

INSTITUTE FOR GLYCOMICS

*Higher Degree Research
opportunities*

2021/2022



Institute for Glycomics

Queensland, Australia

A MESSAGE FROM THE DIRECTOR

It is with great pleasure that I introduce you to the Institute for Glycomics, one of Australia's flagship multidisciplinary and translational research institutes based on the beautiful Gold Coast in Queensland, Australia.

Did you know that more than 17 million people die from infectious diseases and over 9 million people die from cancer every year across the world?

Do you want to help reverse these alarming statistics?

Do you want to contribute to a future free from cancer? A future free from diseases like influenza and COVID-19? So do we.

Our researchers focus on the discovery and development of new drugs, vaccines and diagnostics to combat some of the world's most devastating diseases.

Here at the Institute for Glycomics, we offer a range of exceptional Honours, Masters and PhD opportunities for the world's future scientists.

Study alongside some of the world's most experienced and well-known research leaders and scientists.

Not only will you have access to our state-of-the-art research equipment and facilities, but you will also be living and studying within one of the most beautiful cities in the world.

And best of all, considering a career in biomedical research could quite literally change the world.

I strongly encourage you to explore the Higher Degree Research opportunities we have available here at the Institute for Glycomics.

Research provides hope. Hope in the fight against disease. Hope for our future. Why not help us change the world.

Professor Mark von Itzstein AO
Director & Principal Research Leader, Institute for Glycomics, Griffith University



ABOUT THE INSTITUTE FOR GLYCOMICS

Comprising over 200 researchers, students and support staff, we strive to be world leaders in the discovery and development of next generation drugs, vaccines and diagnostics for diseases of global impact.

Established in 2000, through investment by Griffith University and the Queensland Government, the Institute for Glycomics is a multidisciplinary biomedical research institute based in the heart of Griffith University's Gold Coast campus and the Gold Coast Health and Knowledge Precinct.

The Institute boasts state-of-the-art facilities combined with some of the world's most outstanding researchers focused on 'glycomics', a constantly expanding field that explores the structural and functional properties of carbohydrates (or sugars) and their roles in disease.

Our research engages worldwide partnerships, in projects that cut across multiple disciplines to apply new approaches to the identification, treatment and prevention of diseases.

The Institute's research targets cancers, infectious diseases and neurodegenerative disorders, with a focus on translational research to have a positive impact on human health globally.

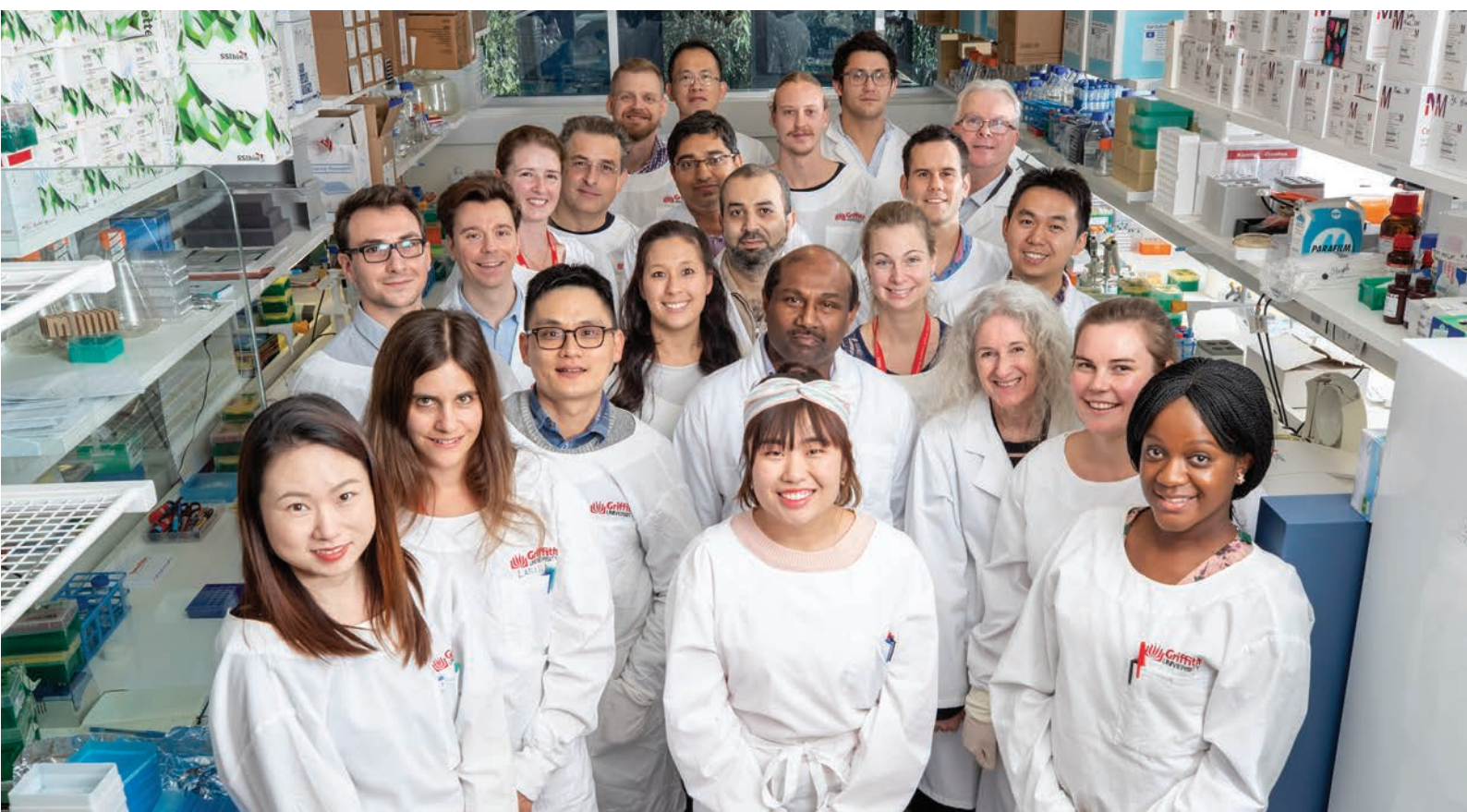
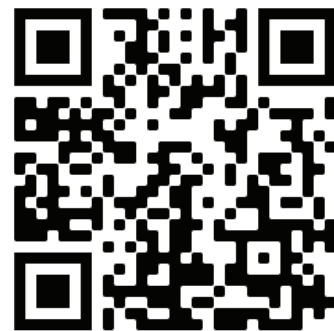
The Institute's rich and enabling research environment provides exceptional Higher Degree Research education programs for future scientists.

The Institute engages with industry, other premier research institutes, philanthropic organisations and governments from across the globe, giving it significant research capacity to provide healthcare solutions to address some of the world's most intractable diseases.

With an outstanding track record in translating biomedical discoveries to the clinic, there is little doubt that our unique approach will play a major role in the discovery and development of next generation drugs, vaccines and diagnostics with the power to change the future of human health.

What is Glycomics?

Scan the QR code for a video illustration



Our Mission

Fighting diseases of global impact through discovery and translational science.



Our Vision

To be a world-leader in the discovery and development of drugs, vaccines and diagnostics through the application of innovative multidisciplinary science in a unique research environment.

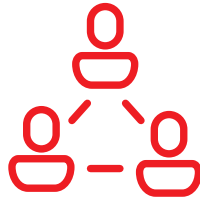


INSTITUTE HIGHLIGHTS



3 Major Research Themes

- Cancer research program
- Infectious diseases research program
- Neurodegenerative diseases research program



Community Engagement

- **PARADISE POINT COMMUNITY BANK** Supporting our COVID-19 research and Summer Student Scholarship scheme
- **WARREN AND SALLY VON BIBRA** Supporting our Honours Student Scholarship scheme
- **SANCTUARY COVE GOLF AND COUNTRY CLUB** Joining forces to fight breast cancer
- **GLYCOMICS CIRCLE** Empowering women in science
- **WOMEN IN RACING** Supporting our glycomics research
- **ROTARY DISTRICT 9640** A powerful partnership to end malaria



200+
Institute Members



Engagement with over 40 industry partners for basic research, translation and commercialisation

Clinical Trials



- **Pilot Phase 1b clinical trial with challenge completed at Griffith University (with support from Rotary)** – Institute vaccine for the prevention of malaria
- **Health Canada CTA submission for Phase 1 clinical trial in Canada in 2021** – Institute vaccine for the prevention of Group A Streptococcus
- **Preparing to enter a Phase 1b clinical trial in collaboration with Murdoch Children's Research Institute (with support from Heart Foundation)** – Institute vaccine for the prevention of Group A Streptococcus
- **Preparing to enter a Phase 2 clinical trial (with support from NHMRC)** – Repurposed vaccine for the prevention of gonorrhoea
- **Phase 1b clinical trial initiated by Grand Medical Ltd** – Institute drug for the treatment of sepsis



Income Sources
for 2020

- Research grant funding \$6,639,125
- Industry, philanthropic & other support \$10,043,387



17,931
Citations
over 10 years



\$1 for \$1
in philanthropic funding supports our research

NEW PHILANTHROPIC ENGAGEMENT

- **Tour de Cure** Supporting our ovarian cancer research
- **Bourne Foundation** Supporting our ovarian cancer research
- **Hay Family Benevolent Fund** Supporting our melanoma research
- **Sanctuary Cove Golf and Country Club** Breast Cancer Awareness month partners
- **Griffith University Film School** A Griffith University cross-collaboration



100+ Publications
per year

OUR REMARKABLE SCIENCE

Our world-renowned research group leaders and their dedicated research teams work around the clock, seeking new opportunities that can lead to novel drugs, vaccines and diagnostics, translating our research into tangible benefits for the global community. Our specialist research programs are centred around cancer, infectious diseases, and neurodegenerative diseases.

Cancer research program

It's estimated that cancer is the second leading cause of death globally and is responsible for over 9 million deaths every year. Globally, about 1 in 6 deaths is due to cancer. Our cancer research specialists aim to reverse these alarming statistics through the discovery and development of new scientific technologies to fight the disease.

Established in 2017, the Australian Centre for Cancer Glycomics (A2CG) is one of our Centres of Excellence housed within the Institute for Glycomics. This unique national resource, dedicated to cancer glycomics research, is the result of significant funding from Griffith University and the community.

Cancer glycomics research involves understanding the role that sugars/carbohydrates play in the development of cancers. Using this knowledge, our researchers can invent new drugs, vaccines and diagnostics to treat, prevent or diagnose cancer.

As the only research institute of its kind in the southern hemisphere, the Institute for Glycomics is already an epicentre of glycomics research globally, and houses many world-leading carbohydrate researchers. The A2CG brings together the Institute's experts in cancer research, while providing an ideal platform for collaboration with other leading cancer researchers and clinicians around the world.

A project with the vision and scale of the A2CG requires substantial human resources, technical knowledge and specialisation. By combining core expertise and infrastructure, the A2CG is a world-class platform for mapping cancer glycomics and glycoproteomics and translating these discoveries into novel diagnostics and therapies.

The state-of-the-art equipment and infrastructure, coupled with the brightest scientific talent in the field of cancer glycomics and glycoproteomics, makes the A2CG an exciting hub of truly revolutionary cancer research.

Our researchers focus on some of the world's most devastating forms of cancer, including (but not limited to) head and neck, leukaemia, lymphoma, breast, ovarian, prostate, and skin cancers.



Infectious diseases research program

Infectious diseases pose some of the world's most significant health challenges, claiming over 17 million lives globally every year.

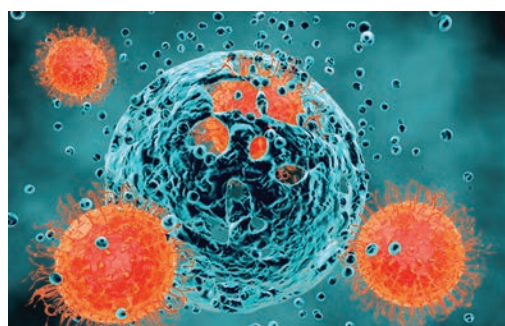
There is an overwhelming need to find new ways to combat diseases caused by bacterial, viral, parasitic and fungal pathogens. The increasing emergence of antibiotic-resistance is also a global concern.

There's an urgent need to discover new approaches to address antibiotic-resistance and the lack of effective vaccines for some of the world's most serious viral and bacterial pathogens.

Our infectious diseases research program tackles these issues, combining our cutting-edge research equipment and facilities with our world-leading scientific expertise in the innovative field of glycomics. Our unique approach to infectious diseases research provides us with a solid platform to discover and develop next generation drugs, vaccines and diagnostics to address some of the world's most debilitating diseases.

Bacterial infections

The Institute's research into the role of sugars/carbohydrates in diseases caused by bacteria represents new and exciting opportunities for the discovery of next generation antibiotics and vaccines. Many of the bacteria that cause some of the world's most devastating diseases are rapidly developing resistance to antibiotics, and to this end we are also developing drugs that break anti-bacterial resistance. Types of bacterial infections included within our infectious diseases research program include Strep A/rheumatic heart disease, tuberculosis, middle ear infections, gonorrhoea, meningitis and gastroenteritis/food poisoning.

