Melbourne Dental School

2020 Honours & Masters Research Project Handbook
Welcome to the Melbourne Dental School

The Melbourne Dental School is proud of its longstanding record of excellence in health research. Research at the School covers a broad range of scientific endeavour from basic science to clinical studies involving various disciplines including microbiology, immunology, cancer cell biology, biochemistry & molecular biology, chemistry, anatomy, and materials engineering.

We are incredibly passionate about the mentoring and the training of future researchers. Indeed, our mission is to continue to be a world-class, research-based school, offering education of the highest quality. To achieve this goal, we provide excellence in research training and support for all laboratory and clinician research students as they develop research knowledge and expertise and help drive new discoveries that lead to better outcomes for patients. So, if you are passionate about improving patient health, we encourage you to join us in the pursuit of knowledge by applying to do Honours or a Masters degree at the Melbourne Dental School. Working closely with researchers, students undertake their project in state-of-the-art research laboratories at the Melbourne Dental School and Bio21 Institute. High-achieving students will automatically be considered for the Noel Arthur Twiss Scholarship ($5,000).

There are a number of factors you might want to consider when making the decision about undertaking an Honours year or Masters degree, such as the amount of time spent on your research project, opportunities to undertake professional skills-based subjects, and which pathway would be most advantageous for possible entry into a PhD program in the future. Regardless of your choice, the School provides a stimulating and challenging intellectual environment that allows you to experience research firsthand and put your scientific knowledge into practice. The diverse range of Australian and international students from many social and ethnic backgrounds at the School greatly enhances the learning experience.

This booklet provides information that will help you decide on potential research projects. Please take your time to identify projects that are of interest and contact potential supervisors for more information. I am very confident they will be eager to discuss your research interests and talk about their own research, show you around their laboratories, and introduce you to other students and researchers.

I look forward to seeing you at the School next year and hearing about your research project.

Professor Mike Morgan
Head of School
# Honours and Masters Research Projects

## Host-Microbe Interactions in Health & Disease
- Investigating mucosal & systemic immune responses to bacteria
- Investigating the host defence functions of the novel epithelial cytokine IL-36 gamma
- How spatial control of cytokine responses maintains host-microbe homeostasis
- Epigenetic control of host-microbe interactions
- Identification & functional characterisation of binding partners of the IRF6 transcription factor
- Maintenance of oral epithelial barrier to infection
- Microbial flow cytometry: developing diagnostic tools for immune responses to bacteria, nano- and micro-materials and vesicles

## Microbiomes in Health & Disease
- Oral microbiomes in health and disease

## Bacterial Virulence
- Characterisation of potential virulence factors secreted by the type 9 secretion system of *Porphyromonas gingivalis*
- Identification of interacting regions between an essential component of the type 9 secretion system, PorV, and secreted virulence factors of the oral pathogen, *Porphyromonas gingivalis*
- Role of PG0189 in the assembly of the type IX secretion system in *Porphyromonas gingivalis*
- Proteomic analysis of gingipain catalysed transpeptidation reactions and its relevance to autoimmunity
- Outer membrane vesicles and polymicrobial chronic disease
- Antimicrobial materials – synthesis of novel peptides, nanoparticles and organic polymers to target antibiotic resistance in bacteria
- Bacterial chemotaxis and chronic disease

## Oral Cancer
- Tumour suppressor functions of the IRF6/RIPK4 axis

## Vaccine Development
- Vaccine design and development to improve immune responses to viral diseases and cancer

## Biomaterials for Tissue Repair & Regeneration
- Prevention of dental caries and promotion of remineralization
- Erosive potential of food products, beverages and oral health care products
**Project Theme:** Host–Microbe Interactions in Health & Disease

Host–microbe interactions: investigating mucosal and systemic immune responses to bacteria

The initial interaction of bacteria and bacterial products with mucosal tissue and the immune response induced are fundamental to bacterial infection and disease. We are focused on investigating how antibiotic susceptible and resistant bacteria differ in their interactions and what materials they produce (e.g. outer membrane vesicles, OMVs) to aid infection. We are also interested in discovering how oral bacteria interact with the host to cause disease and how they are associated with systemic conditions (e.g. oral, pancreatic and bowel cancer). We have already found that there is synergy between pathogenic and non-pathogenic bacteria in causing disease and immunopathology. We are offering a number of projects investigating: (1) mucosal and systemic immune responses to single and multi-bacterial species infection; (2) what and how bacterial factors such as OMVs interact with immune cells; (3) how bacteria affect immune cell trafficking into the mucosa and the effect of infection by multiple bacteria; (4) how OMVs aid infection of antibiotic susceptible and resistant bacteria and oral bacteria that cause chronic periodontitis.

