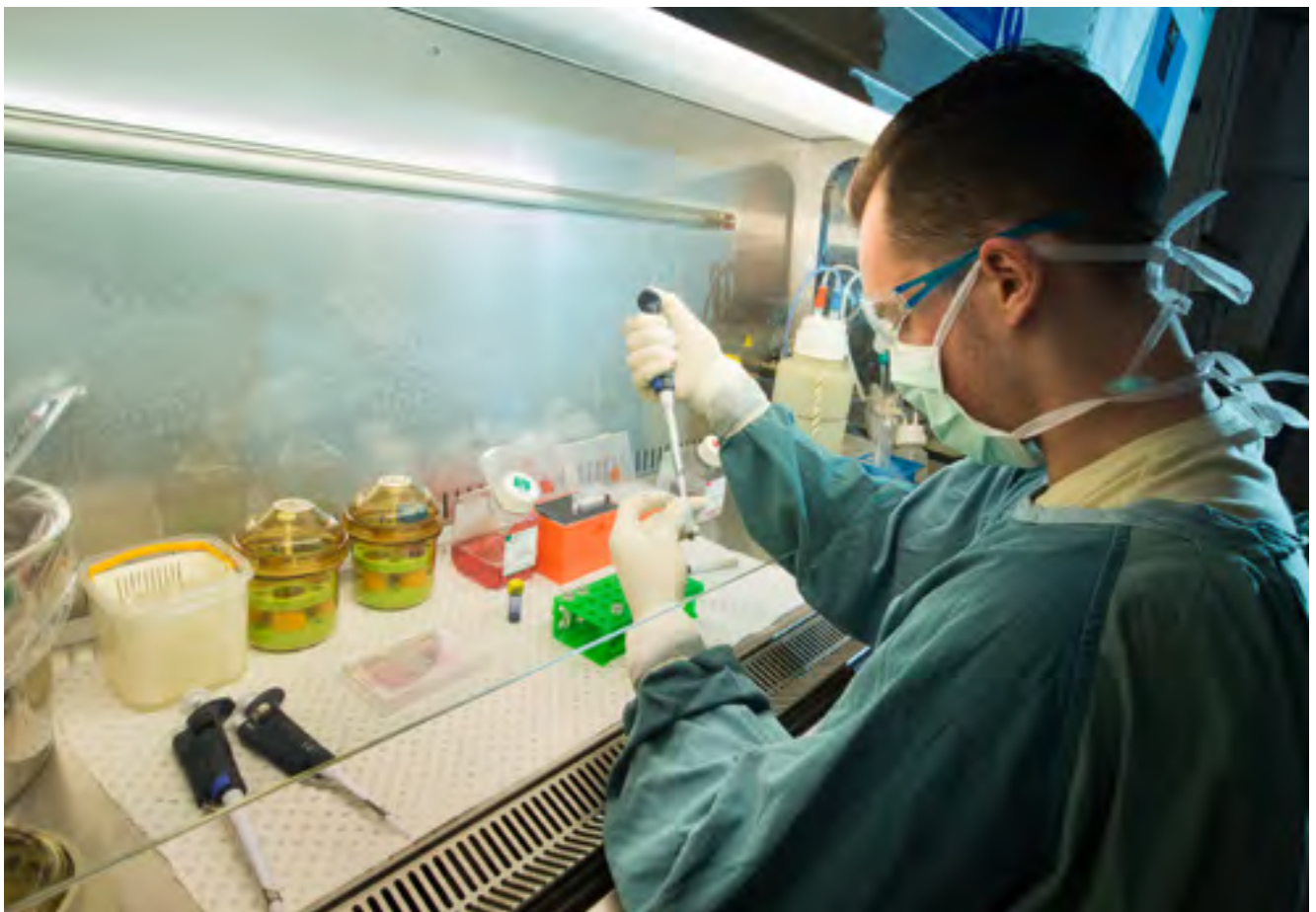
Project supervisor

Associate Professor Catherine Satzke

Project co-supervisor

Dr Jonathan Jacobson

Project availability

- MSc
- Honours

Scott group

Contact name   Dr Nichollas Scott
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Number of vacancies available 2