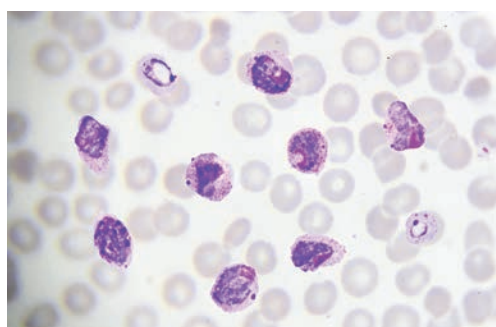


Viral infections

Diseases caused by viruses have plagued humanity for time immemorial. Unfortunately, drugs that combat viruses are extremely limited in number and are not broad spectrum. The Institute's research into viral infections such as hand, foot and mouth disease (HFMD), human immunodeficiency virus (HIV), influenza virus, human parainfluenza virus (hPIV), human metapneumovirus (hMPV), respiratory syncytial virus (RSV), Dengue virus, Ross River virus, Chikungunya virus (CHIKV) and other emerging alphaviruses, seeks to understand how sugars/carbohydrates are utilised in viral infections so that scientists can identify targets for the development of new drugs that will treat and cure these diseases.

Parasitic infections

Parasitic infections such as malaria still present as important public health challenges in tropical environments, with devastating socio-economic consequences in developing countries. It is now becoming clear that some of these parasites rely on carbohydrate-binding proteins for attachment and invasion of human host cells. Our research in this area will yield useful information for the design of diagnostic tools, vaccines and drugs to fight these diseases.



Fungal infections

Fungal infections constitute a broad range of common medical illness from a common superficial or mucosal infection to the more severe systemic invasive fungal infections that affect millions of people worldwide. Fungal infections can occur regardless of the immune status of the host. However, individuals with a compromised immune system are highly susceptible to invasive fungal infections. The Institute is fighting invasive fungal infections through novel therapeutic approaches.

Neurodegenerative diseases research program

Neurodegenerative disease is the umbrella term used to describe a group of disorders that are characterised by the progressive degeneration of the structure and function of the central and peripheral nervous systems.

Neurodegenerative diseases are incurable and debilitating conditions that result in progressive degeneration and/or death of nerve cells. This causes problems with movement or mental functioning.

Neurodegenerative disorders have been predicted by the World Health Organisation to overtake cancer and become the second-most prevalent cause of death in the next 20 years.

The science behind neurodegenerative diseases

Axons (nerve fibres) are the portion of the nerve cells that communicates with other cells by transmitting electrical and chemical signals.

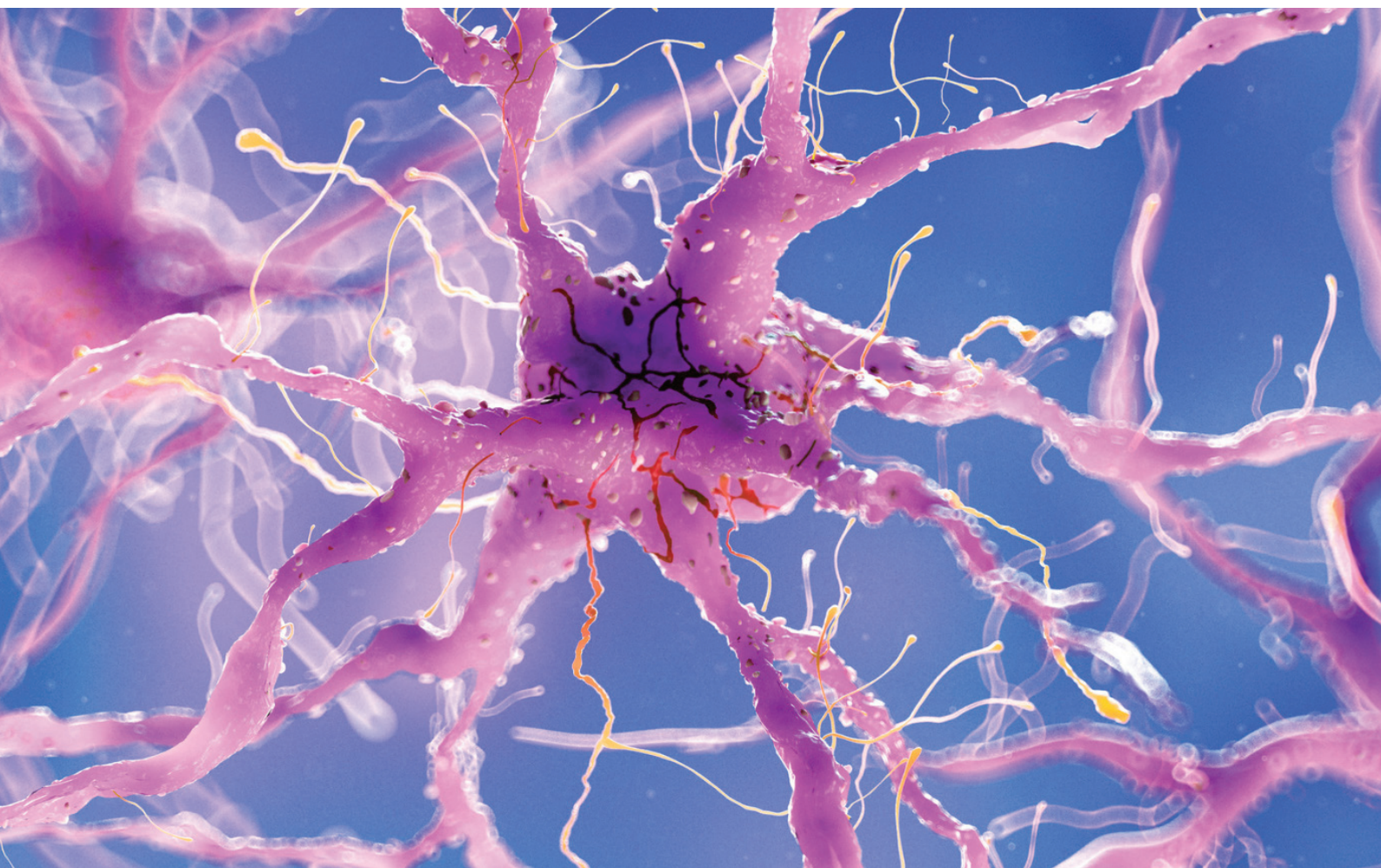
These signals underlie essential processes, such as thinking and memory, movement, language and sense of touch.

When axons are damaged, whether by injury, disease or as a side effect of certain drugs, a program is triggered to make axons self-destruct.

This destruction likely plays an important role in multiple neurodegenerative conditions, including peripheral neuropathy, Parkinson's disease, amyotrophic lateral sclerosis (ALS), traumatic brain injury and glaucoma. There are no current treatments that effectively target axonal breakdown.

The Institute's neurodegenerative diseases research seeks to:

- 1) improve our understanding of the molecular mechanisms involved in axon degeneration
- 2) provide new strategies for the design of targeted inhibitors of axon degeneration, which can be developed into therapeutic agents for neurodegenerative disease.





A MESSAGE FROM OUR HDR CONVENORS

You are not alone in your HDR expedition! At the Institute for Glycomics, you are not travelling alone, but you are supported by a network of HDR colleagues and mentors who will assist you in achieving your scientific and administrative goals.

A Higher Degree by Research (HDR) is an exciting and rewarding, but sometimes also a scary journey. Your HDR convenors, together with your individual supervisory team, will help you to safely navigate the jungles of your degree.

This includes ensuring that you have the resources needed to complete your studies, assisting you with thesis submission, helping you address any changing circumstances during your candidature and guiding you in the completion of your milestones.

On your journey towards an HDR, you will need to complete different milestones to ensure that you are making progress with your research project.

Your supervisors and HDR convenors will help you to successfully complete these milestones towards achieving your degree.

Our doors are always open, and you can approach us to discuss your research progress and milestones. We can support you with individual career advice and will help you tackle challenging situations that can sometimes arise during your research degree.

In short, you are not alone on your journey but can rely on a solid support network. We would like to invite any prospective candidates to contact us with any questions they have about pursuing a research degree at the Institute for Glycomics.

We look forward to discussing possible research projects and options with you and will help you find the ideal supervisor for your research project.

Associate Professor Lara Herrero
Associate Professor Daniel Kolarich
HDR Convenors, Institute for Glycomics

WHY CONSIDER HDR STUDIES AT THE INSTITUTE FOR GLYCOMICS?

The Institute for Glycomics, based at Griffith University's beautiful Gold Coast campus, offers a range of exceptional research degree opportunities. You will have the opportunity to study alongside some of the world's most experienced and well-known scientists on research projects that have the potential to provide solutions to some of the world's most significant health problems.

It's an exciting and supportive research environment

- The Institute for Glycomics is one of only a few multi-disciplinary glycoscience research centres in the world. It has state-of-the-art research facilities which support the full spectrum of research opportunities from basic discovery through to pre-clinical evaluation and clinical translation.
- Collaboration between different research groups enables projects to successfully span multiple research disciplines. This results in novel solutions to global health problems.

There are opportunities for professional development

- HDR students have many opportunities to participate in conferences, networking events and mentoring programs. These may lead to job opportunities and collaborations in the future.
- There are options for industry placements to broaden knowledge, research skills and experience for future career opportunities.

It's an investment in your future

- A postgraduate degree will allow you to develop research skills necessary to progress your career or even help you to explore a new career. It will also allow you to gain other transferable skills which are applicable to many jobs and other aspects of your life.
- A postgraduate degree has enabled many of our previous students to continue on to exciting research positions in academic and research institutions around the world. Other students have transitioned into different careers which benefit from the knowledge and skills that were gained during their degree.

It's an opportunity for you to make a difference

- It is your opportunity to make a substantial and original research contribution towards combatting some of the world's most devastating diseases.

For information on research degree scholarships offered by the Institute for Glycomics, visit: griffith.edu.au/institute-glycomics/study-with-us

For general information on PhDs and other research degrees at Griffith University (including scholarships), visit: griffith.edu.au/research-study/degrees

A selection of Research Projects available at the Institute for Glycomics, including those for summer projects, Honours, Masters and PhDs are listed below. We recommend that you talk to potential institute supervisors to discuss a suitable research project, prior to submitting a scholarship application.

For a full list of projects and contact details of the supervisors, scan the QR code:

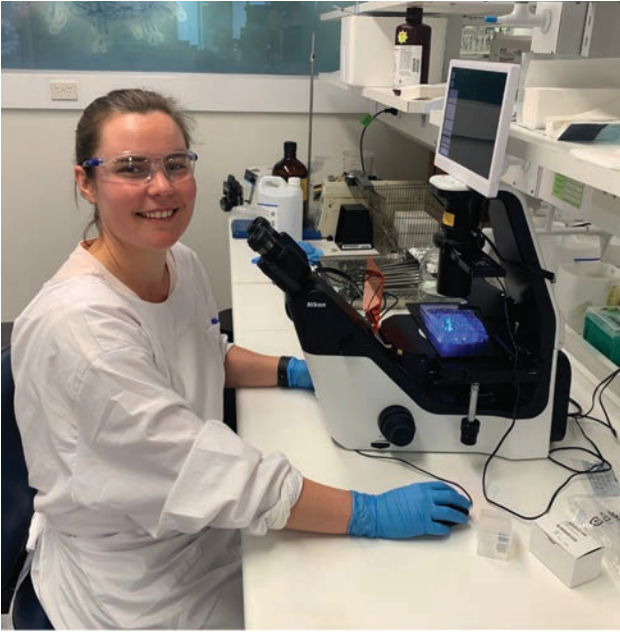


STUDENT EXPERIENCES

Don't just take our word for it...

Annelies Van Den Bergh - PhD student

Annelies works with Professor Mark von Itzstein AO, a world-renowned expert in drug discovery against infectious diseases.



Her research utilises various techniques to understand how the human metapneumovirus (hMPV), a respiratory virus, can bind to human airway cells.

She aims to use her findings to design a drug that is highly potent and with minimal side effects to treat hMPV infections. Annelies says:

“I first came to the Institute for Glycomics in 2017 for my master thesis project in Mark’s group. During this time at the Institute, I became fascinated by the Institute’s research and their cross-disciplinary approach to solve complex problems. After having completed my studies in Belgium, I wanted to join the group in their search for novel antiviral drugs. Now, almost three years into my PhD, I feel very lucky to be a part of the Institute of Glycomics. I have been able to develop my research skills using state-of-the-art facilities while working in an international environment. Additionally, the ongoing translational and commercial projects at the Institute for Glycomics are inspirational and encourage me to pursue a research career.”

Oren Cooper - PhD student

Oren is working with Associate Professor Joe Tiralongo at the Institute for Glycomics on a PhD that focuses on the development of novel micro- and nano-technologies to explore the glyco-interactome.

These biosensors provide researchers with unparalleled sensitivity to explore complex interactions that can be exploited for both biosensing and drug targeting. Oren says:

“I chose to pursue a PhD at the Institute because the facility offers a multi-disciplinary research approach to explore the fascinating world of Glycomics. As a world leader in the development of next generation drugs and diagnostics, the Institute focuses on translational research with real world implications. This fosters a strong scientific community which has helped me to develop valuable skills as a researcher that I will continue to use throughout my scientific career.”