**Areas/techniques in which expertise will be developed**
Flow cytometry (multi-parameter), fluorescence activated sorting, aseptic technique, bacteriology and microbiological techniques, tissue culture, real-time PCR and cytokine DNA microarray, SDS PAGE, ELISA, ELISPOT, cytotoxicity assays, animal and human sample handing and experiments, report writing, paper editing/writing, working as a member of a team, and research management.

**Supervisors**
Prof Neil O’Brien-Simpson – neil.obs@unimelb.edu.au
Dr James Holden – jholden@unimelb.edu.au
Dr Jason Lenzo – jlenzo@unimelb.edu.au

**Degree availability**
Bachelor of Science (Honours)
Bachelor of Biomedicine (Honours)
Master of Biomedical Science

**Location**
Melbourne Dental School & Bio21 Institute

**Number of vacancies**
Two students

**Recent publications**


*Former Honours student; ^former PhD student
Investigating the host defence functions of the novel epithelial cytokine IL-36 gamma

The epithelial cells that cover the external surfaces of the body are the first line of defence against infection. In addition to functioning as a physical barrier to infection, they also produce cytokines that activate and recruit immune cells. We recently discovered that oral epithelial cells produce the novel cytokine IL-36 gamma in response to bacteria. Moreover, we have shown that IL-36 gamma stimulates the production of other cytokines by innate immune cells (e.g. macrophages) to recruit additional immune cells, including adaptive immune cells. In this project, you will use gene knockout mice to investigate the role of IL-36 gamma in preventing infection. This project will provide important new insight into how IL-36 gamma could potentially be used to treat infections, in particular, infections caused by antibiotic-resistant bacteria.

Areas/techniques in which expertise will be developed

Mouse models of bacterial infection, tissue dissection & histological analysis, flow cytometry, cytokine & gene expression analysis, critical thinking & time management, scientific writing & oral communication.

Supervisors
A/Prof Glen Scholz – glenms@unimelb.edu.au
Dr Jacqueline Heath – jhea@unimelb.edu.au

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Recent publications


*Former Honours student; ^former PhD student
How spatial control of cytokine responses maintains host-microbe homeostasis

The oral cavity encounters billions of bacteria, including potential pathogens, on a daily basis. Critically, the epithelial cells that line the oral cavity express receptors which enables the detection of bacteria. However, how the epithelial cells tolerate commensal bacteria, and yet produce cytokines that stimulate inflammation to eliminate pathogens is poorly understood. In contrast to pathogens, commensal bacteria do not typically invade epithelia. Therefore, the spatial control of cytokine-regulated responses likely plays a critical role in delineating between commensal bacteria and pathogens. In this project, you will use cell culture systems to investigate how responses regulated by the cytokine IL 36 gamma are spatially controlled. This project will provide important new insight into how impaired spatial regulation of IL 36 gamma could result in the stimulation of chronic inflammation by commensal bacteria and increased susceptibility to infection.

Areas/techniques in which expertise will be developed

Mammalian & bacterial cell culture, manipulating gene expression, cell signalling & transcriptional regulation, cytokine analysis, immunofluorescence confocal microscopy, critical thinking & time management, scientific writing & oral communication.

Supervisors

A/Prof Glen Scholz – glenms@unimelb.edu.au
Dr Jacqueline Heath – jhea@unimelb.edu.au

Degree availability

Bachelor of Science (Honours)
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Location

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Number of vacancies

Two students

Recent publications

• Huynh J*^, Kwa MQ*^, Cook AD Hamilton JA, Scholz GM. CSF-1 receptor signalling from endosomes mediates the sustained activation of Erk1/2 and Akt in macrophages. Cellular Signalling (2012) 24: 1753-61.

*Former Honours student; ^former PhD student
Epigenetic control of host-microbe interactions

Epigenetic mechanisms play important roles in regulating the functions of immune cells. It has recently emerged that specific metabolites produced by bacteria can effect these epigenetic regulatory mechanisms, and thus may influence susceptibility to infection. Epithelial cells covering the external surfaces of the body (e.g. skin & oral cavity) also have important immune functions; for example, producing anti-microbial proteins and inflammatory cytokines. We have established that the immune functions of oral epithelial cells are regulated by epigenetic mechanisms, and modified by bacterial metabolites. In this project, you will use cell culture systems to investigate how different bacteria affect the immune functions of epithelial cells by producing metabolic products. This project will provide important new insight into how changes in the types of bacteria colonising surface epithelia might promote disease by disrupting epigenetic regulatory mechanisms.

