INSTITUTE FOR GLYCOMICS

Higher Degree Research Opportunities
2023

Griffith UNIVERSITY
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, HIV 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
Founder, Director and Principal Research Leader, Institute for Glycomics, Griffith University

ABOUT THE INSTITUTE FOR GLYCOMICS

The Institute for Glycomics' research targets the identification, prevention and discovery of cures for cancers, infectious diseases and neurological disorders, with a focus on translational research to have a positive impact on human health globally.

Established in 2000, through investment by Griffith University and the Queensland Government, the Institute for Glycomics is one of Australia's flagship interdisciplinary translational biomedical research institutes, 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.

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

The Institute's rich and enabling research environment provides exceptional Honours, Masters and PhD education programs for the nation's future scientists. Research students are given the opportunity to study alongside some of the world's most experienced and well-known research leaders and scientists, with access to state-of-the-art research equipment and facilities.

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 our future.

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
- Infectious diseases research
- Neurological disorders research

300+

Institute members

100+ Publications

per year

Community Engagement

- **Paradise Point Community Bank** supporting our Grand Ball and Summer Student Scholarship Scheme
- **Warren and Sally von Bibra** supporting our honours and masters student scholarship scheme
- **Sanctuary Cove Golf and Country Club** joining forces with our Institute 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

5 Provisional Patents

filed on new Institute technologies

Partnering

Engagement with over 45 industry partners for basic research, translation and commercialisation

Clinical Trials

- **Phase 1 clinical trial began in Canada** – Institute vaccine for the prevention of Streptococcus A infection
- **Phase 2 clinical trial began in Australia** – Repurposed vaccine for prevention of gonorrhoea
- **Phase 1b clinical trial run by Grand Medical continued in Australia** – Institute drug for treatment of sepsis
- **Preparing to enter a Phase 1b clinical trial with challenge in Australia** – Institute vaccine for the prevention of Streptococcus A infection

15,160 Citations

over 10 years

Income Sources

for 2022

- Research grant funding **$6,414,286**
- Industry, philanthropic and other support **$9,931,712**

$1 for $1

in philanthropic funding supports our research

2022 PHILANTHROPIC ENGAGEMENT

- **Bourne Foundation -** supporting prostate cancer research and ovarian cancer research
- **Reuben Pelerman Benevolent Foundation -** supporting the malaria vaccine project
- **The Snow Foundation -** supporting Streptococcus A Streptococcal Toxic Shock Syndrome research
- **GC Value Pty Ltd**
- **Order of St John of Jerusalem Knight Hospitaller the Commandery of SEQ Inc.**
- **Victoria Racing Club**
- **Gold Coast Titans Community Benefit Fund Inc**
- **Southern Paradise Foundation Pty Ltd**
- **National and General Operations Pty Ltd**
- **MyPayNow Pty Ltd**

- all supporting world class research at Institute for Glycomics

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 neurological disorders.

Cancer Research Program

It is 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 ACRF International Centre for Cancer Glycomics (I2CG) 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, the Australian Cancer Research Foundation (ACRF) and the community.

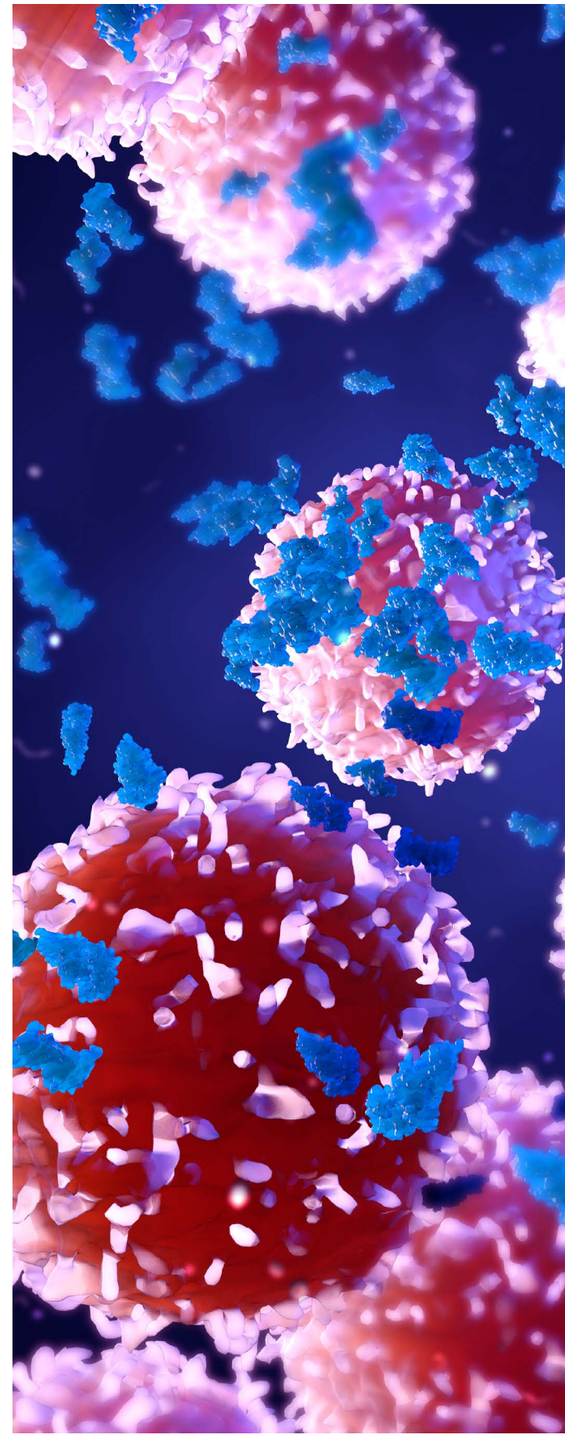
Cancer glycomics research involves understanding the role that sugars/carbohydrates play in the development of cancers. Using this knowledge, our researchers can invent new drugs, vaccines and diagnostics to treat, prevent or diagnose cancer.