Antimicrobial Resistance and Healthcare Associated Infections

Host-pathogen Interactions

Discovery Research

The Scott group focuses on understanding microbial mediate protein glycosylation and microbial pathogenesis. Glycosylation is a post-translational modification, which allows pathogens to radically alter the function of proteins both within microbes and the host cells they infect. Within a range of pathogens such as malaria, salmonella and Burkholderia cenocepacia, protein glycosylation can be used for both defensive and offensive processes. Using mass spectrometry-based approaches, the Scott group seeks to develop methodologies to identify and track microbial glycosylation events and investigate how microbes subvert host proteomes leading to disease.

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, diversity and machinery responsible for glycosylation in *Bukholderia* species. By studying glycosylation within *Burkholderia* we aim to gain a fundamental understanding of this

biological process and how it contributes to bacterial survival. The long-term goal of this project is to learn how we can target protein glycosylation to generate new antimicrobial agents, and how we can exploit bacterial glycosylation systems to generate novel glycoconjugates such as vaccines.
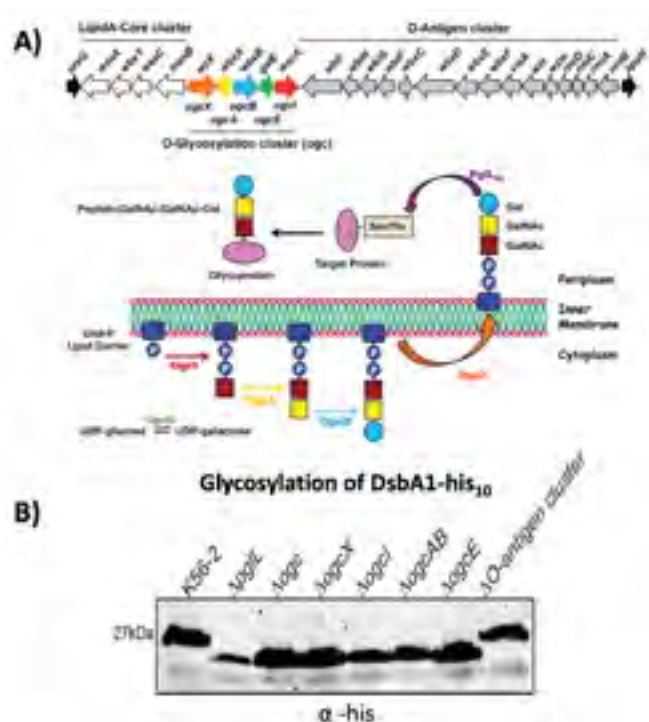
Characterisation of the O-glycosylation cluster in Burkholderia spp. A) Diagrammatic representation of the OGC cluster and O-linked glycosylation system. B) Western analysis of glycosylated substrate DsbA1-his_{10}. Disruption of genes within this pathway lead to alterations within the decorating glycan of DsbA1.

Project supervisor

Dr Nichollas Scott

Project availability

- PhD
- MSc
- Honours

Project: Development of novel proteomic tools to explore *Burkholderia* pathogenesis