Areas/techniques in which expertise will be developed
Mammalian & bacterial cell culture, manipulating gene expression, cell signalling & transcriptional regulation, cytokine analysis, immunofluorescence confocal microscopy, critical thinking & time management, scientific writing & oral communication.

Supervisors
A/Prof Glen Scholz – glenms@unimelb.edu.au
Dr Jacqueline Heath – jhea@unimelb.edu.au

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One student

Recent publications

*Former Honours student; ^former PhD student
Identification and functional characterisation of novel binding partners of the IRF6 transcription factor

The epithelial cells covering the external surfaces of the body (e.g. skin & oral cavity) not only function as an important physical barrier to infection but their expression of immune receptors also enables them to actively particulate in host defence. We have established that the IRF6 transcription factor is an important regulator of the host defence functions of epithelial cells. However, the proteins with which IRF6 interacts to regulate these important functions are poorly understood. In this project, you will use cell culture systems to identify and characterise novel binding partners of IRF6.

Areas/techniques in which expertise will be developed
Mammalian cell culture, mass spectrometry, manipulating gene expression, cell signalling & gene expression analysis, immunofluorescence confocal microscopy, critical thinking & time management, scientific writing & oral communication.

Supervisors
A/Prof Glen Scholz – glenms@unimelb.edu.au
Dr Jacqueline Heath – jhea@unimelb.edu.au

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Recent publications

*Former Honours student; ^former PhD student
Maintenance of oral epithelial barrier to infection

Epithelial surfaces (e.g. skin, oral cavity, gut, lungs) interact directly with the external environment, continuously encountering commensal bacteria as well as potential pathogens. Therefore, mucosal epithelial cells are critical mediators of host defence, acting as a physical barrier against infection. They maintain this essential barrier by undergoing coordinated cycles of cell proliferation and differentiation. During repair of damaged epithelium, epithelial cells at the border of the wound undergo intermediate epithelial-mesenchymal transition (EMT), allowing migration of the cells and remodelling of the tissue, which coincidentally also induces permeability of the barrier. Pathogenic bacteria (e.g. *Salmonella typhimurium*) have been shown to induce EMT to promote colonization and invasion of mucosal epithelia. Oral pathogen *Porphyromonas gingivalis* has been shown to induce EMT in oral epithelial cells. In addition, we have recently shown that oral epithelial cells respond to *P. gingivalis* by producing the novel cytokine IL-36γ. Furthermore, we have shown that IL-36γ plays a role in proliferation and differentiation of oral epithelial cells. Therefore, dysregulation of IL-36γ expression by *P. gingivalis*, may compromise barrier function of the oral mucosa and impair host defence against infection. In this project, you will investigate the role of IL-36γ and a novel protein we have shown to be regulated by IL-36γ, in regulating the molecular mechanisms and processes of barrier function maintenance and EMT, their role in preventing infection, as well as the effect of bacterial exposure (commensals and pathogens) on regulation of these processes.

Areas/techniques in which expertise will be developed

Bacterial & mammalian cell culture, bacterial-challenge assays, manipulating gene expression, transcriptional regulation, proteomics, immunofluorescence confocal microscopy, critical thinking & project management, scientific writing & oral communication.

Supervisors

Dr Jacqueline Heath – jhea@unimelb.edu.au
A/Prof Glen Scholz – glenms@unimelb.edu.au

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Recent publications


*Former Honours student; ^former PhD student
Microbial flow cytometry: developing diagnostic tools for immune responses to bacteria, nano- and micro-materials and vesicles

Analysis of nano-materials and microbes using flow cytometry is a novel area of research. A major issue in studying nano- and micro-particle interaction with mammalian cells or microbes or analysis of microorganisms by flow cytometry has been the sensitivities of flow cytometers. As part of the University’s Cytometry Platform the Melbourne Dental School node has developed methodologies to detect and resolve 100 nm particles, thus allowing detection of exosomes and outer membrane vesicles in biological fluids. The methodologies allow detection and sorting of mixed bacterial populations and enable analysis of rare events in mammalian cells and microbes. The projects offered are in the development of nano- and micro-flow cytometry assays for the detection, analysis and sorting of: (1) bacteria-bacteria interactions, (2) nanoparticle interactions with bacteria and/or mammalian cells, (3) bacterial outer membrane vesicle (OMV) interactions with bacteria and host cells, (4) isolation and identification of bacteria from mixed biofilm and biological samples, (5) isolation of exosomes, OMVs from biological samples and their identification.