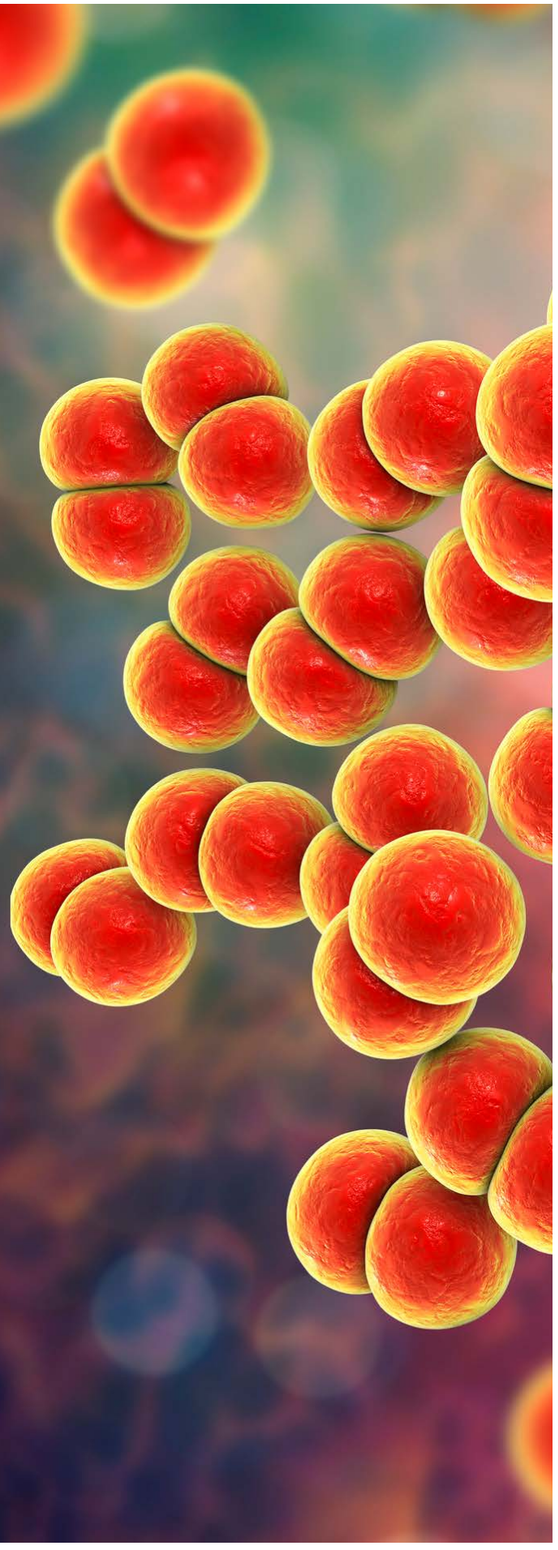
As the only research institute of its kind in the southern hemisphere, the Institute for Glycomics is already an epicentre of glycomics research globally, and houses many world-leading carbohydrate researchers. The I2CG brings together the Institute's experts in cancer research, while providing an ideal platform for collaboration with other leading cancer researchers and clinicians around the world.

A project with the vision and scale of the I2CG requires substantial human resource, technical knowledge and specialisation. By combining core expertise and infrastructure, the I2CG 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 I2CG 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 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 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, multi-disciplinary 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 targets for invasive fungal infections. The Institute is fighting invasive fungal infections through novel therapeutic approaches.

Neurological Disorders Program

The Institute's neurological disorders research encompasses the following key issues:

- **Axon degeneration research:** Axon degeneration represents a pathological feature of many neurodegenerative diseases that form a large part of the global disease burden including Alzheimer's disease, Parkinson's disease, motor neuron disease, and neuropathies. Elucidating the molecular mechanisms regulating the degeneration of injured axons may bring new therapies to a broad range of neurodegenerative diseases.

- **Mental health, PTSD, and pain research**: Glycans play an integral role in the intercommunication of neurons in the brain. We know that for patients who experience pain, trauma and blast exposure, these glycans alter. Investigating this process, known as plasticity, is integral to better understanding, diagnosing and preventing acute neurological conditions transitioning to chronic disease.

Axon degeneration research

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 enzyme SARM1 is a central player in axon loss. In healthy nerve cells, SARM1 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. Interestingly, similar NAD+ consuming enzymes are also found in bacterial immune systems that provide protection against viral (phage) infections.

SARM1 is a potential therapeutic target for many neurodegenerative diseases but, in order to exploit the full promise of targeting SARM1, detailed knowledge of the catalytic mechanism and the molecular mechanisms upstream and downstream of SARM1 enzyme activity is required.

Researchers at the Institute for Glycomics are using structural biology methods such as cryo-Electron Microscopy and X-ray Crystallography, combined with cell and chemistry-based approaches through in collaboration with national and international partnerscollaborators, to characterise SARM1 and related bacterial enzymes at the molecular level; define how they are regulated; and explore the diversity and targets of their nucleotide signals.

The research will unravel general principles of nucleotide-based signalling across all domains of life and will lead to an improved understanding of the molecular mechanisms involved in SARM1 induced axon degeneration.

Importantly, the research will provide new strategies for design of targeted inhibitors of axon degeneration, which can be developed into therapeutic agents for neurodegenerative diseases.

Mental health, PTSD, and pain research

The Institute's translational research in the neuro field centres on MR technology to identify neurochemical changes to the brain associated with pain, Post-Traumatic Stress Disorder (PTSD), injury from blast and impact. Researchers at the Institute for Glycomics have now completed a contract to the USA and Australian military to develop an approach to improve the health of soldiers.

The research team uses clinical 3T scanners to monitor the effect of trauma and pain on the human glycome. They have assigned seven fucosylated glycans in the human brain. These glycans are affected differently in men and women. They are also affected differently by chronic pain, PTSD, and blast exposure. These fucosylated glycans have been shown in animal models by a Caltech team to be implicated in the mechanisms underlying neuronal development, learning and memory and regulation of the nervous system development and neuronal processes.

A MESSAGE FROM OUR HDR CONVENORS

You are not alone in your HDR expedition! At the Institute for Glycomics 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 scary process. Your HDR convenors, together with your individual supervisory team, will help you safely navigate your HDR journey.

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

You can rely on a solid support network. We would like to invite any prospective candidates to contact us with any questions 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 PROFESSORS LARA HERRERO AND DANIEL KOLARICH
HDR Convenors, Institute for Glycomics

WHY CONSIDER HDR STUDIES AT THE INSTITUTE FOR GLYCOMICS?

▶ Study alongside expert scientists in state-of-the-art facilities

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.

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.

▶ It's an exciting and supportive research environment

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 word. 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 to combat some of the world's most devastating diseases.

For information on research degree scholarships offered by the Institute for Glycomics:

griffith.edu.au/institute-glycomics/study-with-us

For general information on PhDs and other research degrees at Griffith University (including scholarships):

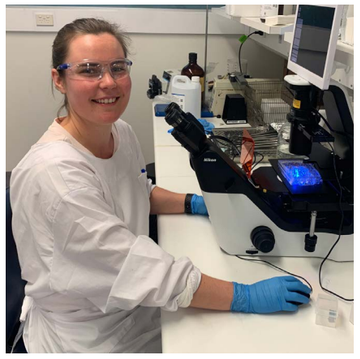
griffith.edu.au/research-study/degrees

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 with minimal side effects to treat hMPV infections.

"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."

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.

"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."

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.