STUDENT EXPERIENCES

Don't just take our word for it...

Winter Okoth - PhD student

Winter is a PhD Student in the Laboratory of Vaccines for the Developing World under the supervision of Dr Danielle Stanisic and Professor Michael Good AO at the Institute for Glycomics.



Winter's project focuses on the development and preclinical evaluation of a whole asexual blood-stage parasite malaria vaccine formulated with cationic liposomes. Winter says:

"Upon completion of my Master of Science degree in the USA, I chose to join Professor Michael Good and his Malaria Research Team in the Laboratory of Vaccines for the Developing World for my PhD studies to further my knowledge on malaria research and novel malaria vaccine development strategies. I was also fascinated by the diverse interdisciplinary research environment, community, network and facilities at the Institute for Glycomics. It has been extremely interesting learning various vaccine research techniques through my studies. My supervisors and colleagues at the Institute have been supportive. Furthermore, at the Institute for Glycomics, HDR students have many different opportunities such as conferences, seminars, scholarships, and industry mentoring which allows them to become well-rounded and develop professionally."

Dr Lucy Shewell's *research journey*

“I have been working as a research scientist at the Institute for Glycomics since November 2009.

I was awarded my PhD from Griffith University in the field of Molecular Microbiology in July 2011.

I also studied my Bachelor of Biomedical Science with Honours at Griffith University.

I knew that the Institute for Glycomics was a leading research institute in the field of glycobiology and was attracting high calibre scientists.

I have witnessed the Institute grow so much over the last 10+ years and this positive growth and the expanding facilities has encouraged me to stay.”



CURRENT RESEARCH PROJECTS

Principal Research Leader | Professor Mark von Itzstein AO

Contact e-mail: m.vonitzstein@griffith.edu.au



From structure to function – rational development of new sialidase inhibitors

Molecular Modelling, Medicinal Chemistry, Biochemistry, Molecular Microbiology, Virology, Structural Biology

Other supervisors | Dr Robin Thomson, Dr Ibrahim El-Deeb, Dr Benjamin Bailly, Dr Patrice Guillon, Dr Larissa Dirr, Dr Xing Yu

Sialidases are involved in the infective cycles of a range of viruses, bacteria, and parasites. These include, for example, the causative agents of influenza, cholera, and African sleeping sickness. The essential roles that the sialidases often play in the infection cycle make them interesting targets for drug design. In the case of influenza virus sialidase, development of potent and selective inhibitors of the enzyme, based on knowledge of the enzyme structure, led to a new drug class to treat influenza. In recent years, new structural and mechanistic characteristics of both microbial sialidases have been discovered, presenting new opportunities for inhibitor design.

The von Itzstein group works on the development of new sialidase inhibitors against pathogenic organisms using a multidisciplinary approach that includes: computational chemistry and structure-based inhibitor

design; synthetic chemistry, working on a range of inhibitor templates; expression and purification of recombinant enzymes; the use of whole virus particles or virus-like particles presenting the enzyme on a non-infectious particle; enzyme assays for evaluation of inhibitor affinity; cell-based evaluation of compounds, and; structural biology studies in solution phase (NMR) or through X-ray crystallography. A student working on this project may specialise in one particular aspect, or be involved with a number of the different interconnected aspects of the project.

Techniques: Computational Chemistry including visualisation and molecular docking; Synthetic carbohydrate chemistry; Protein expression and purification; Virology; Enzyme Assays; Cell-based assays; Advanced NMR techniques including STD-NMR; X-Ray crystallography.

The characterisation of virus binding specificity to host cell receptors

Virology, Structural Biology, Cell Biology

Other supervisors | Dr Benjamin Bailly, Dr Crystal Swarbrick

The hand, foot and mouth disease causing agent enterovirus 71 engages a variety of receptors on the surface of host-cells prior to entry. These receptors include the P-selectin glycoprotein ligand-1 (PSGL-1), the scavenger receptor class B member 2 (SCARB2), glycosaminoglycans (GAG) and sialylated glycans. The interplay between these receptors is still poorly understood. The types of GAGs and sialylated glycans the virus binds to have not been fully investigated, and we believe that given our progress with GAG-like binding inhibitors they may be more important than previously reported. Furthermore, in our experience different cell-types have different susceptibilities to glycan-based

binding inhibitors, suggesting that cell binding events may be more complicated than previously characterised.

This multidisciplinary research project involves the differentiation of various cell types and subsequent functional assays to investigate virus-cell binding events, glycan-array experiments, cell-based chemical combination assays using glycans, competition STD-NMR experiments and crystallography using purified virus particles.

Techniques: Virology; Cell biology; Crystallography; NMR techniques including STD-NMR; Glycan-Array.

Exosomes as cancer biomarkers and therapeutics

Cancer Biology, Biochemistry

Other supervisors | Dr Andrea Maggioni, Dr Arun Everest-Dass

Exosomes are vesicles that are secreted from cells and appear to have roles in the tumour microenvironment, including in metastasis. These vesicles are therefore thought to be invaluable in both a diagnosis setting as well as therapeutic targets. Little is known about the cell surface changes in glycans and glycan-recognition

proteins. This project will explore these changes using a multidisciplinary approach that may identify potential biomarkers and therapeutic targets that could be used in diagnosis and drug discovery, respectively.

Techniques: Cell biology, Biochemistry, Glycoanalytics.

CURRENT RESEARCH PROJECTS

Associate Research Leader | Dr John Atack

Principal Research Leader | Professor Michael Jennings

Contact e-mails: j.atack@griffith.edu.au; m.jennings@griffith.edu.au

Investigating epigenetic gene regulation by phase-variable methyltransferases at the promoter level

Molecular Microbiology; Bacterial Pathogenesis; Genetics

Many host-adapted bacterial pathogens contain phase variable methyltransferases, which control expression of multiple genes, and known as phasevarions (phase variable regulons).

Our studies will investigate the specificity, and the mode of gene regulation through differential methylation by these phase-variable methyltransferases. We will clone and over-express newly identified methyltransferases to determine their recognition sequences.

We have identified a number of genes in both human and animal pathogens that are differentially expressed in several phasevarions: we will investigate how methylation alters regulation of these genes. We will investigate if these genes are regulated directly or indirectly, and determine the effect of removing any recognition sequences from the promoters of these genes.

This project will use protein over-expression and purification methods to allow us to study these methyltransferases *in vitro*.

Surface plasmon resonance will be used to conduct kinetic measurements, and gel-shift assays (EMSA) will be used to study binding affinity and ability. Reporter constructs will be made to observe the effect of methyltransferase phase-variation on the level of expression from individual promoters.



Generation and improvement of an NTHi vaccine

Non-typeable *Haemophilus influenzae* is a major human adapted pathogen, and causes a number of acute and chronic diseases of the human respiratory tract, including middle ear disease, otitis media (OM) in children, exacerbations in chronic obstructive pulmonary disease (COPD) in the elderly, and pneumonias.

Invasive disease (meningitis and septicaemia) caused by NTHi is increasing annually, and is a particular problem in infants under 1 year of age, where the mortality is

close to 20%. Antibiotic resistance is increasing each year, resulting in NTHi being on the World Health Organisation's list of priority pathogens. There is no currently licensed vaccine available for NTHi. Vaccine design is a problem for NTHi as individual strains show high genetic diversity, and many antigenic proteins are phase-variable – their expression is randomly and reversibly switched on or off. If a vaccine target is able to randomly turn off, the vaccine would lose effectiveness.

This project will: 1) determine the best possible combination of conserved protein antigens to include in a universal NTHi vaccine from both current and putative vaccine candidates; 2) study the role and regulation of a number of uncharacterised NTHi proteins that show high sequence and strain conservation; and 3) determine

if known proteins that have been discounted from use in vaccines as they are phase-variable can be used in vaccines as their expression is critical for certain disease stages or colonisation of particular host niches.

Associate Research Leader | Dr John Atack

Contact e-mail: j.atack@griffith.edu.au

*Defining the glycointeractome of the major drug resistant pathogen *Acinetobacter baumannii**

Acinetobacter baumannii is classified by the WHO as a critical top priority pathogen, and is resistant to almost all current antibiotics. This is particularly problematic as there are very few new antibiotics currently in development. The rate at which *A. baumannii* acquires resistance to antibiotics means *A. baumannii* infections may soon become impossible to treat.

A. baumannii is a particular problem in hospitals and aged care units due to its ability to survive harsh environments and cleaning procedures. It is crucial to develop novel treatment methods and therapeutics due to the lack of current new antibiotics in development. Although much is known about *A. baumannii* virulence factors, little is known about the exact host factors *A. baumannii* interacts with during colonisation and disease. Many human adapted pathogens use host glycans (sugars) as to bind to host surfaces and cells.

This project will determine which glycans *A. baumannii* interacts with in the human host, i.e., we will define the *A. baumannii* glycointeractome, by leveraging the innovation of glycan array technology and biophysical approaches to precisely determine the glycans *A. baumannii* interacts with.

We will utilize multiple *in vitro* and *in vivo* models to determine the ability of these glycans and novel compounds to serve as blocking agents for the treatment of MDR *A. baumannii* infections. This will aid in the development of new treatment strategies, and lay the groundwork to develop novel agents to serve as an alternative to, or act in synergy with, existing antibiotics.



CURRENT RESEARCH PROJECTS

Principal Research Leader | Professor Michael Jennings

Associate Research Leader | Dr Christopher Day

Contact e-mails: m.jennings@griffith.edu.au; c.day@griffith.edu.au

Identification of novel carbohydrate binding proteins

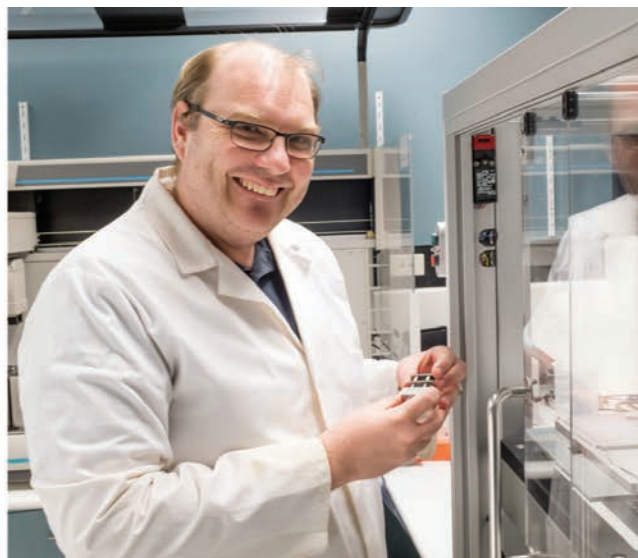
Array Technology; Affinity and Kinetics Measurements

Other supervisors | Dr Jessica Poole

Carbohydrate binding proteins (also known as lectins) are a broad range of proteins with a wide specificity for carbohydrate structures. Recently we have found that a large number of bacterial and eukaryotic proteins have the ability to bind to glycans that had not previously been appreciated. This project will investigate a range of proteins from bacterial and eukaryotic sources for their ability to interact with glycans. This study will utilise the

glycomics arrays that we produce within the Institute for Glycomics as well as studies of affinity and kinetics using surface plasmon resonance (GE Biacore T100) and micro isothermal calorimetry (TA Instruments nanoITC).

Techniques: molecular biology, SPR, affinity and kinetics measurements; cell assays.



Investigation of the glycan binding sites of cholesterol-dependent cytolysins (CDCs)

Molecular Microbiology, Glycobiology

The cholesterol-dependent cytolysins (CDCs) are a family of toxins produced by a number of Gram-positive human pathogens including *Streptococcus*, *Clostridium*, *Listeria*, *Bacillus* and *Gardnerella*. These toxins form pores in cholesterol-containing membranes, hence it was thought that cholesterol was the cellular receptor. We have found that the CDCs bind with high-affinity to glycan targets and that these glycans serve as cellular receptors. This project aims to further investigate the glycan binding of several of the CDCs by using molecular modeling to identify key residues involved in binding

Other supervisors | Dr Lucy Shewell

to the glycan targets. Site-directed mutants of these residues will be generated and analysed using a range of techniques, including surface plasmon resonance (SPR) and cell-based assays, to confirm their role in glycan binding. Identifying key residues of the CDCs involved in glycan binding will provide insight into the function and tropism of these toxins and may assist in the development of inhibitors of these toxins.

Techniques: molecular biology, SPR, affinity and kinetics measurements; cell assays.

Investigation of Neu5Gc tumour antigens in cancer

Glycobiology, Biochemistry, Biophysics, Cancer Biology

Other supervisors | Dr Lucy Shewell

Approximately half or more of all human proteins carry a carbohydrate moiety through the process of glycosylation and it is well established that one of the universal features of cancer cells is aberrant glycosylation. The changes in glycosylation that occur in cancer cells include loss of expression or excessive expression of certain glycans (carbohydrates attached to proteins or lipids), increased expression of incomplete or truncated glycans, and the appearance of novel glycans. Glycoproteins, therefore, make ideal cancer biomarkers because these molecules are secreted or shed into the circulation from tissues or blood cells allowing them to be detected in the serum. Glycans terminating with the sialic acid Neu5Gc are not expressed at significant levels on healthy human tissues, because humans express an inactive cytidine monophosphate *N*-acetylneuraminic acid (Neu5Ac) hydroxylase (CMAH) enzyme, and thus cannot synthesize Neu5Gc. Nevertheless, Neu5Gc-containing glycans are found in human tumour tissues, tumour cells and tumour secretions, and have been proposed as a tumour biomarker.