Areas/techniques in which expertise will be developed

Flow cytometry, fluorescence activated sorting, aseptic technique, bacteriology and microbiological techniques, tissue culture, peptide/polymer chemistry, peptide/protein purification (HPLC/FPLC), SDS-PAGE, ELISA, ELISPOT, cytotoxicity assays, animal and human sample handling and experiments, report writing, paper editing/writing, working as a member of a team, and research management.

Supervisors
Prof Neil O’Brien-Simpson – neil.obs@unimelb.edu.au
Dr Alexis Gonzalez – alexis.gonzalez@unimelb.edu.au
Dr James Holden – jholden@unimelb.edu.au
Dr Jason Lenzo – jlenzo@unimelb.edu.au

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Recent publications

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Honours and Masters Research Project Handbook 2020
Project Theme: Microbiomes in Health & Disease

Oral microbiome in health and disease
The human oral cavity is home to over 700 species of bacteria, many of these species are beneficial to our health whilst others are associated with the development of chronic diseases. During disease initiation there is a shift in the composition of the microbiome that leads to the development of a dysbiotic biofilm community that sustains disease progression. In this project you will determine the oral microbiome in health compared with that in disease states and identify those bacteria associated with disease. Ultimately, we would like to identify microbial biomarkers that can be used as predictors of health or disease.

Areas/techniques in which expertise will be developed
Genomic DNA extraction from different sample types, PCR amplification, next generation sequencing using Ion Torrent technology, bioinformatics, microbial ecology, research management, oral presentation skills, scientific writing skills.

Supervisors
Prof Stuart Dashper – stuartgd@unimelb.edu.au
Dr Catherine Butler – cbutler@unimelb.edu.au
Dr Samantha Byrne – sbyrne@unimelb.edu.au

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Two students

A pseudo-colour image showing percent loading of Ion Sphere Particles (ISPs) across the physical surface of an Ion Chip Plate used for Ion Torrent sequencing.
**Project Theme:** Bacterial Virulence

**Characterisation of potential virulence factors secreted by the type 9 secretion system of Porphyromonas gingivalis**

Chronic periodontitis is an inflammatory disease causing the destruction of the supporting gum and bone of teeth. *Porphyromonas gingivalis* (*Pg*) is the major agent of this disease and is also associated with other diseases/conditions such as cardiovascular diseases, adverse pregnancy outcomes (preterm birth, low birth weight and pre-eclampsia), rheumatoid arthritis, diabetes, non-alcoholic fatty liver disease and Alzheimer’s disease. This emphasizes the importance of *Pg* host dissemination, immune evasion, immune modulatory tactics and *Pg*-induced inflammation. *Pg* possesses a type 9 secretion system (T9SS) which secretes abundant gingipain proteases that are involved in this disease process. Many other proteins are secreted by this T9SS but their functions are unknown. Recent structural analyses have predicted virulence functions for several of these T9SS substrates. The honours projects on offer will characterize these candidate virulence factors to further our understanding of the arsenal of virulence factors that *Pg* deploys and to identify potential vaccine candidates.

**Areas/techniques in which expertise will be developed**

Microbiological, molecular biology, immunological and biochemical techniques, including anaerobic bacterial growth, cell growth inhibition assays, *Pg* gene deletion, PCR, DNA purification, DNA gel electrophoresis, recombinant protein expression, SDS-PAGE, Western blot, 2D Blue-Native PAGE and proteomics, super-resolution fluorescence microscopy and electron microscopy.

**Supervisors**

Dr Michelle Glew – mglew@unimelb.edu.au  
A/Prof Paul Veith – pdv@unimelb.edu.au

**Degree availability**

Bachelor of Science (Honours)  
Master of Biomedical Science

**Location**

Bio21 Institute

**Number of vacancies**

Two students

**Recent publications**

Identification of the interacting regions between an essential component of the type 9 secretion system, PorV, and secreted virulence factors of the oral pathogen, *Porphyromonas gingivalis*

The type 9 secretion system (T9SS) of the oral Gram-negative pathogen, *Porphyromonas gingivalis*, is responsible for secreting many CTD-proteins including abundant gingipain proteases that are major virulence factors and contribute to chronic periodontitis in humans. PorV is an outer membrane beta-barrel protein and we have shown it to be an essential component involved in binding to CTD-proteins and interacting with the attachment complex (PorU, PorQ and PorZ) that is responsible for the covalent linkage of CTD-proteins to anionic lipopolysaccharide (A-LPS) which ultimately anchors them to the cell surface. Recently, the structure of an outer membrane component of the T9SS called Sov was determined by cryo-electron microscopy and found to exist as two separate complexes: Sov-Plug and Sov-PorV. We propose that Sov aids PorV in recruiting and translocating the CTD-proteins across the outer membrane in preparation for linkage to A-LPS. To better understand how PorV interacts with T9SS substrates and Sov, this project will involve mutagenesis of the inner and outer loop amino acids of PorV followed by characterization of the resulting *P. gingivalis* mutants to identify specific secretion defects. Any interaction defects of the mutated PorV protein with either the CTD-proteins and/or Sov will be identified. The student will join a team that are leaders in the field and publishing in high ranking journals.