Multiple bacterial pathogens escape detection and removal by the host immune system by hiding within cells. Understanding how bacteria create hospitable intracellular environments is critical for developing approaches to help prevent infections in immunocompromised individuals, and advancing new therapies to purge these infections from cells. Within this project, we aim to explore new state-of-the-art approaches to track and quantify proteomic changes at the intracellular host pathogen interface. Utilising recent innovations in protein labelling, redox probes and mass spectrometry, both the host and bacterial factors, which contribute to intracellular replication, will be identified. By applying these tools, we will gain valuable insight into how *Burkholderia cenocepacia* (a serious opportunistic infection of CF suffers) survives within human macrophages leading to a deeper understanding of the molecular pathogenesis of *Burkholderia*.
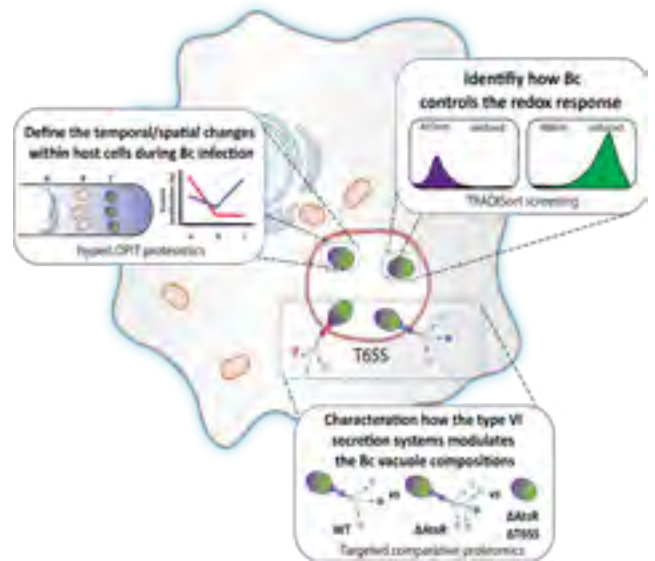
This research seeks to understand how Bc controls and overcomes the host defences to enhance Bc survival using state of the art systems approaches. Aim 1) will seek to characterise the temporal and spatial changes in the host cell in response to infection using MS based approaches; Aim 2) will characterise the composition of the Bc containing vacuole in the presence and absence of the type VI secretion system using protein labelling; and Aim 3) will dissect the bacterial factors which delay the oxidative burst using a novel redox probe.

Project supervisor

Dr Nichollas Scott

Project availability

- PhD
- MSc
- Honours

Stinear group

Contact name   Professor Tim Stinear
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Number of vacancies available 1

Antimicrobial Resistance and Healthcare Associated Infections

Host-pathogen Interactions

Genomics

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

Subbarao group

Contact name Professor Kanta Subbarao
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kanta.subbarao@influenzacentre.org

Number of vacancies available 1

 Viral Infectious Diseases

 Host-pathogen Interactions

 Public Health

 Translational and Clinical Research

The Subbarao group research program incorporates bench-to-bedside studies of influenza viruses, the human host and vaccines to address three major questions in the field of influenza research: how can seasonal influenza vaccines be improved? What makes some seasonal influenza viruses more virulent than others? What is the basis for cross-species transfer and emergence of novel influenza A viruses (IAV) from animal hosts?

Subbarao group
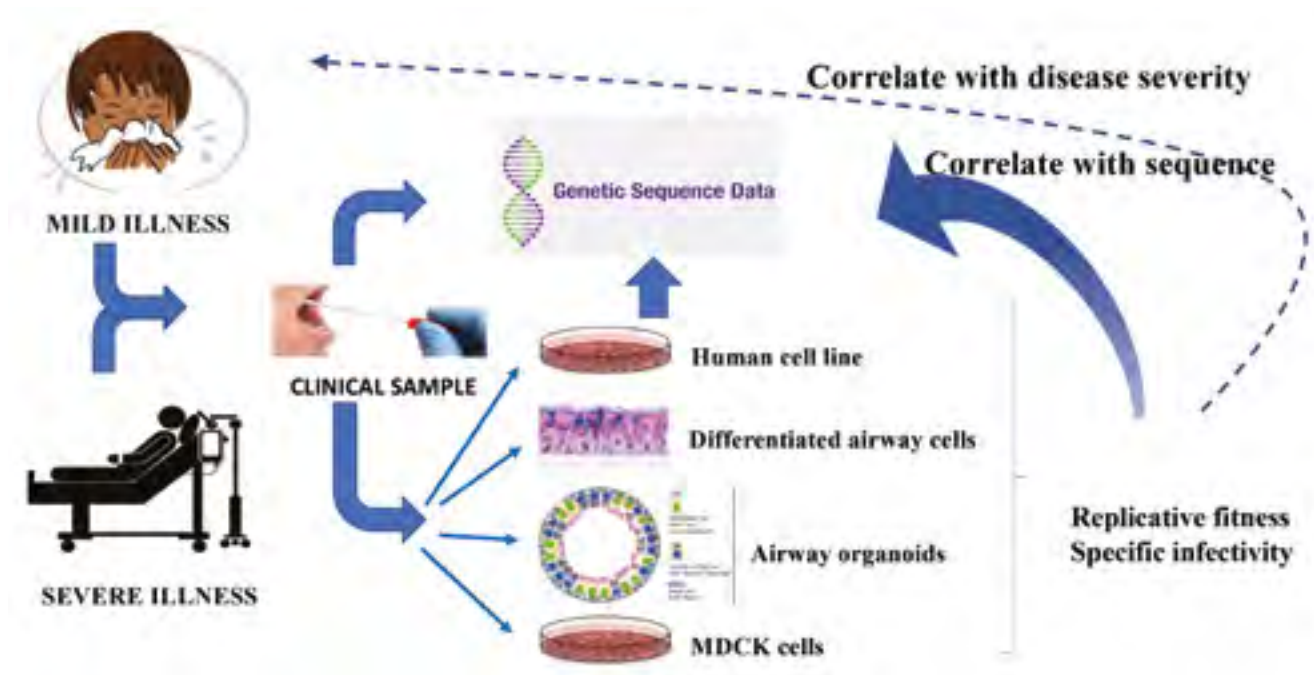
Virulence of seasonal influenza viruses