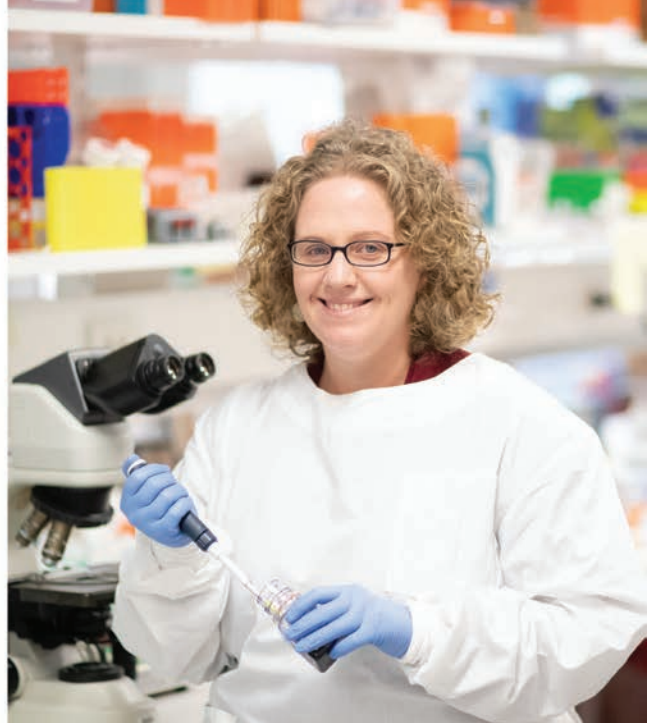
The Shiga toxigenic *Escherichia coli* (STEC) Subtilase cytotoxin (SubAB) recognizes α 2-3 linked Neu5Gc via its pentameric B-subunit SubB. We purpose-engineered the SubB protein to increase specificity and selectivity for Neu5Gc containing glycans and have demonstrated that this mutant protein, termed SubB2M, recognizes Neu5Gc glycans exclusively and is able to detect Neu5Gc-enriched serum glycoproteins. We showed that SubB2M can detect elevated levels of Neu5Gc in serum samples from patients at all stages of ovarian cancer using only very small volumes of serum ($\sim 1\mu\text{l}$) via surface plasmon resonance (SPR). SPR is a biophysical technique for measuring the binding of molecules in real-time without the use of labels. This project will investigate whether serum Neu5Gc levels are elevated in patients with other types of cancers compared to normal controls using a SubB2M-SPR assay. This project will also attempt to discover and characterize Neu5Gc-containing cancer biomarkers.

Techniques: SPR, affinity purification, protein gel electrophoresis, western blotting.

CURRENT RESEARCH PROJECTS

Principal Research Leader | Professor Michael Good AO
Associate Research Leader | Dr Danielle Stanisic

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Pre-clinical development of a whole parasite liposomal vaccine approach to prevent babesiosis

Parasitology, Immunology, Vaccinology

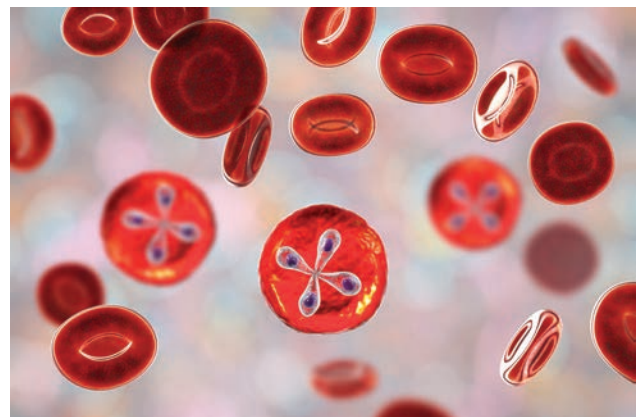
Babesiosis is a tick-borne infectious disease, caused by parasites of the genus *Babesia*. Human babesiosis is typically asymptomatic, or results in mild symptoms that resolve within a few days in healthy individuals. However, *Babesia* infection in the very young, the elderly, splenectomized, and immunocompromised individuals can result in acute anemia, multi-organ failure, or death. There is currently no human vaccine available, with prevention strategies focused on controlling the tick vector. *Babesia* parasites also infect cattle, with bovine babesiosis (or cattle tick fever) having a major economic impact on the livestock industry in South America, Africa, Asia and Australia. The currently used live attenuated cattle vaccine has a number of major drawbacks.

We have previously shown that a whole blood-stage parasite liposomal malaria vaccine is able to induce protective immunity in rodent models of the related Apicomplexan parasite, *Plasmodium*. This vaccine approach has been shown to induce a broad protective immunity. We have recently applied this same approach to the development of a *Babesia* vaccine, using a rodent model of *B. microti*. Further work is required to optimise the vaccine formulation to both maximise protective efficacy and to enable the development of a product that is compatible with administration to humans and

cattle. In this project, different vaccine candidates will be generated containing the whole *Babesia* parasite. For some vaccine candidates, recombinant proteins/peptides derived from the parasite will also be included.

Pre-clinical development of these vaccine candidates will include characterisation, optimisation and evaluation of the vaccine formulations.

Techniques: Parasitology, Vaccinology, Real-Time PCR, Cellular and Humoral Immunology (including Cell Culture, ELISA, Flow Cytometry and Cytokine Analyses).



Development and evaluation of a controlled malaria infection immunization approach for the development of a malaria vaccine

Parasitology, Immunology, Vaccinology, Drug Discovery

Malaria is a parasitic disease prevalent in many developing countries, with transmission reported in 90 countries. It is associated with extensive morbidity and mortality, mainly in pregnant women and young children. Currently available control strategies are becoming increasingly less effective; therefore the development of an effective vaccine is considered to be of critical importance. Many researchers have focused on single parasite-derived proteins in their quest to develop a sub-unit vaccine against malaria. However, many of these proteins are highly variable, and are not useful in eliciting responses that can protect against multiple strains of the parasite. A vaccine approach that uses the whole malaria parasite however, would contain multiple parasite antigens including antigens that are not altered by the parasite i.e. are therefore conserved between different parasite strains.

Using rodent models of malaria, it has previously been shown that different whole parasite asexual blood-stage vaccine approaches are able to induce species and strain-transcending protective immune responses. One such approach is controlled infection immunization (CII). This involves administering a malaria infection at the same time as anti-malarial treatment is commenced. So far, these immunization regimens have required either

multiple days of anti-malarial treatment (which is not viable for a vaccine strategy) or a single large dose of drug that is not currently clinically indicated in humans and may not be tolerated. This may be overcome by using alternative anti-malarial drugs in the context of CII or by the use of slow release drug formulations

This project will involve further pre-clinical development and evaluation of the CII approach. Using rodent models of malaria, pre-clinical development will initially involve characterising and optimising different anti-malarial drug formulations in the context of CII. Their ability to control parasite growth will be examined. If required, slow release drug formulations may be developed. The optimal drug formulations and parasite combinations will be evaluated for their ability to induce protection against subsequent challenge infection. Immunological and functional assays will be used to assess immunogenicity and to examine the immune mechanisms of protection. Results from this project will inform the transition of this vaccine approach into clinical studies.

Techniques: Parasitology, Vaccinology, Real-Time PCR, Cellular and Humoral Immunology (including Cell Culture, ELISA, Flow Cytometry and Cytokine Analyses).

Development and pre-clinical evaluation of a transmission-blocking liposomal malaria vaccine

Parasitology, Immunology, Vaccinology

Malaria is a global public health problem with transmission still being reported in over 90 countries. It is an infectious disease caused by *Plasmodium* parasites which are transmitted by female Anopheline mosquitoes. Current control methods are becoming increasingly less effective, therefore the development of an effective vaccine is considered to be of critical importance. The majority of malaria vaccine candidates are based on single malaria proteins, but many of these are highly variable and are not useful in inducing immune responses that will protect against multiple strains of the malaria parasite. An alternate approach currently being developed, involves using the whole malaria parasite – such a vaccine contains multiple parasite proteins including those that are conserved between different parasite strains.

This study will involve the pre-clinical investigation of a *Plasmodium falciparum* transmission blocking liposomal vaccine. This vaccine type does not prevent an individual from being infected like an asexual blood-stage vaccine aims to do, but rather stops an infected individual from transmitting malaria to other individuals. This is because it targets the parasite life-cycle stage that is infective

to mosquitoes. It is thus seen as a community-based vaccine approach.

In this project, different vaccine candidates will be generated containing the *P. falciparum* gametocyte-stage parasite; this is the life-cycle stage that is found in the blood of malaria-infected individuals and is infective to mosquitoes. For some vaccine candidates, recombinant proteins/peptides derived from the gamete-stage of the parasite, which is the stage of the parasite within the mosquito, will also be included. Pre-clinical development of these vaccine candidates will include characterisation and optimisation of the vaccine formulations. Immunological and functional assays will also be undertaken to characterise the immunogenicity and transmission-blocking activity of the single and multi-component vaccine candidates ie whether the induced immune response impacts on parasite development and/or survival in the mosquito host.

Techniques: Parasitology, Vaccinology, Cellular and Humoral Immunology (including Cell Culture, ELISA, Flow Cytometry and Cytokine Analyses).

CURRENT RESEARCH PROJECTS

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Developing novel peptide-based vaccines for infectious diseases including COVID-19 and rheumatic heart disease

Molecular Immunology and Vaccinology (MIV)

Infectious diseases account for over 17 million deaths per year. Globally, as of August 2021, there have been over 205 million confirmed cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and over 5 million deaths. SARS-CoV-2 is the causal agent of Coronavirus Disease 2019 (COVID-19). A protein called the Spike (S) protein is attached to the viral surface. The interaction between the S protein and a receptor present on human lung cells (angiotensin converting enzyme 2 receptor; ACE2 receptor) initiates viral entry into human cells. There are a total of 8 SARS-CoV-2 vaccines approved for full human use. These vaccines have high efficacy rates against current SARS-CoV-2 strains; however, their efficacy may be compromised against mutant strains.

Another significant pathogen, *Streptococcus pyogenes* is a Gram-positive bacterium that causes multiple diseases. *S. pyogenes* primarily infects the upper respiratory tract (URT) and the skin. If left untreated, invasive (necrotising fasciitis and streptococcal toxic shock syndrome) and post streptococcal sequelae of diseases (rheumatic fever and rheumatic heart disease) can follow. *S. pyogenes* infections and their sequelae are responsible for more than 500,000 deaths each year. Despite the burden of disease, a vaccine is not yet available. Ideally, a vaccine against SARS-CoV-2 and *S. pyogenes* should be immunogenic and protective at the primary sites of infection and against all strains of the infectious agent. Our laboratory focuses on two main elements of vaccine

Other supervisors | Dr Victoria Ozberk

design and development. These include (i) peptide (immunostimulatory) antigens and (ii) vaccine delivery systems. We have identified highly efficacious peptide antigens for use in vaccines against *S. pyogenes*. These peptide antigens, conjugated to a carrier molecule such as diphtheria toxoid (DT) have been tested with various vaccine delivery/adjuvant systems such as Aluminium hydroxide for intramuscular delivery or liposomal platforms for mucosal delivery. Two vaccine combinations for *S. pyogenes* are now being prepared to enter a Phase I Clinical trial. In parallel, using murine models, immunological and molecular biology investigations will continue to unravel mechanism of vaccine mediated strain transcending immunity. Using our expertise in designing peptide vaccines, we are working towards the rapid development of a vaccine against SARS-CoV-2. We have identified peptide antigens from the receptor binding domain (RBD) of the Spike protein and demonstrated their potential as a vaccine candidate. We will now combine these peptide antigens with various vaccine delivery systems to develop a vaccine that is protective at the primary site of infection (URT) and against upcoming viral mutants of concern. Success with this project will lead to the development of vaccines which will have real world impact.

Techniques: ELISA, flow cytometry, SDS-PAGE, MCS-conjugation, in vitro neutralisation assay, cell culture, liposome formulation, in-vivo techniques such as vaccination and sample collection.

Developing an immunotherapy to treat invasive *Streptococcus pyogenes* infection

Bacteriology and Immunology

Seemingly mild streptococcal infections can rapidly escalate to serious invasive infections with a high mortality rate. The overall incidence for invasive *Streptococcus pyogenes* disease (ISD) was reported to vary between 2–4 per 100,000 people in developed countries, although in some developed countries, a marked rise in the incidence of ISD has been reported. In developing countries, very high rates are reported amongst the young and the elderly (up to 75 per 100,000) (Steer et al, 2012). In approximately 20% of cases, ISD is accompanied by a streptococcal toxic shock syndrome (STSS) with multi-organ failure and case fatality rates approaching 50% even in the best-equipped facilities. It can occur after any streptococcal infection but most commonly occurs after infections of the skin and is usually associated with necrotising fasciitis, myositis or deep bruising.