**Areas/techniques in which expertise will be developed**

Microbiological, molecular biology, immunological and biochemical techniques, including anaerobic bacterial growth, gene mutagenesis in *P. gingivalis*, PCR, DNA purification, DNA gel electrophoresis, SDS-PAGE, Western blot, 2D Blue-Native PAGE, proteomics, protein complex purification and electron microscopy.

**Supervisors**

Dr Michelle Glew – mglew@unimelb.edu.au  
A/Prof Paul Veith – pdv@unimelb.edu.au

**Degree availability**

Bachelor of Science (Honours)  
Master of Biomedical Science

**Location**

Bio21 Institute

**Number of vacancies**

One student

**Recent publications**


Proposed mechanism of recruitment and translocation of CTD-proteins by the T9SS Sov-PorV complex prior to ligation to A-LPS
Role of PG0189 in the assembly of the type IX secretion system (T9SS) in Porphyromonas gingivalis

Periodontitis (gum disease) is a major health problem. The main microorganism responsible for periodontitis is the pathogenic bacterium Porphyromonas gingivalis. Infection by this bacterium can cause severe lesions resulting in tooth loss. The major virulence factors of P. gingivalis are cysteine proteinases called gingipains, which are sorted to the cell-surface by the recently identified Type IX secretion system (T9SS). This secretion system is composed of at least 13 proteins, including PorK and PG1058, which are thought to assemble an outer membrane channel that transports the gingipains to the cell-surface. The T9SS is poorly characterised and very little is known about how this system functions to transport the gingipains. More recently, we have identified PG0189 to be a novel component of the T9SS and found that it forms a disulphide bond with PorK. This study aims to understand the role of this conserved cysteine in PG0189. The cysteine will be mutated to alanine and introduced in P. gingivalis. We will then examine the effect of this mutation on the T9SS, i.e. is the formation of the ring structure affected in the absence of the cysteine? This study will improve our understanding of how the T9SS functions to secrete virulence factors to the cell surface.

Areas/techniques in which expertise will be developed

Isolation of genomic DNA, mutagenesis, PCR, DNA gel electrophoresis, plasmid isolation, DNA cloning, growing anaerobic bacteria (P. gingivalis), isolation of large macromolecular complexes using gradient centrifugation, SDS-PAGE, western blots and electron microscopy.

Supervisors
Dr Dhana Gorasia – gorasiad@unimelb.edu.au
A/Prof Paul Veith – pdv@unimelb.edu.au

Degree availability
Bachelor of Science (Honours)
Bachelor of Biomedicine (Honours)
Master of Biomedical Science

Location
Bio21 Institute

Number of vacancies
One student

Recent publications
Proteomic analysis of gingipain catalysed transpeptidation reactions and its relevance to autoimmunity

The gingipains are cell surface cysteine proteases and major virulence factors of Porphyromonas gingivalis, a keystone pathogen of human periodontitis (gum disease). We recently discovered that these proteases not only hydrolyse proteins but also cleave them via transpeptidation leading to rearranged peptide sequences. In vivo, this is expected to generate a staggering number of rearranged host protein sequences which may lead to autoimmune reactions. The aim of this project is to further characterise this transpeptidation activity. First, transpeptidation rates will be measured as a function of environmental variables such as pH and temperature as well as a function of the sequence and length of peptide acceptors. In addition, we have noted that gingipains degrade model substrates including human haemoglobin via both transpeptidation and hydrolysis reactions in vitro. This project will study in detail the degradation pathway of human haemoglobin to help predict the kinds of favoured transpeptidation reactions that may also occur in vivo. Finally, a proteomic study of sub-gingival plaque and surrounding protein fluid (gingival crevicular fluid) obtained from periodontitis patients will be conducted to identify in vivo targets of transpeptidation.

Areas/techniques in which expertise will be developed
Mass spectrometry/proteomics, enzyme characterization, UV-Vis and fluorescence spectrophotometry, enzyme activity assay, polyacrylamide gel electrophoresis and immunoassays, protein purification techniques including liquid chromatography, ultrafiltration and ultracentrifugation.