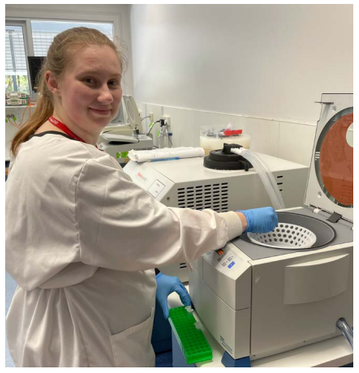
These biosensors provide researchers with unparalleled sensitivity to explore complex interactions that can be exploited for both biosensing and drug targeting.

"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."

Xavier De Bisscop
Masters Student

Xavier has just completed his Masters degree with Professor Michael Jennings and Dr Lucy Shewell. He project involved using novel methods to look for Neu5Gc (a sugar associated with cancer) in blood collected from pancreatic cancer patients. Ultimately, his research may help to develop diagnostic tests that detect pancreatic cancer earlier or improve the specificity of current tests.

"I developed an interest in cancer research as an undergraduate biomedical science student here at Griffith. When choosing a project for the Master of Medical Research program, my attention was directed to the Institute for Glycomics, where the Jennings group was conducting innovative work in cancer detection. Since starting my degree, my understanding of the research process has deepened in a way that could only be possible through firsthand experience. The opportunities for learning such a wide variety of skills and techniques in the lab truly exceeded my expectations. Working at the Institute in the Jennings group has been greatly fulfilling, and I look forward to continuing this work as a PhD candidate."



Jessica Halliday – Masters Student

Jessica is supervised by A/Prof Daniel Kolarich and Dr Darren Grice and her project involves understanding storage associated changes in platelet components using glycomics.

"In 2021 I was awarded an Institute for Glycomics Summer Scholarship which provided me with the opportunity to experience working in a research institute alongside some of the best in their fields. For 4 weeks, I was a part of the Kolarich group where I was given a hands-on learning experience into how glycomic and glycoproteomic samples are prepared for mass spectroscopy analysis. After learning some tricks of the trade, I began processing samples for one of the group's current projects that is investigating the glycomic changes that occur as a result of pre-operative carbohydrate loading in surgical breast cancer patients.

When I learnt about the scholarship, I was nearing the end of my Bachelor's degree with no idea what my next step would be. Luckily, I attended one of the Institute's Open Days where I was given a booklet just like you are reading now which opened my eyes to the variety of opportunities the Institute provides for students. There I met Associate Professor Daniel Kolarich who explained the various applications that glycomics has on multiple scientific and health-related issues, which created a foundation for my scientific curiosity to grow from. This curiosity has continued to develop and has led to me staying at the Institute where I am now undertaking a project for my Master of Medical Research degree. Four weeks of work experience has led to the beginning (hopefully) of my long career in medical research."

CURRENT RESEARCH PROJECTS

Principal Research Leader | Professor Mark von Itzstein AO

Contact email: m.vonitzstein@griffith.edu.au

Development of ionophores as novel antimicrobial therapies

Medicinal Chemistry

Other supervisors: Dr Ibrahim El-Deeb

The increase in bacteria acquiring resistance to current antibiotics, and a reduction in development of new antibiotics by the pharmaceutical industry over the past years, is placing a significant burden on global health care, with the World Health Organization noting that antibiotic-resistant pathogens represent an imminent global health disaster for the 21st century. Our research is focussed on investigating alternative therapeutic strategies to break antibiotic resistance. Metal-ion homeostasis is critical for bacterial survival, and elevated metal ion levels can be toxic to bacterial pathogens. Ionophores are chemical compounds that facilitate transport of metal ions across biological membranes. Together with our collaborators, we have identified ionophores that are able to break antibiotic resistance by destabilizing bacterial metal homeostasis.[1] This project will extend our work in this area, through development and evaluation of new ionophores.

1. Bohlmann L et al., mBio 9:e02391-18 (2018). doi: 10.1128/mBio.02391-18.

Techniques: Synthetic chemistry.

The characterisation of virus binding specificity to host cell receptors

Virology, Structural Biology, Cell Biology

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-recognising proteins on exosomes. 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.

Associate Research Leader | Dr Patrice Guillon
Early Career Research Leader | Dr Larissa Dirr
Principal Research Leader | Professor Mark von Itzstein AO

Contact email: p.guillon@griffith.edu.au; m.vonitzstein@griffith.edu.au; l.dirr@griffith.edu.au

Parainfluenza virus glycan receptor characterisation and structure-based discovery of anti-parainfluenza viral agents

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

Other supervisors: Dr Ibrahim El-Deeb, Dr Robin Thomson, & Dr Alpesh Malde

Human parainfluenza viruses (hPIV) are important respiratory tract pathogens. Infants, young children, the elderly and the immunocompromised are most severely infected, developing croup, pneumonia or bronchiolitis that may need patient hospitalisation. Currently there are neither vaccines nor specific antiviral therapy available to prevent or treat hPIV infections.

Among the hPIV proteins, the surface glycoprotein haemagglutinin-neuraminidase (HN) is crucial in several key steps of the virus life cycle.[1] Virus interaction with the host cell surface carbohydrate sialic acid is the trigger for the HN activities. The research experiments of this project are focused on furthering our understanding of the functions of HN, and the development of high potency inhibitors of the HN–sialic acid interaction.[1]

The X-ray crystal structures of the HN glycoprotein of a number of hPIV sub-types are available and can be used for guiding the design of compounds to inhibit the protein's interactions with sialic acid. While some characterisation of hPIV glycan receptor interaction has been undertaken, a complete systematic study is yet to be done. Furthermore, the combination of molecular modelling, structure-guided design, fragment screening, and synthetic chemistry, may provide new inhibitors of viral replication. Using biochemistry and structural biology techniques on whole virus and recombinant HN glycoprotein, the effect of these new inhibitors on the virus/glycan interaction can be investigated. 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.

1. Reviewed in: Chibanga V et al, Antiviral Res. 167: 89–97 (2019)..doi: 10.1016/j.antiviral.2019.04.001.

Techniques: Computational Chemistry including visualisation and molecular docking; Fragment screening using 19F NMR; Synthetic Chemistry; Protein expression and purification; Virology; Biological Assays; Advanced NMR techniques including STD-NMR, X-ray crystallography.

Early Career Research Leader | Dr Larissa Dirr
Associate Research Leader | Dr Patrice Guillon
Principal Research Leader | Professor Mark von Itzstein AO

Contact email: m.vonitzstein@griffith.edu.au; l.dirr@griffith.edu.au; p.guillon@griffith.edu.au

Structural characterisation and inhibition of human metapneumovirus infections

Structural Biology, Biochemistry, Virology

Human metapneumovirus (HMPV) is an emerging cause, second after the human respiratory syncytial virus (RSV), for lower respiratory disease in infants with currently neither an approved antiviral drug nor a vaccine available. The populations most at risk for developing severe HMPV-associated disease are young children, the elderly, and immunocompromised people.