Streptococcal ‘superantigens’ (SAGs) are thought to play the key role in the pathogenesis of STSS (Proft and Fraser, 2016). However, we have recently demonstrated that the M protein also plays a critical role in the pathogenesis of STSS (M. Pandey et al, 2019). We have

Other supervisors | Dr Victoria Ozberk

developed a model for STSS using HLA-humanized mice and showed that these mice became gravely ill when infected with a SpeC+ (a streptococcal superantigen) positive *S. pyogenes* organism that caused STSS in human patients. The project will utilise humanised mice to model STSS caused by SpeA+ organisms and will examine critical roles for both the M protein and SpeA in pathogenesis. It will further assess whether vaccination with our lead vaccine candidate (J8/p*17) can prevent disease and whether passive immunotherapy can rapidly ablate the mitogenic and inflammatory activity of SpeA+ *S. pyogenes* organisms, and clear infection. The project will further advance to test combination therapy utilising monoclonal antibody to J8/p*17 and antibiotics with a view to reduce repeated antibiotic administration and thus antibiotic resistance. Success with this project could quickly lead to novel therapies to treat STSS.

Techniques: Culturing of bacteria, mouse infection model, PCR, Enzyme Linked Immunosorbent Assays (ELISA), *in-vitro* cell culture assays, *in-vivo* techniques such as bacteria challenge, vaccination and sample collection.

Modelling development of naturally acquired immunity to *S. pyogenes* to decipher protective immune mechanisms to aid vaccine design

Bacteriology, Immunology, Vaccinology

Streptococcus pyogenes is a Gram-positive bacterial pathogen of humans. It causes a broad spectrum of diseases ranging from self-limiting throat and skin infections to life-threatening streptococcal toxic shock syndrome and rheumatic heart disease. Altogether, these infections result in over 500,000 deaths annually. Naturally acquired immunity to *S. pyogenes* takes several years to develop and its slow acquisition has been attributed specific virulence factors impeding innate immunity and significant antigenic diversity of the type-specific M protein, hindering acquired immunity. There are known to be in excess of 250 different M types and limited evidence suggest that M-type-specific immunity can protect in a type-specific manner. This also poses a significant hinderance to vaccine development, as an effective vaccine will need to protect against most, if not all, existing *S. pyogenes* serotypes. In addition, it is yet to be defined if a single vaccine will protect against both skin and mucosal infections which are the primary infection sites.

To understand protective immune mechanisms against *S. pyogenes* infection, this project will investigate immune responses following natural infection and/or vaccination in mice and humans. *S. pyogenes* can infect via skin or mucosa and it is not clear whether infection at one site would induce immunity to protect at another site. Therefore, understanding the mechanisms of cross-

compartment immunity i.e. skin infection protecting against mucosal infection and vice-versa, is critical. These investigations will tease apart the role of specific immune cell populations contributing towards protective immunity against multiple serotypes as well as at various infection sites. Deciphering immune mechanisms involved in site-specific and cross-compartment immunity will have significant implications for vaccine designs and vaccination strategies.

Techniques: Culturing of bacteria, mouse infection models, PCR, Enzyme Linked Immunosorbent Assays (ELISA), *in-vitro* bacterial and cell culture assays, flow cytometry, *in-vivo* techniques such as bacteria challenge, vaccination and sample collection.



CURRENT RESEARCH PROJECTS

Research Leader | Professor Johnson Mak

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Pseudotyped virus-like-particles as platform for vaccine development

Other supervisors | Dr Belinda de Villiers

Pseudotyped virus-like-particles (VLPs) are non-infectious, nano-scale biological materials that can be used for vaccination purposes. VLPs have benefited from the evolutionary processes that impart exceptional efficiency to deliver the payload to animal hosts, thereby eliciting strong immune responses. Our laboratory uses two types of VLP systems for evaluation, which include: (i) lentiviral vector (LV) system; and (ii) vesicular stomatitis viral (VSV) vector system. Both systems have proven successful in clinical settings, including the use of LV system in gene therapy and CART cell therapy; and the use of VSV system as an Ebola vaccine.

Our lab explores the potential of using these two systems to develop effective vaccines against viral pathogens. Some of the viral pathogens being evaluated using these systems include HIV, SARS-CoV-2, and African Swine Fever Virus (ASFV). This work requires: molecular virology-based approaches to produce VLPs via tissue culture; biochemical and biophysical evaluation to dissect mechanism; imaging analyses to track the movement of VLPs; structural biology and glycan biology to refine the design of our system; and preclinical animal work to determine the effectiveness of some of these specific vaccine designs. This project has both PC2 and PC3 components, and they complement each other. The



PC3 component is reserved to PhD students and post-doctoral fellows, in which live infectious materials or PC3 related genetic modified organisms will be used.

The successful applicant will be part of a larger research team to work on aspect(s) of the project that are based on: (i) practicality; (ii) project objective; plus (iii) mutual research interest between the appointee and the host lab.

Techniques: Virology, Biochemistry, Biophysics, Molecular Biology, Structural Biology, Glycan Biology, Animal Works.

Mechanisms of assembly and entry of viruses that enhance virus transmission

Other supervisors | Dr Belinda de Villiers

Viruses are 'obligate parasites' that completely rely on their hosts to propagate. The constant navigation and exploitation of their hosts have allowed viruses to hijack (and to adopt) selected aspects of these host cell systems to facilitate effective virus transmission. These events include: (i) utilising directional trafficking of viral proteins during virus formation to maximise efficiency of cell-cell transmission; and (ii) incorporating glycan-shield on virus surface to block the anti-viral immune response and/or to mediate virus attachment during progeny virus infection. Our lab investigates the directional trafficking and release of viral particles using retrovirus systems, including HIV, Koala retrovirus (KoRV), and Human T-cell-leukemia virus. We also use viral proteins from a wide range of enveloped viruses to study the glycan biology of viral proteins, such as HIV, KoRV, SARS-CoV-2, ASFV, influenza and respiratory syncytia virus (RSV). This work requires: molecular virology-based approaches to produce viruses via tissue culture; biochemical and biophysical evaluation to dissect mechanism; imaging

analyses to delineate directional trafficking; structural and glycan biology to reveal molecular interactions. This project has both PC2 and PC3 components, and they complement each other. The PC3 component is reserved to PhD students and post-doctoral fellows, in which live infectious materials or PC3 related genetic modified organisms will be used.

The successful applicant will be part of a larger research team to work on aspect(s) of the project that are based on: (i) practicality; (ii) project objective; plus (iii) mutual research interest between the appointee and the host lab.

Techniques: Virology, Biochemistry, Biophysics, Cell Biology, Molecular Biology, Glycan Biology, Structural Biology.

Mobile device compatible rapid diagnostics suitable for remote settings

Other supervisors | Dr Belinda de Villiers

Accurate and rapid diagnostic assays are critical in controlling the spread of infection events. The current COVID-19 pandemic highlights a major shortcoming of the gold-standard, lab-based, quantitative polymerase chain reaction (qPCR) diagnostics in an evolving-crisis situation. The relative lengthy turn-around time of qPCR plus the requirement of trained staff and high-end equipment in diagnostic processes are the bottlenecks for clinical assessments of patients (subjects) in remote settings. These practical challenges are further amplified in low- to middle-income countries where highly trained staff and pricy infrastructure are often in short supply. Our laboratory is trying to address this technological gap by developing rapid point of care diagnostics, which include the evaluation and development of loop-mediated isothermal amplification (LAMP) and CRISPR-based diagnostics. We are focusing our work on HTLV-1 and ASFV, which have a major impact on the health of our indigenous people within Central Australia and the global pig farming industry respectively.

This work requires: molecular biology-based approaches to design and to refine our detection system; molecular virology techniques to generate relevant samples for evaluation; biochemical assessment to evaluate detection system; pre-clinical evaluation of diagnostic system using precious clinical samples. This project has both PC2 and PC3 components, and they complement each other. The PC3 component is reserved to PhD students and post-doctoral fellows, in which live infectious materials or PC3 related genetic modified organisms will be used.

The successful applicant will be part of a larger research team to work on aspect(s) of the project that are based on: (i) practicality; (ii) project objective; plus (iii) mutual research interest between the appointee and the host lab.

Techniques: Virology, Biochemistry, Biophysics, Molecular Biology, Clinical Integration.

CURRENT RESEARCH PROJECTS

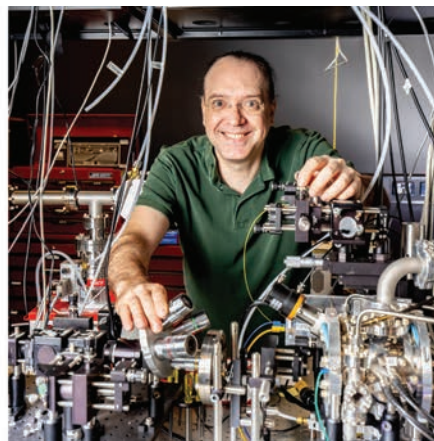
Research Leader | Associate Professor Erik Streed

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Levitating yeast cells in an ion trap

Biophysics

Other supervisors | Associate Professor Joe Tiralongo



Techniques from physics have often been adapted to solve problems in the life sciences. Notable examples include microscopy, x-ray diffraction, and fluorescent labelling.

We are interested in developing new ways to investigate the properties of cells, subcellular structures, and large biomolecules using ion trapping techniques from quantum physics.

Project students will be involved in a subset of the

following project aspects: culturing and fluorescent labelling of yeast cells, loading yeast cells into an ion trap, and then measuring the physical properties & manipulating the cell using electrical, hydrodynamic, and laser methods.

There are also projects available on mathematical modelling of the particles. Physics or Biological laboratory course experience preferred for in-lab components.

CURRENT RESEARCH PROJECTS

Research Leader | Professor Kate Seib

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Does a licensed meningococcal vaccine protect against Neisseria gonorrhoeae?

Molecular Biology, Microbiology, Vaccine Development, Immunology

Other supervisors | Dr Evgeny Semchenko & Dr Taha

There are >100 million cases of gonorrhoea per year, and infection can cause severe sequelae including pelvic inflammatory disease, adverse pregnancy outcomes, neonatal complications, infertility, and increased risk of HIV. Gonorrhoea disproportionately impacts women, particularly in the developing world, and has been recognised by the World Health Organization (WHO), USA Centers for Disease Control (CDC), and Australian National Antimicrobial Resistance Strategy as an urgent threat to global health. There is currently no gonococcal vaccine, and due to multidrug resistance there are concerns that *N. gonorrhoeae* may become untreatable in the near future.

A recent retrospective case-control study found that individuals vaccinated with the meningococcal

serogroup B (MenB) outer membrane vesicle (OMV) vaccine MeNZB were significantly less likely to contract gonorrhoea compared with unvaccinated controls. We have shown that a newer MenB vaccine, induced antibodies in humans that are cross-reactive with *N. gonorrhoeae*. A randomised control trial is now underway to test the efficacy of 4CMenB against gonorrhoea. Human serum samples from this trial will be assessed to understand the vaccine-induced immune response and determine whether antibodies raised to 4CMenB can kill *N. gonorrhoeae* or block its adherence to host epithelial cells.

Techniques: Cloning, protein expression and purification, Western analysis, ELISA, serum bactericidal assays, cell adherence assays, opsonophagocytosis assays.

Vaccine development for Neisseria gonorrhoeae

Molecular Biology, Microbiology, Vaccine Development

Other supervisors | Dr Evgeny Semchenko & Dr Taha

Neisseria gonorrhoeae, the causative agent of gonorrhoea, is a significant health problem worldwide. The control of gonorrhoea depends on the development of a vaccine due to the continuing increase of antibiotic resistance and the staggering outcomes of infection, including infertility and increased transmission of HIV.

This project aims to characterise potential vaccine candidates to aid in the development of a gonococcal vaccine. The distribution of the identified vaccine candidates will be investigated in a diverse range of *N. gonorrhoeae* strains. The functions of candidates will be examined by generating a mutant strain of *N. gonorrhoeae* that does not express the vaccine candidate, and comparing the wild type and mutant

strains in a panel of antimicrobial stress assays. The vaccine potential of these candidates will be assessed by expressing and purifying the protein from *Escherichia coli*, immunising mice to generate antibodies to the protein, and then testing the ability of these antibodies to mediate killing of *N. gonorrhoeae* in various assays (e.g., serum bactericidal assays and neutrophil opsonophagocytic assays to measure killing of the bacteria; adherence assays to test if the antibodies can inhibit association and invasion of human epithelial cells).

Techniques: Cloning, protein expression and purification, construction of gene deletions in *N. gonorrhoeae*, Western analysis, ELISA, serum bactericidal assays, cell adherence assays, opsonophagocytosis assays.

Characterising the role of sugars in host-pathogen interactions

Microbiology, Glycobiology, Molecular Biology

Other supervisors | Dr Evgeny Semchenko & Dr Taha

Human mucosal surfaces, such as the airway, contain a range of carbohydrate structures (glycans) and many bacteria have evolved carbohydrate-binding proteins (lectins) that enable cell attachment, colonisation and invasion of host cells. Our aim is to identify glycans that host-adapted bacterial pathogens bind to during colonisation and disease.