Project: Defining the association between virulence and fitness of seasonal influenza viruses

The severity of influenza illness is influenced by host and viral factors. Host factors include age, prior immunity, underlying health conditions and genetic susceptibility. Some influenza viruses, particularly A(H3N2) viruses, are clearly associated with more severe illness and epidemics than others. Viral determinants include antigenic drift that permits escape from immunity, tropism and replicative fitness in the human respiratory tract. Additionally, the ratio of infectious and non-infectious (defective) viral particles produced from different substrates can differ; this can be measured as specific infectivity. Madin Darby canine kidney (MDCK) cells are the standard cell line used for propagation of influenza viruses in laboratories but they are not the natural substrate for human influenza viruses. We hypothesise that influenza viruses associated with severe disease will replicate more efficiently in cells derived from the human respiratory tract than viruses associated with mild outbreaks. As part of global virologic surveillance activities, the World Health Organization Collaborating Centre for Reference and Research on Influenza (WHOCCRI) monitors genetic and antigenic drift by characterising approximately 4000 influenza viruses each year. Seasonal influenza viruses associated with severe or mild illness will be identified among viruses submitted to the WHOCCRI. Their replicative fitness and

specific infectivity will be assessed by measuring virus titre and number of infectious virions by plaque assay/number of genome copies by digital drop PCR, respectively in (1) monolayers of A549 cells, a cell line derived from a human lung adenocarcinoma; (2) normal human tracheobronchial epithelial (NHBE) cells grown at an air liquid interface from a commercial source, and (3) recently described human airway organoids established through a collaboration with Professor Elizabeth Vincan from the Doherty Institute, Professor Michael Chan from the University of Hong Kong, and Professor Hans Clever from the University of Utrecht, in addition to (4) standard MDCK cells. Data on replication and specific infectivity will be correlated with nucleotide sequences generated by next generation sequencing, which is routinely performed in the WHOCCRI. We expect to detect a correlation between severity of illness and virus titre, fitness and/or specific infectivity achieved in human respiratory tract cells.

Project supervisor

Professor Kanta Subbarao

Project availability

- MSc
- Honours

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

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

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

Purcell 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. This 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

Further information

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

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

Project: Influenza epidemiology in the Northern Territory – analyses of linked datasets