Human metapneumoviruses are decorated with three surface glycoproteins: fusion protein (F), attachment protein (G), and small hydrophobic protein (SH). The F protein plays important key roles during various stages of the HMPV lifecycle such as recognition and binding to host receptor, fusion of virus envelope with host cell membrane, and fusion of infected cell membrane with neighbouring cells' membrane. As a result, the F protein is considered as a promising target for antiviral drug discovery. The F protein expressed at the virus surface contains a mucin-like domain that has been shown to participate in the virus/cell binding event by recognizing DC-SIGN and L-SIGN, both C-type lectins. Moreover, glycan recognition and binding are fundamental to the HMPV/cell attachment binding event(s). As such, heparan sulfate (HS), a glycosaminoglycan (GAGs) has been proposed to act as primary receptor. However, the structural basis for how the F protein coordinates selective binding to specific glycans, such as HS is completely unknown. Recently, our group has identified new host cell glycan receptors of hMPV and has also made progress with GAG-like binding inhibitors.

This project will a combination of biophysical and cell-biology approaches to further understand how HMPV interacts with their host cell glycan receptors (glycointeractome) at a molecular level, 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, saturation transfer difference nuclear magnetic resonance (STD NMR), library screening, surface plasmon resonance (SPR), glycan arrays, viral infection assays and advanced in vitro human airway epithelium model.

Early Career Research Leader | Dr Mehfuz Zaman
Principal Research Leader | Professor Mark von Itzstein AO

Contact email: m.vonitzstein@griffith.edu.au; m.zaman@griffith.edu.au

Vaccine development against respiratory pathogens

Vaccinology, liposome design and formulation, drug delivery, immunology, virology, microbiology

The upper respiratory tract (URT) is the major entry site for multiple pathogens including Influenza A-B, *Streptococcus pyogenes* (group A streptococci, GAS) and coronaviruses. We are establishing a 'modular' multi-pathogen vaccine platform using liposomes (phospholipid vesicles). The liposomal delivery system allows the incorporation of both viral and bacterial peptide epitopes (a part of a protein recognised by antibodies and cells of the immune system) to prevent URT infection. The liposomal formulation can be stored as a lyophilised powder and reconstituted prior to immunisation, yielding a stable product that potentially does not require a cold-chain from production to needle-free administration. Incorporating lipid-linked sugars (glycolipids) enhances secretory immunoglobulin A (IgA)-mediated mucosal immunity that may reduce infectivity of human secretions and transmission.

This multidisciplinary research project involves liposome formulation, testing in pre-clinical models and immunological and functional assays to examine the mechanisms of protection.

Techniques: Vaccine design, Enzyme Linked Immunosorbent Assays (ELISA), *in-vitro* cell culture assays such as viral propagation and plaque forming assays, in-vivo techniques such as viral and bacterial challenges, immunization and sample collection from pre-clinical models.

Research Leader | Dr John Atack
Principal Research Leader | Professor Michael Jennings

Contact email: 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 pneumoniae.

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 know 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.

Research Leader | Dr John Atack

Contact email: 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.

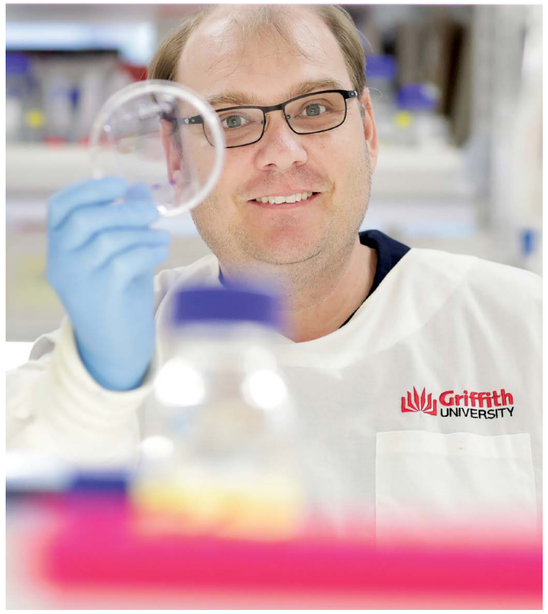
We will utilise multiple *in vitro* and *in vivo* models to determine the ability of these glycans and novel compounds to serve as blocking agents for the treatment of MDR *A. baumannii* infections. This will aid in the development of new treatment strategies, and lay the groundwork to develop novel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

Characterisation of gene expression and virulence factors in bacterial otopathogens

Non-typeable Haemophilus influenzae (NTHi) and Streptococcus pneumoniae (Spn) both colonise the human nasopharynx asymptomatically. Transition to other niches in the body results in a variety of diseases, such as middle ear infection (otitis media, OM) in young children, exacerbations in chronic obstructive pulmonary disease (COPD) in the elderly, pneumonia across all age-groups, and serious invasive diseases, such as sepsis and meningitis. Co-infections involving the two species are common, but the molecular basis for their interactions is poorly understood.

There are current vaccines available to protect against Spn, but these are only effective against a limited number of serotypes. No current vaccine exists to protect against NTHi. A major hurdle to vaccine development against both species is the random and reversible switching of gene expression in both pathogens. Both species encode randomly switching epigenetic regulators called phasevarions, which control multiple virulence traits that trigger infection. We will investigate if specific alleles and expression states of these systems are under selection pressure by undertaking detailed in-vitro studies using model strains. This will also allow identification of other factors required for interactions between these two species. Additionally, we will use the ORChID collection, samples from a 4-year birth cohort study of children in SE QLD over their first 2-years of life for an epidemiological determination of the role of co-colonisation events on disease incidence, severity, and burden.

Our studies will examine if certain gene(s) are required for NTHi-pneumococcal interactions. We will determine the role phasevarions play in this interaction, and if specific genes/alleles of each methyltransferase provide an advantage to either species during interaction. Detailed analysis of chronological samples from the ORChID collection will determine if co-colonisation events precede disease, and if particular strains/serotypes are more associated with colonisation and/or disease. This information will allow development of better vaccines and treatments for two pathogens of major importance to human health.



Principal Research Leader | Professor Michael Jennings
Associate Research Leader | Dr Christopher Day

Contact email: m.jennings@griffith.edu.au; c.day@griffith.edu.au

Identification of novel carbohydrate binding proteins

Array Technology; Affinity and Kinetics Measurements

Other supervisor: 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 plamon 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

Other supervisors: Dr Lucy Shewell

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 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 (~1µl) 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.