This project will focus on bacteria including *Moraxella catarrhalis* (causes middle ear infections and exacerbations of chronic obstructive pulmonary disease), *Neisseria gonorrhoeae* (causes gonorrhoea) and *Neisseria meningitidis* (causes sepsis and meningitis). We will probe Glycan Arrays (consisting of >400 sugars immobilised onto glass-slides) using recombinant proteins and wild type bacteria and a series of mutant strains lacking key

outer membrane structures. The affinity and kinetics of interactions will be investigated using surface plasmon resonance. We will also use epithelial cell adherence and invasion assays to investigate the functional role of glycan-based host-pathogen interactions. These findings will contribute to understanding key bacterial and host factors involved in colonisation and disease, and may direct development of new drugs and vaccines for these bacteria.

Techniques: Cloning, protein expression and purification, construction of gene deletions in bacteria, array technology, surface plasmon resonance, cell adherence assays.

CURRENT RESEARCH PROJECTS

Research Leader | Professor Victoria Korolik

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Understanding the role of chemosensory perception in pathogenicity of Campylobacter jejuni

Molecular Microbiology

The natural habitat of campylobacters is the intestine of warm-blooded animals, and therefore chemotactic motility is an important mechanism involved in the colonisation and pathogenicity of this microorganism. Bacterial motility is subject to sensory control mechanisms that introduce a bias into the swimming direction of the organism towards beneficial environments and away from unfavourable conditions. Although chemotaxis has been demonstrated for *Campylobacter* the chemical substrates, mechanisms involved in the sensory control of motility and the role of chemotaxis in disease, are poorly understood. We, therefore hypothesise that the chemosensory receptor proteins play a key role in chemotaxis and are involved in the pathogenicity of this organism as the first line of bacterial – host interaction and thus provide rational targets for the design of novel antimicrobial agents.

This project involves characterisation of interactions of one of the chemoreceptors of *C. jejuni*, named Tlp7 with environmental molecules. The major aim of this project is to identify which chemicals are responsible for triggering chemotactic responses governed by Tlp7. This will be determined using site-specific mutagenesis followed by analysis of the wild type and mutated proteins using small molecule and glycan arrays, chemotaxis assays and mammalian cell culture.

Other supervisors | Dr Bassam Elgamoudi

This project will further the studies to elucidate the role of Tlp7 chemoreceptor in chemotaxis and pathogenicity of *C. jejuni*, which can potentially provide a tremendous insight into the mechanisms of chemotaxis of this organism.



Understanding the role of multifunctional periplasmic proteins in bacterial sensory perception

Molecular Microbiology

Other supervisors | Dr Bassam Elgamoudi

The natural habitat of campylobacters is the intestine of warm-blooded animals, and therefore chemotactic motility is an important mechanism involved in the colonisation and pathogenicity of this microorganism. Bacterial motility is subject to sensory control mechanisms that introduce a bias into the swimming direction of the organism towards beneficial environments and away from unfavourable conditions. Although chemotaxis has been demonstrated for *Campylobacter* the chemical substrates, mechanisms involved in the sensory control of motility and the role of chemotaxis in disease, are poorly understood. We therefore hypothesise that the chemosensory receptor proteins play a key role in chemotaxis and are involved in the pathogenicity of this organism as the first line of bacterial – host interaction and thus provide rational targets for the design of novel antimicrobial agents.

This project involves characterisation of interactions of the chemoreceptors of *C. jejuni*, named Tlps, with periplasmic ligand-binding proteins. The major aim of this project is to identify how periplasmic ligand binding proteins induce directed bacterial motility to nutrients and host targets through small molecule arrays, chemotaxis assays, systematic mutagenesis followed by analysis of the mutated proteins using yeast 2-hybrid protein-protein interaction system, mammalian cell culture and animal models.

This project will further the studies to elucidate the role of chemosensors in chemotaxis and pathogenicity of *C. jejuni*, which can potentially provide a tremendous insight into the mechanisms of chemotaxis of this organism.

*Role of multispecies biofilms in transmission of bacterial pathogen *Campylobacter jejuni**

Molecular Microbiology

Other supervisors | Dr Bassam Elgamoudi

Biofilms and complex multi-species communities are a preferred manner by which bacteria exist within the host or grow on various surfaces. In this mode, the cells exude gelatinous exopolymeric substances that are mostly polysaccharides, proteins and DNA.

Progressively, a structured biofilm matrix or a gel, consisting of cells and exuded elements, is formed in which cells are protected from physical trauma, immune clearance mechanisms, desiccation and antimicrobial agents. In nature, most biofilms are complex and are formed by many different microbes in a multi-species community. *Campylobacter jejuni*, a ubiquitous pathogen, is known to be associated with complex gel and surface biofilms, and is an ideal model for studies of naturally occurring multi-species biofilms. *C. jejuni* is recognised as one of the most important human food-borne pathogens to date, and is the leading cause of acute human bacterial gastroenteritis worldwide. *C. jejuni* survives in foods, animal products and aquatic environments.

We hypothesise that it does so by integration into complex microbial communities and biofilms. The formation of complex multi-species communities involving *C. jejuni*, and their role in transmission of infection, are poorly understood.

We aim to use a comprehensive, biologically valid multidisciplinary approach to quantify the composition, both microbial and host-related, of naturally occurring complex communities involving *C. jejuni*. We will use transcriptome and mass spectroscopy analysis with wild type and mutated *C. jejuni* strains contained in chicken caeca and in laboratory created biofilms. This will allow us to understand how this pathogen integrates into complex microbial communities and biofilms, how to break the chain of transmission of *C. jejuni* from animals and animal food sources, how to reduce incidence of campylobacteriosis in human population, and ultimately, how to develop novel strategies for biological intervention in disease transmission to humans.



CURRENT RESEARCH PROJECTS

Research Leader | Associate Professor Thomas Haselhorst

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Novel antibody-independent targeted therapy for the treatment of B cell Lymphomas

Medicinal Chemistry, Structural Biology, NMR Spectroscopy, Cell Culture

Other supervisors | Dr Santosh Rudrawar

Lymphoma is the most common lymphoid malignancy and is among the 10th most prevalent cancers worldwide. Non-Hodgkin's Lymphoma (NHL) accounts for 80–85% of all lymphomas, including the common B-cell NHLs (B-NHLs). Current standard of care for relapsed/refractory NHLs are anthracyclines that are associated with cumulative cardiotoxicity with limited repeated clinical use. Rituximab-based therapy relies on complement and antibody dependent cell-mediated cytotoxicity to effect cell killing and is associated with severe side effects and in some cases form tumour lysis syndrome. This PhD project aims to develop novel

therapies with an alternative mechanism for B cell killing and improved outcome by synthesising novel carbohydrate-based ligands and conjugating ligands to toxin-loaded liposomes.

Techniques: Synthetic carbohydrate chemistry; Lipid and peptide chemistry, Medicinal chemistry, Cell biology, Cell culture, Computational Chemistry including visualisation and molecular docking, NMR spectroscopy, drug discovery and design.

Novel agents for antifungal drug development

Structural Biology, Computational Chemistry, Microbiology, Cell Culture, Molecular Biology, NMR Spectroscopy

Other supervisors | Associate Professor Joe Tiralongo

The opportunistic human pathogenic fungus *Aspergillus fumigatus* causes severe systemic infections including Invasive Aspergillosis (IA), a major cause of life-threatening fungal infections in immuno-compromised patients.

An overwhelming number of reports appeared in 2020 demonstrating that COVID-19-associated pulmonary Aspergillosis (CAPA) is one of the leading factor affecting morbidity in critically ill COVID-19 patients [2] with some reports even classifying Aspergillosis as a significantly under-recognized 'Superinfection' in COVID-19.

Drug resistance among fungal pathogens is continuing to develop into an increasingly serious threat to public health and health-care systems worldwide. This PhD projects entails the development of novel antifungal therapies that are urgently needed using our established and unique combined in-silico/SPR drug discovery pipeline evaluating a number of new protein targets.

Techniques: Computational Chemistry including visualisation and molecular docking, in-silico screening, microbiology, protein expression, drug discovery and design.

Development of novel non-antibiotic strategies to ensure food safety in Australia

Structural Biology, Computational Chemistry, NMR Spectroscopy, Microbiology

Other supervisors | Dr Chris Day

The decade long overuse of antibiotics in poultry agriculture and consequently the transferral of antibiotic resistance to humans and the associated health problems underlines the urgent need for novel antibiotic-independent strategies, such as feed supplements (prebiotics) that augment commercial poultry performance and provide food safety.

This PhD project aims to develop prebiotic treatment options to reduce the colonisation of *Campylobacter jejuni* in the chicken intestinal tract. Structural and biophysical investigations of glycan-glycan interactions

followed by monitoring the bacterial load in chickens and potential cross-contamination into chicken will form the main part of the thesis. Expected outcomes will be the development of a potentially commercially viable non-antibiotic treatment option for poultry farmers in Australia.

Techniques: Structural investigations on Glycans in solution with NMR spectroscopy, biophysical methods and molecular modelling, developing of a virtual glycan array approach, monitoring *Campylobacter* bacterial strains.

CURRENT RESEARCH PROJECTS

Research Leader | Dr Ian Peak

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Host immune responses to bacterial signaling molecules

Molecular Microbiology, Molecular Biology

**Other supervisors | Dr Chris Day,
Professor Michael Jennings**

The immune system responds to infections after it has recognised infectious agents. All bacteria secrete products, and some of these have profound effects on the host immune system, either acting as recognition molecules for immune attack, or by modifying the immune response to assist the microbe to survive. We are investigating how secreted molecules from pathogenic bacteria are detected. We are characterising host receptors for these secreted products, which will help understand diseases such as cholera, legionnaire's disease, as well as infections caused by *Pseudomonas* in burned, and cystic fibrosis patients.



Techniques: Molecular genetics techniques, immunofluorescence microscopy, protein expression and purification, FACS analysis, cell culture and *in vitro* infections, *in vivo* infections using mouse models of disease, analyzing immune markers such as cytokine and chemokine responses of the host cell, small molecule purification and analysis by Mass Spectrometry and other techniques.

Improving delivery of antimicrobials across biological barriers

Cell Biology, Microbiology, Medicinal Chemistry

Other supervisors | Dr Matt Zunk, Associate Professor Gary Grant, Professor Vicky Avery

Antimicrobial resistance is an increasingly urgent challenge to human health, with a growing number of multidrug resistant (MDR) and extensively resistant (XDR) species. Several antimicrobials considered "last resort" can only be delivered intravenously, as they do not easily cross from the gut into the blood stream if taken orally. However, long term use of intravenous antimicrobials causes higher rates of complications, resulting in more deaths, and contributes to emergence of further resistance. Our approach for improved delivery is to temporarily improve the permeability of the gut, using "permeation enhancer" compounds: by making the gut temporarily more permeable, the oral delivery of "last resort" antimicrobials can be improved.

This multidisciplinary project includes leaders from across Griffith. You can develop skills in one or more of the following: chemical synthesis of the novel permeation enhancer molecules: cell biology and analysis of mucosal cell permeability: analyse delivery & antimicrobial effect on resistant bacteria; high throughput image analysis. In the future, we will collaborate with other Glycomics investigators who are developing novel antimicrobials, and we will investigate using the permeation enhancers to target other diseases such as neurological conditions, and cancers.

Techniques Cell biology; Synthetic chemistry; Hi-content image analysis microscopy.

CURRENT RESEARCH PROJECTS

Research Leader | Associate Professor Daniel Kolarich

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The role of glycosylation in transmission of zoonotic diseases

Glycomics, Glycoproteomics, Infection, Evolution, Zoonotic Disease

Other supervisors | Dr Chris Day, Associate Professor Joe Tiralongo, Dr Alison Peel

Animals such as bats are considered prime hosts for zoonotic diseases before they “jump” to humans. Viruses such as influenza or COVID-19 are known to infect different host species, where they can gain novel functions and increase their virulence.

The cell surface of mucosal barriers in the respiratory tract plays a fundamental role in this interplay. This cell surface, but also any body fluid proteins are extensively modified with species specific sugars called glycans. These glycans build a universal language used by cells but also abused by pathogens. Though eukaryotic organisms share one alphabet, evolution made them speak multiple different languages and dialects. We have developed glycomics & glycoproteomics tools to translate these languages and uncover how pathogens learned to speak and interpret glyco-languages between different species. Understanding this relationship is crucial as viral, bacterial and parasite pathogens have developed elaborate strategies to jump between hosts – and many of these strategies involve cell surface glycans. The influenza virus is just one fairly well understood example that uses this strategy.

As part of this project several student projects are available that include 1.) characterisation of the plasma/serum glycome across several vertebrate species;

2.) investigation and understanding cross-species recognition of pathogen adhesins; 3.) novel, cutting-edge science to understand the role of glycosylation and infection in flying foxes; 4.) working in and with an interdisciplinary and international team delivering first-hand knowledge and skills in a variety of biochemical and immunological skills and techniques.