Supervisors
A/Prof Paul Veith – pdv@unimelb.edu.au
Dr Lianyi Zhang – lizhang@unimelb.edu.au

Degree availability
Bachelor of Science (Honours)
Bachelor of Biomedicine (Honours)
Master of Biomedical Science

Location
Bio21 Institute

Number of vacancies
One student

Recent publications
Outer membrane vesicles and polymicrobial chronic disease

*Porphyromonas gingivalis* and *Treponema denticola* display a range of synergistic behaviours including polymicrobial biofilm formation and development, and nutrient acquisition, which together enable them to cause chronic disease. Both bacteria produce and release outer membrane vesicles that preferentially bind to the other species. In this project you will determine how this binding occurs and the benefits to each species of binding outer membrane vesicles.

Areas/techniques in which expertise will be developed

Confocal microscopy, molecular biology, anaerobic bacterial culture, flow cytometry

Supervisors

Prof Stuart Dashper – stuartgd@unimelb.edu.au
Dr Catherine Butler – cbutler@unimelb.edu.au
Dr Nada Slakeski – n.slakeski@unimelb.edu.au
Dr Alexis Gonzalez – alexis.gonzalez@unimelb.edu.au

Degree availability

Bachelor of Science (Honours)
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Location

Melbourne Dental School & Bio21 Institute

Number of vacancies

Two students

Recent publications


*Former Honours student; ^former PhD student
Antimicrobial materials – synthesis of novel peptides, nanoparticles and organic polymers to target antibiotic resistance in bacteria

By 2050, it is predicted that more people will die from bacterial infections than cancer. Currently, multidrug resistant (MDR) bacterial infections cause >700,000 deaths/year and incur an estimated annual treatment cost of >US $20 billion. Antimicrobial resistance is considered “one of our most serious health threats” and thus new, potent and selective antimicrobial agents that do not induce resistance like traditional antibiotics are urgently required. We wish to recruit students into 3 areas of research: (1) Antimicrobial nanomaterials – we are investigating antimicrobial nanomaterials, termed Structurally Nanoengineered Antimicrobial Peptide Polymers (SNAPPs). This project will use novel and established assays in an iterative chemical biology approach to modify antimicrobial nanomaterials to enhance killing of MDR bacteria. (2) Antimicrobial peptides targeting oral bacteria – the oral cavity is a reservoir for transferable antibiotic resistance, a phenomenon increased in patients with chronic periodontitis. This project will investigate methods for narrowing the activity spectrum of AMPs to target only periodontal pathogens, reduce cytotoxicity, and leave unharmed bacteria associated with oral health. (3) Antibiotic adjuvants – one approach to address antibiotic resistance is to combine antibiotics with an “antibiotic adjuvant”, which potentiates or restores the activity of the antibiotic towards MDR bacteria. This project will use an iterative chemical biology approach to modify AMPs or SNAPPs to enhance their antibiotic adjuvant properties.

Areas/techniques in which expertise will be developed
Bacteriology & microbiological techniques, mammalian tissue culture, peptide & polymer chemistry, peptide & protein purification (HPLC, FPLC), SDS-PAGE, ELISA, ELISPOT, cytotoxicity assays, animal handing and experiments, paper editing & writing, working as a member of a team, and research management.

Supervisors
Prof Neil O’Brien-Simpson – neil.obs@unimelb.edu.au
Dr James Holden – jholden@unimelb.edu.au
Dr Jason Lenzo – jlenzo@unimelb.edu.au

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Honours and Masters Research Project Handbook 2020
Bacterial chemotaxis and chronic disease

*Treponema denticola* is a chemotactic, motile spirochaete that is an aetiological agent of chronic periodontitis. Its unique form of motility and chemotaxis enable it to move through highly viscous environments. It has twenty chemoreceptor proteins that enable it to respond to a range of stimulatory substances. In this project you will determine how *T. denticola* moves in response to stimuli using a custom-built flow cell and confocal scanning laser microscopy. You will have the opportunity to clone and express the *T. denticola* chemotaxis proteins and determine their substrate specificity using highly novel microarray technologies.