Principal Research Leader | Professor Michael Jennings
Associate Research Leader | Dr Freda Jen

Contact email: m.jennings@griffith.edu.au; f.jen@griffith.edu.au

Fighting Infectious Diseases - Engineering carbohydrate-based vaccines against Gram-negative bacteria

Microbiology, Molecular biology

Nontypeable *Haemophilus influenzae* (NTHi) is known to cause middle ear infections in children, sinusitis in adults, acute bronchitis, and exacerbations of chronic obstructive lung disease. *Neisseria gonorrhoeae (*Ng) infects human mucosal surfaces, leading to the sexually transmitted infection gonorrhea. However, both of these bacteria are becoming increasingly resistant to antimicrobial treatments, posing a significant challenge to healthcare systems and endangering our ability to treat these prevalent infectious diseases. Currently, there are no vaccines available for either of these pathogens, and they have evolved mechanisms to evade the human immune system, making it difficult to develop effective vaccines. Our laboratory has discovered a shared characteristic between these two bacteria: they both have aberrant expression of a unique sugar. The project aims to use different approaches to design and synthesize various versions of carbohydrate-based vaccine antigens, which will be tested in mice. Successful completion of the proposal will enable the development of a potential vaccine into clinical development and provide a new solution for the treatment and prevention of NTHi and Ng infections in the near future.

The Battle Against Antimicrobial Resistance in Neisseria Pathogens

Microbiology, Molecular biology

Antimicrobial resistance is a growing concern in pathogenic Neisseria species such as *Neisseria gonorrhoeae* and *Neisseria meningitidis*, which are responsible for causing sexually transmitted infections and meningitis, respectively. These bacteria have developed resistance to multiple antibiotics, including penicillin, tetracycline, and fluoroquinolones, which were previously used to treat these infections. The emergence and spread of antimicrobial resistance in pathogenic Neisseria is primarily driven by the acquisition of resistance genes through horizontal gene transfer. This has led to the development of multidrug-resistant strains that are becoming increasingly difficult to treat, posing a significant threat to public health. To address this issue, there is a need for the development of new antibiotics and alternative therapies that are effective against multidrug-resistant strains. The goal of this project is to develop a novel treatment for pathogenic Neisseria.

Discovering How Gonorrhea Bacteria Survive: Investigating CMP-Neu5Ac Transport in Neisseria

Microbiology, Molecular biology

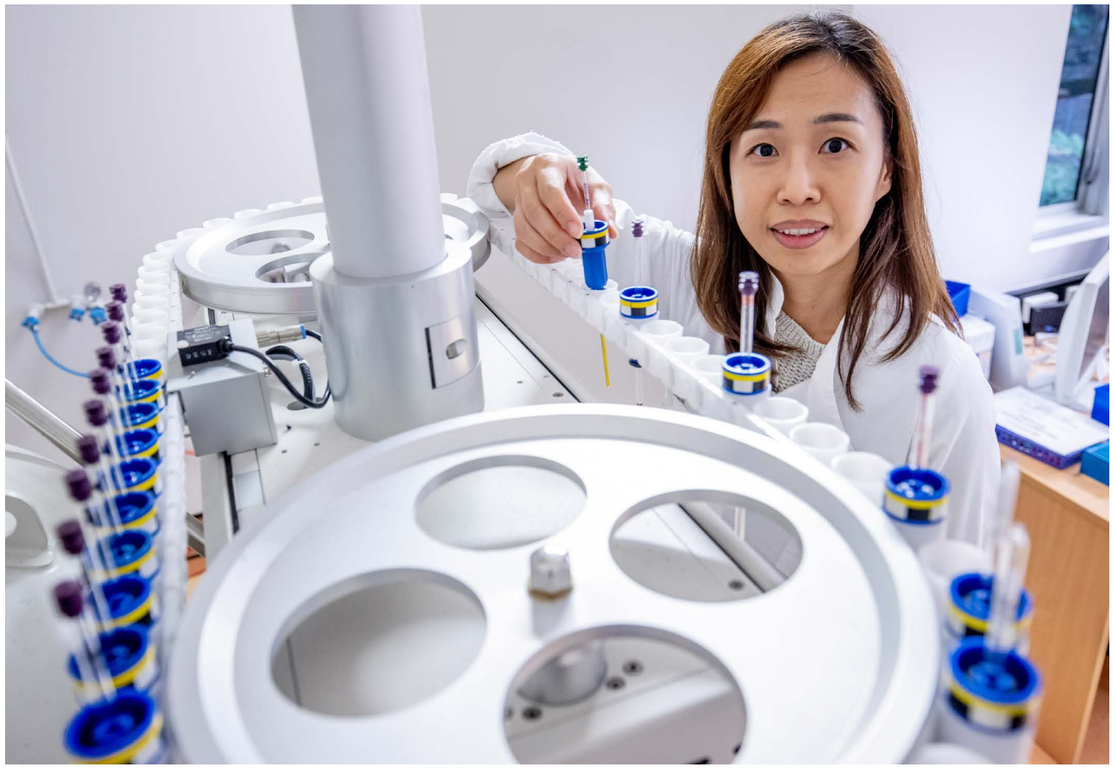
Neisseria gonorrhoeae is a bacterial pathogen that causes the sexually transmitted disease gonorrhea by infecting male urethral and female cervical tissues. One of the major virulence factors of N. gonorrhoeae is Lipooligosaccharides (LOS), which can take on multiple glycoforms due to the phase variation of the genes involved in LOS biosynthesis. The structure of gonococcal LOS is capped with N-acetyl-5-neuraminic acid (Neu5Ac), but the bacterium cannot synthesize the CMP-Neu5Ac required for LOS biosynthesis and must acquire it from the host. While the core-oligosaccharide of LOS is assembled in the cytoplasm, our published study revealed that the alpha-2,3-sialyltransferase Lst, previously thought to be a surface-exposed outer membrane protein, is located inside the cell. This suggests the existence of a transport system or trans-sialidase to transport CMP-Neu5Ac from the host to inside the cell. The goal of this project is to identify a novel CMP Neu5Ac transporter in Neisseria.

Uncovering the Secrets of Guinea Pig Serum

Cancer, Molecular biology

Other supervisors: Professor Ifor Beacham

Over 65 years ago, Guinea pig serum was fortuitously discovered as an effective anti-tumour agent against transplantable lymphomas. Subsequent investigations revealed that L-asparaginase in the serum was responsible for this remarkable anti-tumour property. The anti-tumour properties of L-asparaginases are primarily due to the depletion of exogenous L-asparagine, which is crucial for the growth of tumour cells, as they are essentially auxotrophic for L-asparagine. Despite its discovery, the identification of guinea pig serum L-asparaginase has been problematic, as it has only been found in guinea pig serum and not in the sera of other species studied, including mice and rats. This project aims to determine the genetic and biochemical origins of liver and serum enzymes in guinea pigs and related species, which also have both isozymes.