The outcomes of these highly collaborative (across Griffith, national and international partners) projects will provide novel clues how infectious diseases can spread and uncover novel targets to stop their distribution and uncover novel biology in animal species of primary interest for the distribution of zoonotic pathogens. Students will be introduced to biochemistry and immunology laboratory workflows that include (but are not limited to) SDS-PAGE, Western blotting, Proteomics and Glycomics sample preparation, acquisition and data analyses and gain general knowledge in Biochemistry, Glycobiology and Immunology.

Techniques: mass spectrometry, glycomics, proteomics, microarray, Immunoglobulins, protein purification, immunological techniques.

Understanding the impact of glycosylation on stem-cell-factor (SCF) and stem-cell-factor receptor signalling in stem cell biology, health and cancer pathogenesis

Glycoproteomics, Biochemistry, Signaling, Protein Structure

Other supervisors | Dr Larissa Dirr, Dr Alpesh Malde, Associate Professor Joe Tiralongo, Professor Mark von Itzstein AO

Receptor glycoproteins are highly important signalling molecules in controlling cell communication and interaction. Dysregulation of these signalling pathways is frequently associated with diseases such as cancer and chronic inflammatory conditions. However, the role their glycosylation plays for protein structure and interaction is still poorly understood. Type III family of receptor tyrosine kinases such as c-KIT (also known as Stem Cell Factor receptor or CD117, PDGF-receptor- α and β , CSF-1 receptor and the FLT3 receptor play a vital role in the pathogenesis across different types of cancer.

As part of a larger, collaborative project (Mater Research, Brisbane and Australian Red Cross Lifeblood) a variety of student projects are available that include aspects of mass spectrometry applications (proteomics, glycomics and glycoproteomics) next to structure biology, molecular dynamics simulation, cell culture, Western Blot, electrophoresis and other standard biochemistry

techniques. In combination these techniques are being employed to characterise and modulate the glycosylation of these important signalling molecules to understand how protein-specific glycosylation impacts protein function and cell signalling. This knowledge will provide opportunities for developing novel therapeutic strategies targeting these receptor proteins.

As part of this project, students will be introduced to biochemistry laboratory workflows that include (but not limited to) SDS-PAGE, Western blotting, Proteomics and Glycomics sample preparation, acquisition and data analyses and gain general knowledge in Biochemistry and Glycobiology.

Techniques: mass spectrometry, glycomics, proteomics, cell culture, Western blotting, protein structure, basic biochemical workflows.

Cracking the cancer-glycocode to guide novel cancer diagnostics and therapeutics

Glycomics, Proteomics, Cancer, Cancer-biomarkers, Cancer Microenvironment, Cancer Diagnostics, Multi-omics

Other supervisors | Dr Arun Everest-Dass, Associate Professor Chamindie Punyadeera, Professor Mark von Itzstein AO

Understanding cancer and patient-specific dynamics of protein glycosylation holds enormous yet unmined potential for cancer precision medicine. Glycosylation is a dynamic protein post translational modification in which defined sugars (so called glycans) are attached to proteins by highly individual biosynthetic pathways. Human blood groups are one example of the individuality and clinical relevance of protein glycosylation, as specific glycans form the molecular basis of the human ABO blood group system. About 2% of human genes are dedicated to biosynthetic pathways of this glycosylation machinery. Genomics and transcriptomics can provide some information about the presence or absence of glycosylation-relevant genes. However, the biosynthetic events that regulate the glycosylation machinery are beyond direct genomic and transcriptional regulation. Glycomics and glycoproteomics approaches thus are the only technologies that can be employed to sequence the cancer glycocode.

In close collaboration with national and international clinical partners we are studying cancer glycocode to understand why cancer forms, what makes individual cancers specific and to identify the weak points that allow us to develop novel strategies to fight cancer. With a focus on cancers such as Leukaemia, Prostate cancer, Melanoma, Ovarian cancer, Head & Neck Cancer or Colon

cancer we use highly sensitive and selective glycan/glycoprotein sequencing tools to study cell surface glycoconjugates and their role in pathological processes. One technology involves cutting-edge Laser Capture Microdissection that allows the specific cutting of cancer cells from tissue that has revolutionised how we can read the language of cancer. As part of the Australian Centre for Cancer Glycomics (A2CG) we are now systematically applying our glycan-sequencing technologies to sequence cancer glycomes in a variety of cancers. Be part of the cancer glyco-revolution. A number of student projects are available supporting this important endeavour that will result in a new generation of diagnostic and prognostic cancer markers. As part of this project, students will be introduced to biochemistry laboratory workflows that include (but not limited to) SDS-PAGE, Western blotting, Proteomics and Glycomics sample preparation, acquisition and data analyses and gain general knowledge in Biochemistry and Glycobiology. They will work in an interdisciplinary and multi-national team at the direct interface between the clinic and the research lab.

Techniques: mass spectrometry, glycomics, proteomics, Western blotting, Laser Capture Microdissection microscopy, basic biochemical workflows.

CURRENT RESEARCH PROJECTS

Research Leader | Associate Professor Todd Houston

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Design and synthesis of synthetic receptors for cell-surface carbohydrates

Medicinal Chemistry



Other supervisors | Dr Milton Kiefel

Boronic acids form covalent, but reversible, interactions with polyols such as sugars in aqueous solution. We have developed boronate receptors selective for cell-surface carbohydrates from both mammalian and bacterial cells (specifically sialic acid and KDO). Our receptors display a unique and divergent fluorescent response that can be exploited for selective detection in biological media. Ultimately, these receptors will be developed into boronolectins that target specific cell types and may be used in drug targeting. These synthetic receptors can identify targets complementary to those of nature's antibodies and lectins that normally survey cell surfaces. In addition, we have identified anti-bacterial activity in some of these compounds implying there is potential to develop these into medicinal agents.

Techniques: Synthetic chemistry; fluorescence detection.

Development of novel antibacterial treatments

Medicinal Chemistry

**Other supervisors | Dr Darren Grice,
Associate Professor Nick West**

Deadly infectious bacteria such as *Mycobacterium tuberculosis* and MRSA are able to survive within macrophages in a human host and this makes treatment particularly challenging. Incomplete or ineffective antibiotic treatment leads to development of drug resistant bacteria, a problem of growing global concern. We are currently developing antibacterial compounds that can be formulated into nanoparticles with drug targeting epitopes to improve uptake and drug delivery into macrophages. This allows for improved bactericidal activity and diminishes the opportunity for the development of drug resistance.



Techniques: Synthetic carbohydrate chemistry; liposome formulation; bacterial cell growth assays.

Improving Affinity of Glycosidase Inhibitors for Drug Development

Medicinal Chemistry

Other supervisors | Dr Michela Simone

Exo-glycosidases are an important family of enzymes involved in a number of vital biological process and pathologies. Glycosidase inhibitors have a wide range of medically-relevant activities including anti-cancer, anti-viral and anti-diabetic properties. Unfortunately, these compounds often have a relatively low affinity for their target enzyme. We have identified an important structural motif that improves binding affinity of a

number of glycosidase inhibitors and this can be modified to improve drug targeting to cell surfaces where a number of enzyme targets are displayed. In this way, the inhibitor can be placed in close proximity to the substrates the glycosidase enzyme

Techniques: Synthetic carbohydrate chemistry; molecular modelling; enzyme assays.

CURRENT RESEARCH PROJECTS

Research Leader | Associate Professor Lara Herrero

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The pathobiology of emerging viral diseases; from the nerves to the joints

Virology, Immunology, Cellular and Molecular Biology

Other supervisors | Dr Penny Rudd, Collaborators from the USA

Mosquito-borne alphaviruses such as chikungunya virus (CHIKV) and Ross River virus (RRV) cause large epidemics of severe musculoskeletal disease and have been progressively expanding their global distribution emerging in new regions of the world. The hallmark of alphavirus disease is crippling pain and joint arthritis, which often has an extended duration leaving patients bed-ridden and incapacitated. In some instances, these viruses are known to cause life-threatening complications including neurological disorders leading to life-long cognitive impairment. Although greatly understudied, neurological complications are seen in up to 24.1% of all CHIKV cases – this is the major cause of intensive care unit admissions and death during CHIKV infections.

Combatting mosquito-borne diseases is one of our most pressing global health challenges. This project has two main goals, 1) to study the pathobiology of infection in the joint and deciphering the mechanisms of viral-arthritis and 2) dissect the pathways neurovirulence which lead to neurological sequelae.

Techniques: mouse model of viral arthritis, clinical disease and joint hypersensitivity measurement, primary neuronal cell culture, ELISA, real-time PCR, viral plaque assays, flow cytometry, histopathology, western blotting, immunohistochemistry.

How mosquitoes transmit deadly viruses

Virology, Viral-ecology, Cell Biology, Molecular Biology

Other supervisors | Dr Penny Rudd, Dr Arun Everest-Dass, external supervisors in Australia-wide state health departments

The incidence of human and animal diseases caused by mosquito-borne pathogens has increased at an alarming rate globally. In nature, arboviruses are maintained in continuous transmission cycles between mosquito vectors and susceptible vertebrate hosts. The early interactions between the arbovirus and initially infected mosquitoes is likely to be a crucial step in determining whether the virus is able to successfully establish infection. Understanding how viruses infect these cells will significantly expand our knowledge of how arboviruses are transmitted and cause disease. This project utilises glyco-analytical approaches, unique mosquito cells and an arbovirus model system to identify new markers associated with virus transmission by

mosquitoes. Markers associated with transmission will be identified by establishing global glycome and lectin profiles of the cells derived from a major mosquito species. The overall objective of this proposal is to explore the glycomics of mosquito cells and its role in arbovirus mosquito infection.

Techniques: Handling of primary mosquito cells, cell culture, viral plaque assays, flow cytometry, molecular biology, glyco-analytical techniques using mass spectrometry and liquid chromatography. Experiments will be undertaken in the state-of-the-art glycobioanalytical facility.

Bat Borne Viral Zoonosis; glycans and the host

Virology, Epidemiology, Cell Biology, Glycobiology, Public Health

Other supervisors | Dr Penny Rudd, Professor Linfa Wang, Dr Michelle Baker

Zoonotic pathogens pose major threats including catastrophic social and economic impacts. Zoonotic infections are triggered by the ability of a pathogen to cross from animal to human. Bats have been shown to carry more than 200 viruses and a significant proportion of these viruses are zoonotic however very little is known about what makes bats unique hosts. This project aims to investigate the mechanisms of viral host interactions focusing on viruses of pandemic potential. Utilising innovative glycobiological technologies this research seeks to be the first ever to identify the "natural" glycome of the bat leading to better prediction

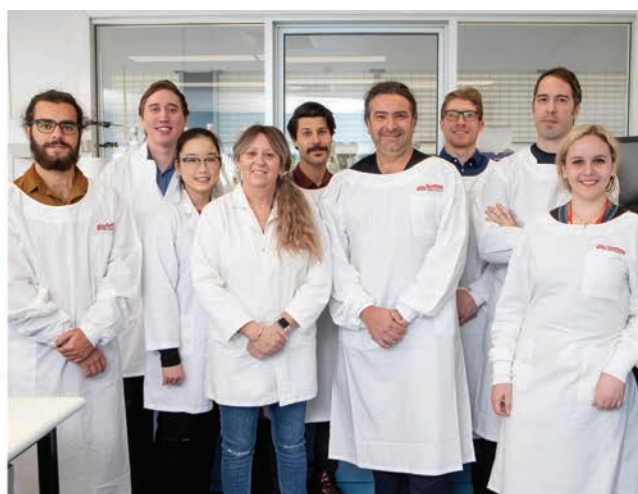
and understanding of why bats are uniquely susceptible to a multitude of important zoonotic viruses. This will fill a significant gap in our knowledge of bat physiology and the unique nature of bats in harbouring viral infections.

Techniques: Handling of primary bat cells, cell culture, viral plaque assays, flow cytometry, molecular biology, glyco-analytical techniques using mass spectrometry and liquid chromatography. Experiments will be undertaken in the state-of-the-art glycobioanalytical facility.

CURRENT RESEARCH PROJECTS

Research Leader | Associate Professor Joe Tiralongo

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When Glycobiology meets Nanotechnology

Materials Science, Nanotechnology, Interaction Biology, Glycobiology, Biochemistry

Micro-technologies in the form of Micro-Electro-Mechanical Systems (MEMS) and micro-plasmonics platforms offer the potential for high-resolution, high-throughput label-free sensing of biological and chemical analytes. Silicon carbide (SiC) is an ideal material for augmenting both MEMS and plasmonics routes, however such inorganic surfaces need to appropriately and efficiently functionalised to allow subsequent immobilization of functional biomolecules.

To this end we trialled various organosilane-based self-assembled monolayers for the covalent functionalization of 2-dimensional SiC films, and have now developed an affordable, facile one-step method. Using high-throughput glycan arrays as our model system a novel platform that has the potential to combine established array technology with the label-free capabilities of

MEMS or plasmonic systems is one step closer. Using a similar functionalisation route, we have extended the use of organosilanes to biofunctionalise the surface of 3-dimensional nanoparticles, specifically carbon dots. Carbon dots are cheap, biocompatible, chemically stable, heavy-metal free quantum dots, of low toxicity that offer an alternative approach for bio-imaging and -sensing applications. Again, employing glycans as our model system, we are now using our biofunctionalization approach to generate glycan-coated carbon dots that we are using to explore complex glyco-interactions.