Areas/techniques in which expertise will be developed
Confocal microscopy, molecular biology, anaerobic bacterial culture, protein expression

**Supervisors**  
Prof Stuart Dashper – stuartgd@unimelb.edu.au  
Dr Catherine Butler – cbutler@unimelb.edu.au  
Dr Nada Slakeski – n.slakeski@unimelb.edu.au

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Two students

**Recent publications**

*Former Honours student; ^former PhD student
**Project Theme: Oral Cancer**

**Tumour suppressor functions of the IRF6/RIPK4 axis**

Many cancers, including skin, breast, and oral cancer, are caused by mutations that dysregulate the normal programs of epithelial cell proliferation and differentiation. The IRF6 transcription factor plays an important role in promoting normal epithelial cell differentiation. We have discovered that IRF6 is directly regulated by the protein kinase RIPK4, and shown that they function together as a regulatory axis to promote epithelial cell differentiation. Notably, IRF6 and RIPK4 were recently discovered to be mutated in human cancers of epithelial origin. In this project, you will investigate the effects of cancer-associated mutations on the regulation and function of IRF6 by RIPK4. You will also identify novel proteins that interact with IRF6 and RIPK4.

**Areas/techniques in which expertise will be developed**

Mammalian cell culture, mutagenesis & manipulating gene expression, mass spectrometry, gene expression analysis, immunofluorescence confocal microscopy, critical thinking & time management, scientific writing & oral communication...

**Supervisors**

A/Prof Glen Scholz – glenms@unimelb.edu.au
Dr Jacqueline Heath – jhea@unimelb.edu.au

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**Recent publications**


*Former Honours student; **former PhD student
Project Theme: Vaccine Development

Vaccine design and development to improve immune responses to viral diseases and cancer

Cytotoxic T lymphocytes (CTL) are critical for immunosurveillance and killing of virus-infected cells and cancer cells. Many viral infections and squamous cell carcinomas (SCC) occur at mucosal sites; however, parenteral vaccination does not induce mucosal immunity. For the vaccine to induce a protective CTL response, it needs to be administered via a mucosal route and deliver its antigen cargo to dendritic cells. Further, the vaccine will need to activate these cells to induce both CTL and T helper (Th) cell antigen-specific responses, which is necessary for strong effector and memory CTL responses. We have demonstrated that nanoparticles are effective mucosal vaccine delivery vehicles and different pattern recognition receptor (PRR) ligands used to functionalise antigen-loaded nanoparticles can enhance or abrogate CTL and Th responses. Our research has shown that protein-coated and PRR functionalised nanoparticles are more rapidly phagocytosed and induce stronger CTL and Th cell immune responses. Finally, we have developed a novel and reliable method for producing different sized calcium phosphate nanoparticles that has applicability for a broad range of vaccines. The overall aim of our research is to combine these new technologies for an integrated, preclinical evaluation of novel calcium phosphate nanoparticle vaccines and compare their ability to induce CTL responses via mucosal or parenteral immunisation. We wish to recruit students into 3 areas of research: (1) Determining the immuno-stimulatory capability of antigen and molecular adjuvant loaded calcium phosphate nanoparticles in vitro. (2) Determining the immuno-stimulatory capability of calcium phosphate nanoparticle vaccines in vivo. (3) Evaluating the efficacy of calcium phosphate nanoparticles as mucosal vaccines to induce protective CTL responses.

Areas/techniques in which expertise will be developed
Flow cytometry, fluorescence activated sorting, aseptic technique and mammalian tissue culture, real-time PCR and cytokine array, SDS-PAGE, ELISA, ELISPOT, cytotoxicity assays, animal and human sample handing and experiments, paper writing/editing, working as a member of a team, and research management.

Supervisors
Prof Neil O’Brien-Simpson – neil.obs@unimelb.edu.au
Dr James Holden – jholden@unimelb.edu.au
Dr Jason Lenzo – jlenzo@unimelb.edu.au

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Relevant publications

\(^*\)Former Honours student; \(^\text{\^}\)former PhD student

Honours and Masters Research Project Handbook 2020
**Project Theme:** Biomaterials for Tissue Repair & Regeneration

**Prevention of dental caries and promotion of remineralization**

Dental decay, or caries, starts when bacteria in plaque produces an organic acid which dissolves the tooth enamel, breaking down the calcium and phosphate in tooth enamel. Enamel remineralization is the process of net mineral uptake into partially demineralized tooth structure to prevent and repair early dental decay. Projects are available to study the process of enamel demineralization and remineralization to increase our understanding of dental caries and will study ways of inhibiting enamel demineralization and enhancing remineralization and quantify the effects of these treatments using state-of-the art quantification methods. Projects are available to test novel oral health products and functional foods designed to assist in the prevention of dental caries. The preventive products that include toothpastes, dental cremes, mouth rinse solutions, gels, and varnishes for topical application will contain anti-caries agents. Alternatively, commonly consumed foods and beverages will be modified to minimize their potential to cause loss of mineral from teeth such as during dental caries or modified to provide a positive health effect. The projects may include laboratory and/or in situ studies.