There is a disproportionate burden of influenza upon Indigenous Australians in the Northern Territory (NT) with regards to incidence of diagnoses. However, the broader impact of influenza is not well understood within the context of a geographically dispersed population in the tropical and arid regions of the NT. We have linked all influenza tests (with positive and negative results) performed in the NT from 2007 to 2015 to primary care and hospital administrative datasets and the NT Immunisation registry. This project would suit a student with a desire to develop and apply skills in analyses of a large linked dataset to address questions of the impact of influenza on primary and tertiary level presentations; the economic cost of influenza; understanding testing patterns over time; and assessing the influence of remoteness, ethnicity, comorbidities and climate upon influenza diagnoses and related outcomes.
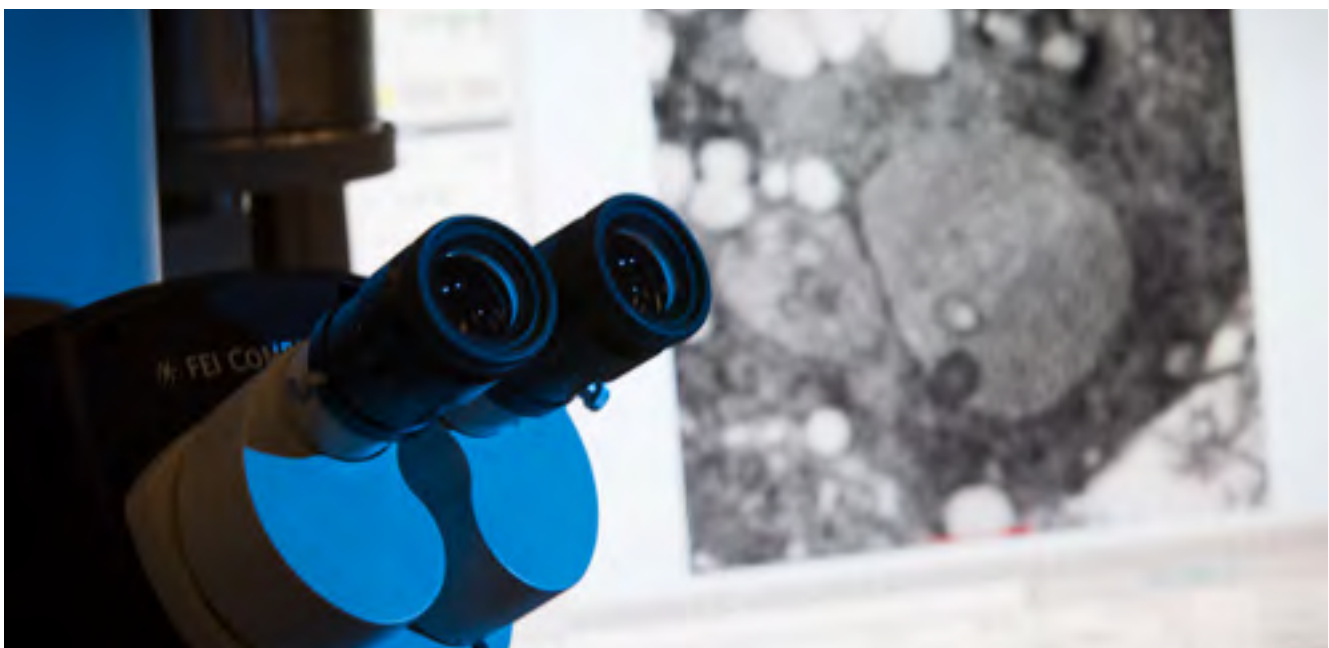
Project supervisor

Associate Professor Steven Tong

Project co-supervisor

Associate Professor Sheena Sullivan

Project availability

- PhD
- MSc

VICNISS group

Contact name Associate Professor Leon Worth
Email address leon.worth@mh.org.au

Number of vacancies available 1

Antimicrobial Resistance and Healthcare Associated Infections

Public Health

The Victorian Healthcare Associated Infection Surveillance System Coordinating Centre (VICNISS) is responsible for surveillance of healthcare-associated infections in Victorian public and private hospitals, and the aged care sector. As a funded service to the Victorian Department of Health and Human Services, data collation, analysis and reporting are provided, together with a platform for health services research. The group includes clinical, epidemiology, biostatistics, and information technology skillsets. We have developed novel and timely methods for detection of new and emerging infections, enhanced data utility through linkage with relevant registries, and contribute to healthcare policy at the national level.