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

Contact email: michael.good@griffith.edu.au; d.stanisic@griffith.edu.au

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).

Principal Research Leader | Professor Michael Good AO
Research Leader | Associate Professor Manisha Pandey

Contact email: michael.good@griffith.edu.au; m.pandey@griffith.edu.au

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

Molecular Immunology and Vaccinology (MIV)

Other supervisors Dr Victoria Ozberk

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 sequalae 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 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

Other supervisors: Dr Victoria Ozberk

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 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.

Research Leader | Professor Johnson Mak

Contact email: j.mak@griffith.edu.au | Other supervisors: Dr Belinda de Villiers

Cell-Cell transmission of HIV-1 and other retroviruses via polarized targeting of virological synapses

Directional delivery of protein complexes to their destinations is fundamental to cellular homeostasis, but mechanisms underpinning intracellular protein trafficking are not well-understood. Cell polarity demands a robust yet simple framework to control intracellular cargo movements. This network is vital for cells to expedite responses across biological processes, including (i) firing of neurotransmitters through neurological synapses, (ii) dispatching exosomes via exocytosis, and (iii) mounting immune responses through immunological synapses. Directional movement of HIV protein during HIV synapses formation during virus production is another example of polarised targeting of protein complexes. HIV synapse formation enables HIV cell-cell transmission and overcomes anti-retroviral therapeutics and broadly neutralising antibodies, which hinders the prospect in achieving HIV cure.

Our reported Ca2+-facilitated HIV synapses formation offers a unified (and testable) principle, illustrating how Ca2+ guided trafficking of HIV assembly is responsible for the directional movement of protein complexes, and reveals novel therapeutic targets as potential treatment strategy. This work requires: molecular virology-based approaches to produce virus-like-particles (VLPs) via tissue culture; biochemical and biophysical evaluation to dissect mechanism; imaging analyses to track the movement of fluorescent tagged viral proteins; electron microscopy analyses to delineate the contextual biological process; mass spectrometry imaging to interrogate the dynamics of virus-host cell interplay; and artificial intelligence to correlate multi-modal biological events. 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 multidisciplinary 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: Molecular Virology; Protein Biochemistry, Protein Biophysics, Molecular Biology, Cell Biology, Imaging (Fluorescent, Electron Microscopy, Mass Spectrometry), Humanised Mice, and Artificial Intelligence.

Glycan-mediated attachment as a general principle amongst viruses-microbes-host interplay

Cell entry of human immunodeficiency virus (HIV) is mediated via the envelope glycoprotein (Env). Glycans comprise up to 40% of the mass of HIV Env and these glycan molecules are best known for their role as a "glycan shield" to prevent access of antibodies to non-glycan Env epitopes. Our lab has made a paradigm shifting discovery that interactions between a specific pair of glycans are vital to potentiate HIV-host cell attachment. This strategy of glycan-mediated adhesion acts as the first contact between viruses and cells, thereby increasing the HIV "dwell time" on the host cell surface, facilitating location of the known viral receptors on the cell surface for virus entry.

As the presence of a glycocalyx is a ubiquitous feature of membrane-enveloped structures (including viruses, bacteria, and cells), we will explore how these glycan-mediated attachment strategies are applicable to virus invasion in general, including (but not limited to): (i) the interplay between HIV, vaginal microbes, and host cell during transmission; (ii) the inter-species jump of zoonotic viruses; and (iii) the inflammation and/or immune activation via glycan-mediated interactions. This work requires: molecular virology and molecular biology tools in virus production in tissue culture; biochemical and biophysical evaluation to dissect mechanism; imaging analyses to track the movement of fluorescent tagged viral proteins; electron microscopy analyses to delineate the contextual biological process; and glycan-related mass spectrometry in glycan analyses. 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 multidisciplinary 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: Molecular Virology; Protein Biochemistry, Protein Biophysics, Molecular Biology, Cell Biology, Imaging (Fluorescent, Electron Microscopy, Mass Spectrometry), Glycobiology, Humanised Mice.

Nucleic Acids Based Rapid Point of Care Rapid Diagnostics

A major gap in the clinical diagnosis of infectious diseases is the lack of an accessible yet simple assay that possesses both the speed of rapid antigen test (RAT) and the accuracy of lab-based polymerase chain reaction (PCR). The development of GeneXpert cartridge-based PCR 3 has partially addressed this gap by reducing the requirement of skilled personnel, but the high cost of entry plus the ongoing maintenance of the GeneXpert device have limited the utility of GeneXpert in most resource-constrained settings. Early diagnoses to discern clinically indistinguishable viruses that require specific/precision treatment options are invaluable. Clustered regularly interspaced short palindromic repeats (CRISPR) was initially discovered as a microbial adaptive immunity against invaded pathogens via specific nucleic acids sequences recognition, and CRISPR-Diagnostic (CRISPR-Dx) has the potential to provide a rapid, accurate, and inexpensive diagnostic for point of care (POC).

Our lab has successfully applied CRISPR-Dx to detect, distinguish, and quantify highly related pathogens (including SARS-CoV-2 variants of concerns) under an hour. We will now apply this technology for the development of rapid diagnostics against both human and animal pathogens. This work requires: molecular biology approaches in sample preparation; biochemical analyses in detection; engineering microfluidic approaches to maximise detection; RNA biology, protein biochemistry, and dynamic structural biology to dissect mechanism; computational RNA biology in RNA modelling; chemical RNA probing and nanopore high-throughput sequencing in empirical RNA structure determination, and artificial intelligence to improve efficiency and field application of CRISPR-Dx. This project is PC2 based that is suitable to undergraduate students, PhD students and post-doctoral fellows. The successful applicant will be part of a larger multidisciplinary 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: Molecular Biology; RNA and Protein Biochemistry, Dynamic Structural Biology, Computational and Chemical Probing RNA Biology, High-Throughput Sequencing, and Artificial Intelligence.

Neutralising Biological Threats against Australian Native and Farm Animals

The Koala is the most celebrated iconic species in Australia. Pathogenic and non-pathogenic koala retroviruses (KoRVs) are prevalent in koalas and contributes to their decline in numbers in the wild. No simple solution can readily distinguish pathogenic KoRV-infected koalas from healthy koalas. Furthermore, there is no easy solution to cure koala from a pathogenic KoRV infection. The Australia Koala Foundation has estimated that the value of the koala to Australia equates to $3.2 billion per year and 30,000 jobs.

The frequency of infections via insect borne swine pathogens are expected to increase due to climate change. For example, infections with swine pathogens such as African Swine Fever Virus (ASFV) and Japanese Encephalitis Virus (JEV) have led to dire consequences to both the global and the Australian pig farming industry. The 2018-19 outbreak of ASFV wiped out USD$300 billion from the global economy. The 2022 JEV outbreak in Australia affected over 50 pig farms across multiple states southern Australia, which may have permanently impacted on future Australian pig farming.