**Areas/techniques in which expertise will be developed**

Demineralization, dental erosion, remineralization, transverse microradiography, microhardness.

**Supervisors**

Dr Peiyan Shen – peiyan@unimelb.edu.au
Dr Glenn Walker – gdwalker@unimelb.edu.au

**Degree availability**

Bachelor of Science (Honours)
Bachelor of Biomedicine (Honours)
Master of Biomedical Science

**Location**

Melbourne Dental School

**Number of vacancies**

One student

**Relevant publications**

Erosive potential of food products, beverages and oral health care products

Tooth erosion is caused by dissolution of the tooth surface by acids that do not originate from bacteria. Both tooth enamel and dentine can be eroded over time following long term exposure to acids in the mouth originating from acid-containing food products and beverages. Some acid-containing oral health care products may also have erosive potential. Tooth erosion is becoming a more significant clinical problem due to increased consumption of acidic foods and beverages. Erosion of tooth surfaces can lead to poor aesthetics and weakening of the tooth structure. In addition, erosion of dentine can lead to tooth sensitivity due to opening and widening of microscopic dentinal tubules that extend from the surface of the dentine to the pulp (nerve) of the tooth. Projects are available to increase our understanding of tooth erosion and to develop strategies to prevent erosion using established state-of-the-art methods for quantifying loss of the tooth surface, measuring tooth mineral content changes and observing changes to dentinal tubules. Specifically, projects are available to: 1) measure erosion of tooth surfaces exposed to various food, beverage and oral health care products; 2) test the ability of novel oral health care products to prevent or repair dental erosion. One compound with the potential to prevent dental erosion is a derivative of the major milk protein casein combined with calcium and phosphate called casein phosphopeptide-amorphous calcium phosphate (CPP-ACP). Oral health care products designed to prevent dental erosion may be tested and may include mouth rinses, toothpastes, gels, dental cremes and dental varnishes containing CPP-ACP with or without fluoride. Methods to decrease or eliminate the erosive potential of some of these products by addition of calcium or CPP-ACP with or without fluoride may also be tested. These projects will be laboratory experiments on pre-sterilized human tooth enamel or dentine. Erosive potential can be investigated using established chemical analytical techniques such as measurement of pH, titratable acidity and chemical composition. Measurement of erosion on enamel and dentine surfaces may include a variety of techniques including surface profilometry, surface microhardness, confocal laser scanning microscopy and transverse microradiography. Changes in the architecture of tooth surfaces and diameters of dentinal tubules may be observed using scanning electron microscopy.

Areas/techniques in which expertise will be developed

Demineralization, dental erosion, remineralization, transverse microradiography, microhardness.

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Master of Biomedical Science

Location
Melbourne Dental School

Number of vacancies
One student

Relevant publications
Becoming an Honours or Masters Student at the Melbourne Dental School

Entry to the Honours and Masters programs is based on available projects, suitability and academic background.

HOW TO APPLY FOR HONOURS

1. Identify projects in this handbook that are of interest to you
2. Contact the relevant project supervisor to discuss your interest in their research. It is a good idea to email them a copy of your CV and your academic transcripts to help them understand your background, interests and academic strengths
3. Make a time to meet with potential supervisors to discuss your project interests and discuss your academic record
4. Visit the laboratory and meet other students and researchers
5. In some cases, supervisors may be willing to offer you a provisional place in their laboratory (a provisional offer indicates that you have a guaranteed place in the Honours course, providing you satisfy all other entry requirements)
6. Apply online through the Faculty of Medicine, Dentistry and Health Sciences website: http://mdhs-study.unimelb.edu.au/degrees/honours/apply-now#apply-now

HOW TO APPLY FOR MASTER OF BIOMEDICAL SCIENCE

1. Identify projects in this handbook that are of interest to you
2. Contact the relevant project supervisor to discuss your interest in their research. It is a good idea to email them a copy of your CV and your academic transcripts to help them understand your background, interests and academic strengths
3. Make a time to meet with potential supervisors to discuss your project interests and discuss your academic record
4. Visit the laboratory and meet other students and researchers
5. In some cases, supervisors may be willing to offer you a provisional place in their laboratory (a provisional offer indicates that you have a guaranteed place in the Honours course, providing you satisfy all other entry requirements)
6. Apply online through the Faculty of Medicine, Dentistry and Health Sciences website: http://mdhs-study.unimelb.edu.au/degrees/master-of-biomedical-science/overview

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