Project: *Staphylococcus aureus* bloodstream infections in Victorian hospitals: regional differences in disease burden and epidemiology

Staphylococcus aureus bloodstream infections (SABs) are associated with significant mortality and healthcare expenditure. Many hospitals, therefore, have structured infection prevention programs to reduce the risk of these infections. VICNISS facilitates surveillance of healthcare associated infections in Victorian hospitals, including SAB. The objective of this study is to evaluate the burden of SAB across the spectrum of Victorian healthcare facilities, including analysis according to hospital size. These data will assist in understanding if burden of illness varies according to location (metropolitan versus regional facilities) and findings will assist individual hospitals to benchmark SAB outcomes appropriately with hospitals of similar size or location.

Project supervisor

Associate Professor Leon Worth

Project co-supervisor

Associate Professor Noleen Bennett

Project availability

- MSc
- Honours

Villadangos group

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

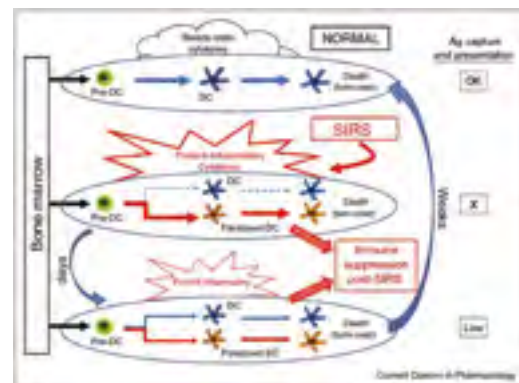**Number of vacancies available** 3

Immunology

Host-pathogen Interactions

Translational and Clinical Research

Discovery Research

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.

Induction of DC paralysis following SIRS.

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 availability

- PhD
- MSc
- Honours

Project: MR1 – a molecular alarm system for bacterial infection

MR1 is a molecular alarm to alert the immune system during bacterial infection. It captures metabolite by-products from bacteria and presents them to a highly abundant T cell subset, called mucosal-associated invariant T (MAIT) cells. The MR1-MAIT cell system is a highly conserved piece of the immune repertoire to detect important bacterial pathogens, yet basic aspects are not understood, such as which cells express MR1 *in vivo*. This project will use a novel MR1-reporter mouse model to discover which cells are armed with MR1 during various disease settings, and CRISPR/Cas9 gene editing to understand how MR1 works in these cells.

Project supervisor

Dr Hamish McWilliam

Project co-supervisor

Professor Jose Villadangos

Project availability

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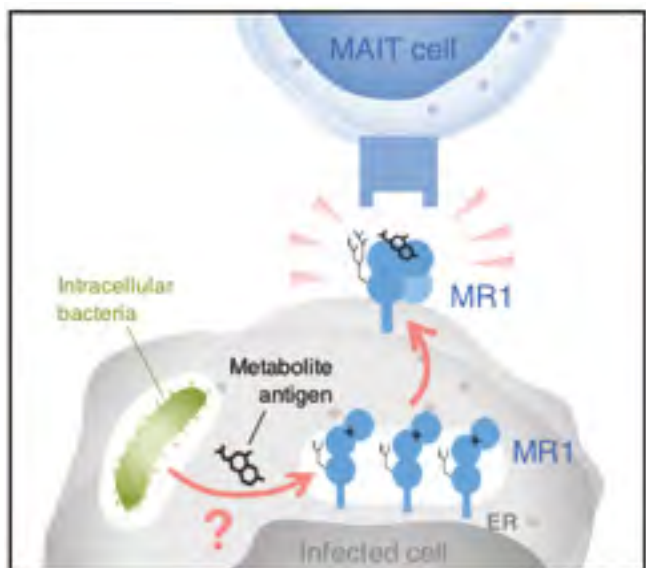
Pathogens (in this case an intracellular bacterium, green) produce unique metabolic products (antigens) that bind to MR1 molecules (blue) expressed by host cells. The MR1 molecules are displayed on the cell surface, enabling MAIT cells specialised in fighting bacterial infections to detect the bacterial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