This project will execute proof-of-concept experiments to develop a practical solution to eliminate pathogenic KoRV from infected koalas. We will also develop a novel platform of swine-specific vaccine with built-in boosters that are expected to bypass the requirement of repeated vaccinations as seen with other vaccines. This work requires: molecular virology-based approaches via tissue culture; biochemical and biophysical evaluation to dissect mechanism; imaging analyses to track the movement of fluorescent tagged viral proteins; and electron microscopy analyses to delineate the contextual biological process;. This project is PC2 based that is suitable to undergraduate students, PhD students and post-doctoral fellows. The successful applicant will be part of a larger multidisciplinary 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: Molecular Virology; Protein Biochemistry, Protein Biophysics, Molecular Biology, Cell Biology, Imaging (Fluorescent, and Electron Microscopy).

Research Leader | Professor Kate Seib
Associate Research Leader | Dr Evgeny Semchenko

Contact email: k.seib@griffith.edu.au; e.semchenko@griffith.edu.au

Does a licensed meningococcal vaccine protect against Neisseria gonorrhoeae?

Molecular Biology, Microbiology, Vaccine Development, Immunology

Other supervisors: Dr Evgeny Semchenko, Dr Taha and Dr Sherry Eskandari

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 disproportionally 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 and Dr Sherry Eskandari

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 and Dr Sherry Eskandari

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 middles 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.

Research Leader | Professor Victoria Korolik

Contact email: v.korolik@griffith.edu.au

Understanding the role of chemosenory perception in pathogenicity of Campylobacter jejuniMolecular Biology, Microbiology, Vaccine Development, Immunology

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 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.

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 though 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 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 a 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.

Research Leader | Associate Professor Thomas Haselhorst

Contact email: t.haselhorst@griffith.edu.au

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: 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

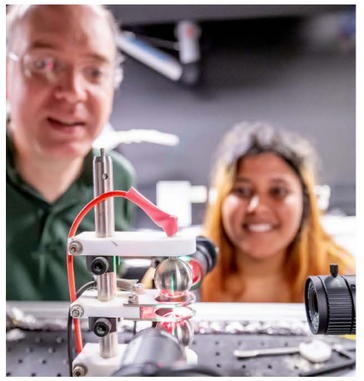
Structural Biology, Computational Chemistry, NMR Spectroscopy, Microbiology

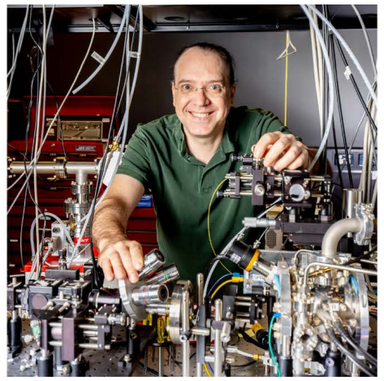
Other supervisors: Dr Chris Day

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.





Research Leader | Associate Professor Erik Streed

Contact email: e.streed@griffith.edu.au

Levitating yeast cells in an ion trap

Biophysics

Other supervisors: 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 and 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.

Research Leader | Associate Professor Daniel Kolarich

Contact email: d.kolarich@griffith.edu.au

Understanding protein glycosylation for precision immunotherapy

Glycoproteomics, cancer biology, Understanding cancer immunotherapy

Other supervisors: Professor Nicolle Packer, Professor Riccardo Dolcetti, Professor Mark von Itzstein AO

Cancer therapies have experienced a tremendous revolution with the introduction of therapies that use monoclonal antibodies that specifically target cancer cell surface targets and immune-checkpoint receptors. More than 95% of the protein receptors targeted by these immunotherapy agents are in fact glycoproteins, but to date the impact of receptor glycosylation in precision medicine is still not understood.

In this close collaboration with colleagues from the Peter MacCallum Cancer Centre students will be introduced to biochemistry and immunology 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. Cancers that are being targeted in this project include Leukaemia, prostate cancer, melanoma, Head and Neck Cancer, Hepatocellular carcinoma or Colon cancer are investigated.

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

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

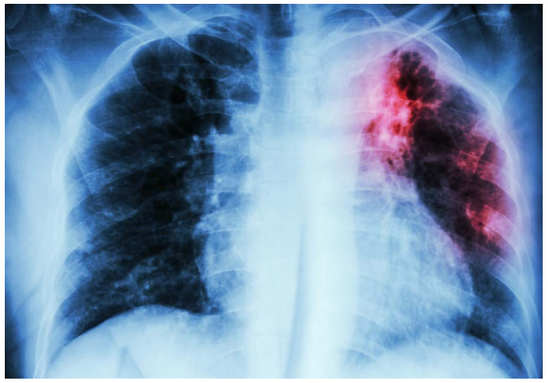
Other supervisors: Dr Arun Everest-Dass, Associate Professor Chamindie Punyadeera, Professor Mark von Itzstein AO

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.



Research Leader | Associate Professor Todd Houston

Contact email: t.houston@griffith.edu.au

Design and synthesis of synthetic receptors for cell-surface carbohydrates

Medicinal Chemistry

Other supervisors: Associate Professor 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 medicinally-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.

Research Leader | Dr Ian Peak

Contact email: i.peak@griffith.edu.au

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 and 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.

Research Leader | Associate Professor Lara Herrero

Contact email: l.herrero@griffith.edu.au

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 undertaking 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 susceptibility 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 undertaking in the state-of-the-art glycobioanalytical facility.

The quest to find treatments for mosquito-transmitted viruses

Virology, Immunology, Cellular and Molecular Biology

Other supervisors: Professor Mark von Itzstein AO

Mosquito-transmitted viruses (arboviruses) cause a range of clinical manifestations including encephalitis, arthritis, arthralgia and myalgia. Viruses in this group include the arthritogenic chikungunya virus (CHIKV), Ross River virus (RRV) and the deadly Japanese Encephalitis virus (JEV). With climate change and increasing globalisation, emerging arboviruses such as JEV, CHIKV and RRV are all examples of viruses which could follow Zika and be the next pandemic. Combatting mosquito-borne diseases is one of our most pressing global health challenges. We recently demonstrated that viral-induced disease is largely driven by activation of the host innate inflammatory response. We now aim to define the mechanisms underlying this inflammatory-mediated pathology. This project (backed by a prestigious NHMRC Synergy grant) will identify new host targets for the rapid development of innovative therapies against arboviruses of pandemic potential.

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

Research Leader | Professor Joe Tiralongo

Contact email: l.tiralongo@griffith.edu.au

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.