Techniques: Organic chemistry; surface plasmon resonance, microarray technology, flow cytometry, microscopy.

Exploring the immuno-modulatory effect of fungal β -glucans

Separation Chemistry, Immunology, Glycobiology

Other supervisors | Dr Darren Grice

Mushrooms are increasingly attracting attention for their immuno-modulatory activities, which are primarily due to β -glucans. β -Glucans comprise a group of glucose (Glc) polysaccharides that are chemically diverse, with a common β -glucan being cellulose (β -(1,4)-linked Glc. It is non-cellulosic β -glucans, mainly β -(1,3)-linked Glc that have been shown to be potent immunological stimulators in humans, and some are now used clinically in China and Japan, as well as being commercially available in Australia.

Due to the complexity of β -glucan chemistry and structure a detailed understanding of the mechanism of action, specifically the structural components that dictate specific immunological responses, are yet to be fully resolved. In collaboration with Integria Healthcare,

the overall objective of the project is to explore the immuno-modulatory effects of mushroom β -glucans, specifically the project aims to structurally characterise commercially available mushroom polysaccharides rich in β -glucans and correlate this with their associated immuno-modulatory effects. The outcomes from this project will lead to a clearer understanding of the properties of β -glucans associated with commercially available mushroom polysaccharides that induce specific immuno-modulatory effects.

Techniques: Carbohydrate chemistry, ELISA assays, separation chemistry, polysaccharide structure determination.

Glycomics of cancer stem cells

Glycobiology, Biochemistry, Cell Biology, Cancer Biology

Other supervisors | Associate Professor Daniel Kolarich

We are interested in better understanding the glycomics (display of glycans on the cell surface) of stem cells predominantly cancer stem cells, specifically cancer cells cultured under spheroid forming conditions. Cancer cells grown as spheroids take on stem-like properties, and we have been assessing changes in the glycomics of these cells relative to cells not cultured in this way. The main techniques we have used to evaluate these cells has been using lectin arrays and flow cytometry. This has identified a number of key changes that we have been evaluating.

We would now like to assess additional/different cancer cells grown as spheroids, including cells that have been genetically engineered to lack certain enzymes involved in glycosylation using lectin arrays and flow cytometry, as well as assess our panel of cancer stem cells using mass spectrometry techniques for specific and potentially more subtle changes in glycosylation.

Techniques: Cell culture, Mass spectrometry, Protein purification.

CURRENT RESEARCH PROJECTS

Research Leader | Dr Thomas Ve

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Structural basis and therapeutic targeting of neurodegeneration

Structural Biology, Biochemistry, Medicinal Chemistry

Other supervisors | Dr Yun Shi, Professor Mark von Itzstein AO

Axon loss is a common theme in some of the most prevalent neurological diseases, including peripheral neuropathies, traumatic brain injury, Parkinson's disease and glaucoma, but no treatments currently exists that effectively target axonal breakdown. The protein SARM1 is a central player in axon loss. In healthy nerve cells, SARM1 (sterile alpha and TIR motif 1) is present but inactive. Disease and injury activate SARM1, which results in rapid breakdown of the essential "helper molecule" nicotinamide adenine dinucleotide (NAD+) and ultimately destruction of the axon. We have demonstrated that it is SARM1 itself that cleaves

NAD+ upon activation through self-association and we hypothesise that detailed structural knowledge of the SARM1 catalytic mechanism and defining the molecular mechanisms upstream and downstream of SARM1 enzyme activity can yield inhibitors as leads to anti-neurodegenerative disease therapeutics. This project can include work in one, or several, areas, including Cryo-EM, X-ray crystallography, NMR and inhibitor design.

Techniques: Cryo-EM, X-ray Crystallography, NMR, Enzyme assays, Computational Chemistry including visualisation and molecular docking; Synthetic Chemistry.

Molecular basis of nucleotide signalling by bacterial TIR domain containing proteins

Structural Biology, Biochemistry, Microbiology, Innate Immunity

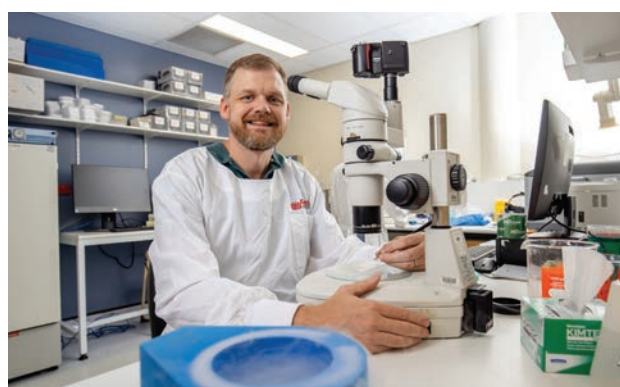
Other supervisors | Dr Yun Shi, Associate Professor Daniel Kolarich

In both animals and plants TIR domain enzymes have important immune functions. While bacterial TIR proteins have long been recognised, their biochemistry and function remain poorly understood. Some TIR domain containing proteins with NAD⁺ cleavage activity have been reported to be involved in (i) subversion of host innate immunity (4) and (ii) in antiphage defence systems, but the mechanism of how these proteins utilise NAD⁺ and its metabolites to modulate the immune system, or provide resistance against phage infection has not yet been explored. As the bacterial TIR domain family is widespread and highly sequence diverse the characterised NAD⁺ cleaving bacterial TIR domains is likely to only comprise a small fraction of this family's enzyme diversity and a kingdom wide analysis of them will allow systematic identification of new bacterial signalling nucleotides as well as potential agonists/antagonists of the innate immune system in animals and plants.

Mechanistic understanding of bacterial defence systems has previously led to the development of revolutionary biotechnological tools such as restriction enzymes and CRISPR-Cas. Understanding the mechanism of new defence systems such as the ones containing TIR

domains may facilitate strategies for developing new useful molecular tools. This multidisciplinary project can include work on one, or several, topic, including: (i) Characterise the structural basis of TIR domain NADase activity; (ii) Explore the diversity of nucleotide signals produced by bacterial TIR domain containing proteins (iii) Identify the mechanisms that regulate TIR domain NADase activity; and (iv) Define the interactome of TIR domain produced nucleotide signals.

Techniques: X-ray Crystallography, Cryo-EM, NMR, Enzyme assays, HPLC, mass spectrometry.



Structural characterisation and inhibition of Nipah and Hendra virus infections

Structural Biology, Biochemistry, Virology

Other supervisors | Dr Yun Shi, Dr Andrea Maggioni, Professor Johnson Mak, Professor Mark von Itzstein AO

Nipah virus (NiV) is a highly lethal (risk group 4) zoonotic paramyxovirus causing severe, rapidly progressive encephalitis in humans with the case fatality rate ranging from 40–70%. NiV is closely related to Hendra virus (HeV), another risk group 4 paramyxovirus that is native to Australia and infects both horses and humans. NiV is widely distributed in Southeast Asia, India, and Africa. WHO has earmarked NiV on a priority list of eight pathogens that is expected to cause severe outbreaks in the near future. While a one-health approach of vaccinating the intermediate host (horse in the case of Hendra) is able to block the transmission of Hendra virus, the limited uptake of the Hendra vaccine by horse owners could potentially make such approach ineffective. Furthermore, transmission of NiV to humans may occur after direct contact with infected bats, infected pigs, or from other NiV infected people making a one-health preventive approach not practical to NiV, due to the lack of reliance of an intermediate host.

The NiV envelope proteins, glycoprotein G and fusion protein F, are the determinants of viral entry. G and F achieve this via their recognition of the host-cell surface proteins Ephrin-B2 and -B3, and the glycosaminoglycan

heparan sulfate (HS). Although detailed structural information is available for the G/Ephrin-B2/B3 interactions, the structural basis for how the G protein coordinates selective binding to specific glycans, such as HS is completely unknown. Furthermore, the mechanistic details of how any of the host-cell receptors trigger viral fusion are poorly defined.

This project will involve a combination of biophysical and cell-biology approaches and aims to define the molecular basis of NiV/HeV interaction with host-cell glycans (glycointeractome), define the molecular mechanisms underlying fusion activation and identify inhibitors targeting these processes. A student working on this project may specialise in one particular aspect, or be involved with a number of the different aspects of the project.

Techniques: X-ray crystallography, cryo electron microscopy (cryo-EM), saturation transfer difference nuclear magnetic resonance (STD NMR), library screening, surface plasmon resonance (SPR), glycan arrays, and viral infection assays using pseudotyped particles.

CURRENT RESEARCH PROJECTS

Research Leader | Dr Milton Kiefel

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Synthesis of ulosonic acids

Medicinal Chemistry

Ulosonic acids are a family of higher order sugars that are intimately associated with a number of human diseases. Keto-deoxy octulosonic acids are key components of the outer membrane of Gram-negative bacteria, whilst nonulosonic acids include the sialic acids, pseudaminic acids, and legionaminic acids, all of which are known to be associated with human disease and bacterial virulence. Whilst the role of these sugars as virulence factors is generally well understood, much remains to be discovered. One of the current limitations in this field of research is the limited availability of synthetic derivatives

and analogues of these important sugars. This project aims to expand on some of our preliminary work into developing a new highly efficient synthesis of ulosonic acids using an aldol condensation as the key step.

Students undertaking this project will learn modern synthetic chemistry methodology in state-of-the-art chemistry research laboratories. They will also gain “hands-on” experience with the use of high field NMR spectroscopy, and will produce compounds that will ultimately be used as biological probes.

Synthesis of butenolides with anticancer or antimicrobial properties

Medicinal Chemistry

Other supervisors | Associate Professor Shai Anoopkumar-Dukie

Butenolides are naturally occurring molecules characterised by a central 5-membered lactone ring. There is vast structural diversity and biological activity within this group of naturally occurring compounds. We have recently developed a highly efficient and flexible synthesis of this important class of natural products. This project will focus on expanding our

synthetic chemistry method to allow the synthesis of novel butenolides, and then evaluate the synthesised compounds for their biological activity. Currently we have research looking at the anticancer activity of butenolides, but this can be expanded to include antimicrobial activity as well.

Synthesis of novel natural product analogues

Medicinal Chemistry

Other supervisors | Professor Tony Carroll

Natural products represent an important source of novel chemical entities with unique biological activity. This project involves the synthesis of compounds that are structurally related to specific classes of natural products that have biological activity (e.g. anticancer activity). The aim of the synthetic chemistry is to provide novel compounds with potentially improved pharmacological profiles in comparison to the natural compounds.

The specific types of compounds to be made will be determined upon discussion with the student. Students undertaking this project will learn modern synthetic chemistry methodology in state-of-the-art chemistry research laboratories, as well as gaining hands-on experience with a number of important spectroscopic instrumentation.

CURRENT RESEARCH PROJECTS

Research Leader | Dr Darren Grice

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Analysis of surface carbohydrate structures from Gram-negative Moraxellaceae bacteria

Medicinal Chemistry, Molecular Microbiology

Other supervisors | Dr Ian Peak, Dr Jennifer Wilson

The aim of this project is to isolate surface carbohydrate components from bacteria in the *Moraxellaceae* family, then determine the structures and biological significance of these carbohydrate molecules. Many bacteria in this family are commensals of the human upper respiratory tract and are important in protecting against disease. Obtaining structural carbohydrate information will enable us to determine the role of these carbohydrates, and potentially developing new strategies to promote upper-respiratory tract health.

The project will require the development of knowledge and skills in the areas of cell culture, chemical and biochemical extraction and manipulation strategies, nuclear magnetic resonance (NMR) and mass spectrometry (MS) of isolated carbohydrate materials.

1. De Castro, Grice, Daal, Peak, Molinaro, Wilson. *Carb. Res.* (2014) 388:81–86.
2. Wilson, Hitchen, Frank, Peak, Collins, Morris, Dell and Grice. *Carb. Res.* (2005) 340:4, 765–769.

Degradation of cancer-associated proteins using proteolysis targeted chimeras (PROTACs)

Medicinal Chemistry

Other supervisors | Professor Mark von Itzstein AO

From previous studies^{1,2}, it is clear that the use of Proteolysis-targeting chimera (PROTAC) molecules can result in the effective degradation of target-proteins. PROTAC techniques involve the exploitation of normal protein degradation essential for cellular maintenance and hijacking the system to specifically target proteins of interest (POI) for degradation.

To achieve an effective PROTAC design the molecule must provide high affinity binding to both the protein of interest and a suitable ubiquitin ligase, and maintain these interactions whilst not inhibiting the overall ubiquitination (or tagging for destruction) process.

Work is underway within the Institute for Glycomics to synthesise novel PROTAC molecules to achieve the

successful proteolysis of a cancer-associated protein, which is known to be intimately involved in cancer progression. This research will be further progressed in this ongoing project.

Techniques: The project will involve synthetic organic/ carbohydrate chemistry, along with NMR spectroscopy, mass spectrometry and other associated techniques for structural characterisation of the synthesised PROTACs followed by assessment of biological activity.

1. Winter, *et al. Science.* (2015) Jun 19;348(6241):1376–81.
2. Gu, Cui, Chen, Xiong, Zhao. (2018). *Bioessays* Apr 40(4), e1700247.





Queensland, Australia



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