## 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 availability

- PhD
- MSc
- Honours
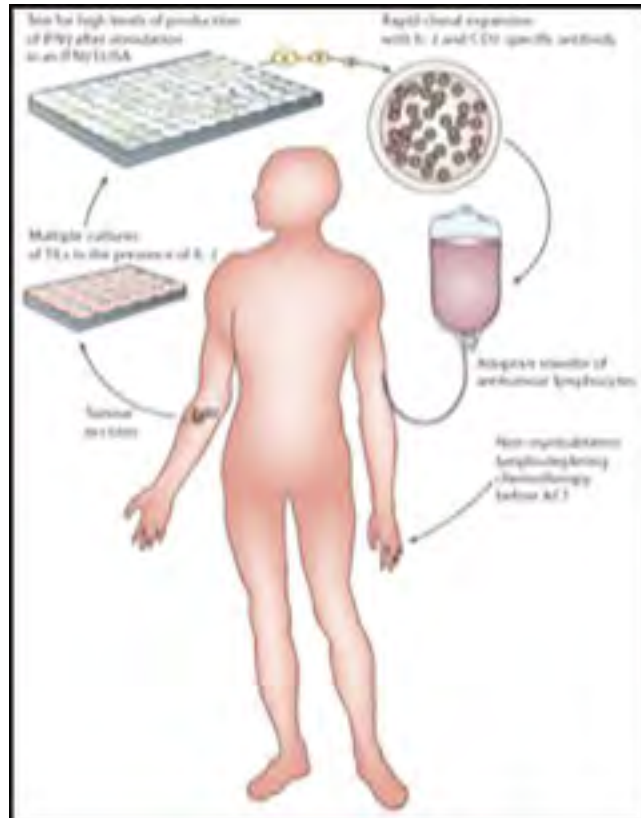
Overview of adoptive cell therapy against cancer (taken from Gattinoni L. et al., Nat Rev Immunol, 2006).

Villadangos group

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.
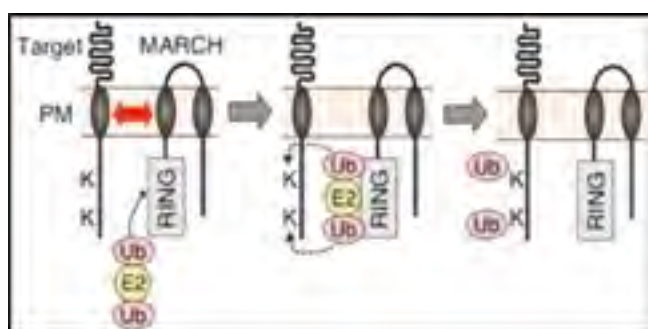
Project supervisor

Professor Jose Villadangos

Project co-supervisor

Dr Justine Mintern

Project availability

- PhD
- MSc
- Honours

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.
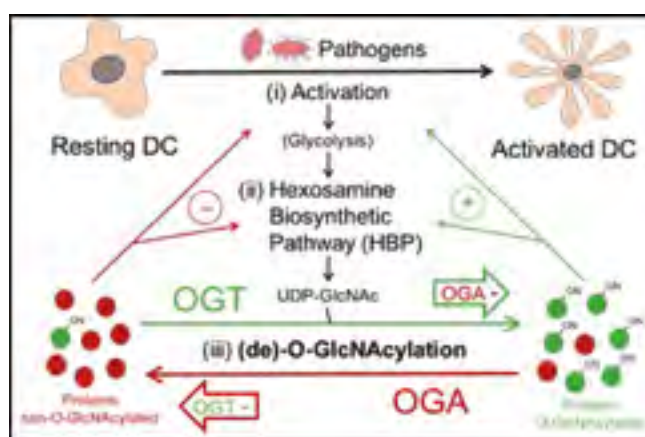
Project supervisor

Professor Jose Villadangos

Project co-supervisor

Dr Nishma Gupta

Project availability

- PhD
- MSc
- Honours

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).