Research Leader | Associate Professor Thomas Ve

Contact email: t.ve@griffith.edu.au

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

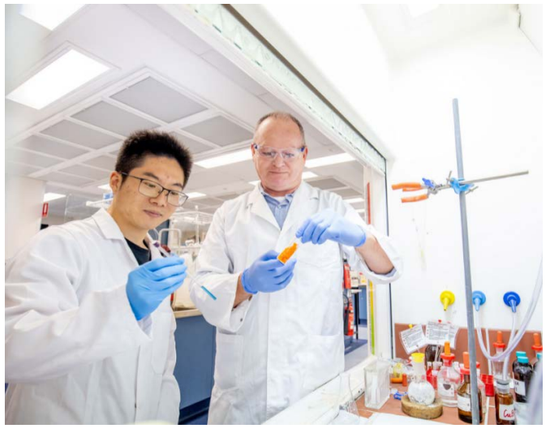
Other supervisors: Dr Yun Shi, Dr Andrea Maggioni, Professor Johnson Mak, Professor Mark von Itzstein AO

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.



Research Leader | Associate Professor Milton Kiefel

Contact email: m.kiefel@griffith.edu.au

Synthesis of ulosonic acids

Medicinal Chemistry

Ulosonic acids are a family of higher order sugars the 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.

Research Leader | Dr Darren Grice

Contact email: d.grice@griffith.edu.au

Analysis of surface carbohydrate structures from Gram-negative Moraxellaceae bacteria

Medicinal Chemistry

Other supervisors: Dr Ian Peak, Dr Jennifer Wilson

The aim of this project is to isolate surface carbohydrate components from bacteria in the Moraxellacae 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.

Research Leader | Dr Santosh Rudrawar

Contact email: s.rudrawar@griffith.edu.au

Development of novel molecular probes targeting neurodegenerative diseases

Neurodegeneration, Medicinal Chemistry, Biochemical assay and screening

Other supervisors: Professor George Mellick and Professor Anthony Carroll

Neurodegenerative diseases are characterised by the progressive loss of neuron function and structure. The most prevalent neurodegenerative diseases are hypothesized to be due to the misfolding and accumulation of specific proteins in the brain. Alzheimer's disease (AD) is suspected to result from the aggregation of amyloid-β (Aβ) or tau proteins, Parkinson's disease (PD) from the aggregation of α-synuclein (α-syn), and so on for numerous other diseases including Huntington's disease, amyotrophic lateral sclerosis, and Creutzfeldt-Jakob disease. There are no curative therapies for any of these fatal diseases, only palliative care is available in some cases currently. Research is currently focussed on modulating the aggregation processes common amongst the diseases. Various projects are dedicated to targeting the protein monomers, or small oligomeric assemblies, present at the early stages toward therapy. Modern strategies to target these proteins involve the use of peptide-based agents, effective at selectively binding the proteins through engaging with multiple sites along the protein sequences; and multi-target directed ligands (MTDL), which engage with multiple pathological factors to produce an overall beneficial effect.

Here we set out to investigate various novel chemical scaffolds that we envisaged may prove effective at inhibiting protein aggregation mechanisms in the hopes of identifying new strategies and promising leads. Following review of the literature, compound scaffolds will be designed based on existing data and then synthetic chemistry will be employed to construct panels of candidate inhibitors. The compounds synthesised will be then screened against protein aggregation including Aβ α-syn and prion formation.

Techniques: Carbohydrate chemistry, organic synthesis, enzyme assays, cell based assays

Development of metabolic chemical reporter as tools to investigate protein glycosylation

Neurodegeneration, Cancer, Medicinal Chemistry, Chemical biology, Biochemical assay and screening

Other supervisors: Dr Arun Everest-Dass

Glycoproteins are a class of proteins that are modified by the addition of glycans (sugar molecules) to specific amino acid residues. *O*-Glycosylation affects protein structure, stability, and function, and aberrant glycosylation has been linked to various diseases such as cancer and neurodegenerative disorders. *N*-Glycosylation (cell-surface glycans) is a complex process and glycans are involved in cell-cell communication, membrane protein trafficking, cell-pathogen interactions, immune signalling, development, and disease progression. Investigating the glycosylation of proteins is therefore important for deciphering their biological roles and developing new therapies.

Metabolic chemical reporters are small molecules that can be incorporated into glycans during glycosylation and then used to label and track glycoproteins. By designing and synthesising metabolic reporter reagents that are specific for certain glycan structures, it is possible to target cell surface glycans and investigate the glycosylation of specific glycoproteins in a highly selective manner.

In this project proposal, we aim to design and synthesise metabolic reporter reagents for investigating glycoproteins. We will focus on developing reagents that can be used to label glycoproteins (glycan editing) with specific glycan structures, such as sialic acid, glucose, galactose, mannose, *N*-acetylglucosamine containing glycans. The synthesised reagents will be tested on various glycoproteins, and their efficacy in labelling and tracking these proteins will be evaluated using a range of techniques, including mass spectrometry.

Techniques: Carbohydrate chemistry, organic synthesis, chemical biology, cell biology, glycoanalytics

Antimalarial drug development

Medicinal Chemistry, Chemical biology, Biochemical assay and screening

Other supervisors: Professor Katherine Andrews

The aim of this research is to contribute to improving and saving the lives of people suffering from malaria through the discovery of new malaria drug leads. Malaria is a parasitic disease that causes ~200 million clinical cases and >400,000 deaths each year. There is currently no broadly effective malaria vaccine and while antimalarial drugs are a front line defence, they are continually under threat because malaria parasites can develop resistance. This means that there is an urgent and unmet need for new drugs to prevent and treat malaria.

In this project, chemical compound libraries held at the Compounds Australia facility will be screened against P. falciparum parasites to identify new drug leads. In addition, compound will be tested against several unique P. falciparum lines to identify agents that act against new drug targets that we have identified. Following review of the literature, compound scaffolds will be designed based on existing data and synthetic chemistry will be employed to construct panels of candidate inhibitors for structure-activity relationship investigation.

Techniques: Carbohydrate chemistry, organic synthesis, chemical biology, cell biology, enzyme and cell-based assays

Griffith UNIVERSITY
Queensland, Australia

WHY CHOOSE GRIFFITH UNIVERSITY?

Ranked in the top 2% of universities worldwide

State-of-the-art facilities

Innovative teaching and learning

Support to reach your goals

International network of graduates

Australia's top teachers

Globally connected

Online or on campus study options

Flexible study options

Over 85% employer satisfaction with graduates

Contact us

Institute for Glycomics
Griffith University Gold Coast
Queensland, Australia 4222

Phone: (07) 5552 8051
Fax: (07) 5552 8098
Email: glycomics@griffith.edu.au

griffith.edu.au/glycomics

CRICOS No. 00233E

Griffith UNIVERSITY
Institute for Glycomics
Queensland, Australia