Reciprocal regulation of immunity and metabolism via O-GlcNAcylation.

Wakim group

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Email address wakiml@unimelb.edu.au

Number of vacancies available 2

Immunology

Viral Infectious Diseases

Translational and Clinical Research

Discovery 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: Location, location, location – lodging virus specific T cells in the lung as an approach to protecting 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
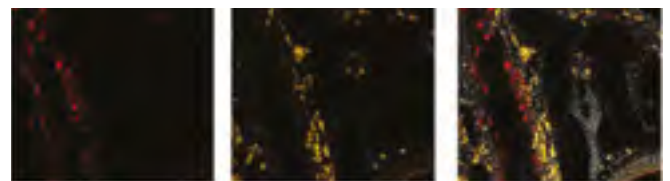
T cells (CD3+) along the respiratory tract surrounding influenza virus (NP+) infected cells.

Wakim group

## 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 per cent 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
- Honours
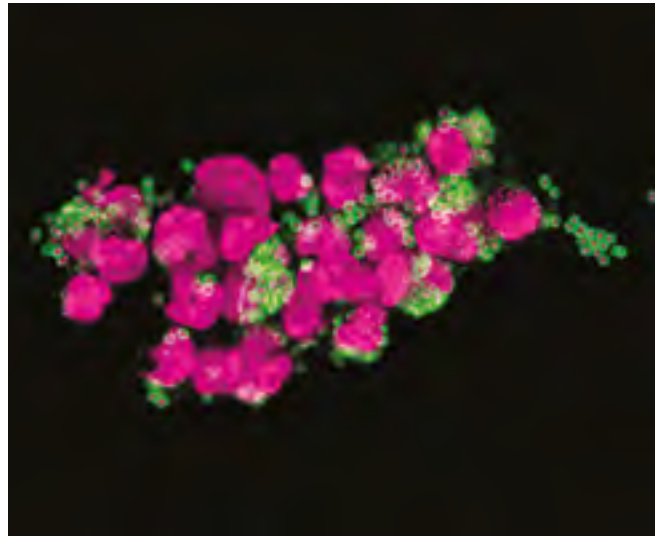
Immune cells in the nasal airways surrounding Staphylococcus aureus.

WHO Collaborating Centre for Reference and Research on Influenza

Contact name Dr Michelle Wille
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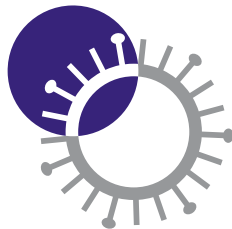**Number of vacancies available** 1

- Viral Infectious Diseases
- Host-pathogen Interactions
- Genomics
- Discovery Research

WHO Collaborating Centre
for Reference and
Research on Influenza
VIDRL

Ruddy Turnstone is an important reservoir species for avian influenza A in wild birds.

The WHO Collaborating Centre for Reference and Research on Influenza (WHOCCRI) is a world-class influenza virus surveillance laboratory. Although the main focus of the WHOCCRI is human influenza viruses, it is well recognised that understanding avian influenza is important to evaluate the risk of future pandemics. Therefore, we also conduct research in avian virus ecology, broadly, with a focus on avian influenza A ecology in wild birds.

Project: Evolutionary Genetics of avian influenza A viruses in Australia

The main reservoir for avian influenza viruses is wild birds, and most of what we know about the ecology of these viruses is derived from surveillance systems in the Northern Hemisphere. Based on a few studies, the dynamics of avian influenza A viruses in Australia appear to be affected by multiple drivers. The aim of this project is to disentangle avian influenza ecology and evolution in Australian wild birds. Specifically, through the generation of sequence data, the results of this project will allow us to place the dynamics of avian influenza A viruses in Australia into a global context. This project will involve an array of laboratory techniques including RNA extraction, qPCR, virus isolation in chicken eggs, and sequencing of virus isolates. The student will learn both PC2 and PC3 laboratory techniques. There is potential for sample collection in the field (January to March) and there is further room for sequencing original specimens and comparing sequencing technologies.

Project supervisor

Dr Michelle Wille

Project availability

- Honours