

# Queensland Infectious Disease Research Capabilities



August 2023

# Preface

The Queensland research community is committed to working together to enhance infectious disease research capabilities to tackle future pandemics and the continued threats posed by viruses, microbes and pathogens, including antimicrobial resistance. This Queensland Infectious Disease Research Capabilities document is the outcome of a comprehensive audit of infectious disease research capabilities across the state conducted in conjunction with Griffith University, QIMR Berghofer, University of Queensland, Queensland University of Technology, Bond University, University of the Sunshine Coast, James Cook University and the Translational Research Institute.

## Key messages

**Together we are a network of infectious disease scientists and clinicians recognised internationally for research excellence.**

### As a collective, we are:

Ready to respond to Australia's and the world's current and emerging infectious disease clinical and public health challenges.

Advancing Australia's capacity to respond to present and future global threats, including pandemics, through our collective infectious disease expertise, knowledge sharing and reach.

Positioned to partner with infectious disease collaboratives and initiatives across Australia.

Ideally placed to lead national efforts in tropical health biosecurity and diseases of high burden due to our proximity and close relationships with our neighbours in the Asia Pacific, including Papua New Guinea.

**Queensland's world-leading infectious disease research, development and translation sits across 4 key themes:**

## 1 Diseases

- Tropical and vector-borne
- Virus associated diseases and cancers
- Chronic and acute respiratory infections
- Pathogenesis and immunity
- Prevention and control
- Rural and remote communities

## 2 Diagnostics

- Development and optimisation
- Clinical translation
- Genomics and biobanking

## 3 Drugs

- Discovery and development
- Optimisation and stewardship
- Antimicrobial resistance

## 4 Vaccines

- Development
- RNA vaccines and therapeutics
- Platform and delivery technologies



# Fast facts

Queensland is home to:



160+

infectious disease  
group leaders  
or independent  
researchers



Collective outputs include (past 5 years):



40

highly cited papers  
(past 5 years)

\$1.0B+

in funding



Includes:

>\$257m

NHMRC, MRFF and  
ARC funding as lead  
Investigator

\$50m

in funding for UQ's  
molecular clamp  
vaccine platform

\$280m

partnership between  
Sanofi, Queensland  
Government, University  
of Queensland (UQ) and  
Griffith University to  
establish a Translational  
Science Hub for  
mRNA vaccines

\$90m

in commercial  
revenue from cellular  
therapies developed  
by QIMR Berghofer

## Queensland's end-to-end capabilities in infectious disease are supported by world-class infrastructure

Queensland's demonstrated end-to-end capabilities in infectious disease supports the critical pipeline required to translate research discoveries into clinical trials, leading to better treatments and care.

Queensland possesses extensive therapeutic and vaccine pre-GMP infrastructure and expertise across multiple modalities, including:

Basic Understanding of Disease

Prevention, Protection & Preparedness

Diagnostics & Interventions

Manufacturing

Treatments, Vaccines & Platforms

Clinical Trials

Better Policy, Practice & Care

### Biologics

National Biologics Facility - QLD Node

Protein Expression Facility (UQ)

### RNA Therapies and Vaccines

BASE Facility (UQ)

Queensland Translational Science Hub  
(Queensland Government, Sanofi, UQ and Griffith University)

Southern RNA

Griffith University's Nanomedicine Biofoundry

### Cell and Gene Therapy

Q-Gen (QIMR Berghofer)

University of Queensland Advanced Cell Therapy Manufacturing Initiative

Prorenata Biotech

### Small Molecule and Glycomic-based Therapeutics

Queensland Emory Drug Discovery Initiative (UQ)

Griffith Institute for Drug Discovery

Community for Open Antimicrobial Drug Discovery (UQ)

Institute for Glycomics (Griffith University)

### Enabling Infrastructure

Australian Infectious Diseases Research Centre  
(UQ – QIMR Berghofer)

Queensland Digital Health Centre (UQ)

Centre for Advanced Imaging (UQ)

National Imaging Facility Queensland-Node

Herston Imaging Research Facility

Herston Biofabrication Institute

Herston Infectious Diseases Institute

TRI Clinical Research Facility

University of the Sunshine Coast Clinical Trials Centre

Griffith University's Clinical Trial Unit

University of Queensland's ULTRA Clinical Trials Program

Queensland's capability has been further enhanced with the new Translational Manufacturing Institute at the Translational Research Institute (TMI@TRI) to provide Australia's first scale-up facility.

## 4 Key Themes of Excellence and Impact

# 1. Diseases

### Tropical and vector-borne diseases

Queensland (especially in the north) has a long history of research into the highest burden tropical diseases (predominantly malaria and tuberculosis (TB)) and neglected tropical diseases (including schistosomiasis, lymphatic filariasis, dengue, Chikungunya, Zika and scabies). For the past 20 years, James Cook University (JCU) has been a World Health Organization (WHO) Collaborating Centre

(WHOCC) for Vector-borne and Neglected Tropical Diseases, including melioidosis, with JCU Directors Profs Maxine Whittaker and Peter Leggat. University of Queensland (UQ), JCU and QIMR Berghofer have also hosted tropical disease research groups, working on dengue, arboviruses, malaria and TB for many decades.

**The State's research capabilities and expertise include:**

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#### Surveillance and control

- vector-borne disease surveillance, transmission and control, including building country-led capacity and engagement programs in our neighbouring South Pacific Islands. The PacMOSSI program based in JCU's Australian Institute of Tropical Health and Medicine (AITHM) is building capacity for vector surveillance and control in 22 Pacific Island and neighbouring countries
- developing new strategies to control and eliminate parasitic worm infections
- surveillance and transmission modelling of TB in PNG and Torres Strait Islands; zoonotic malaria vectors in Indonesia; and the Asian Tiger Mosquito in the Torres Strait Islands using novel male Aedes sound traps
- the impact of climate change on the emergence and transmission of infectious diseases, particularly zoonotic diseases, vector-borne diseases, environmental infectious diseases and methodological expertise in disease mapping and modelling, including estimation of Australia-wide Japanese encephalitis risks
- expertise in genomic and evolutionary analysis of emerging viruses, with the largest collection of dengue virus strains from Asia-Pacific over last 3 decades
- the most extensive collection, surveillance and genomic analysis of environmental and clinical Burkholderia pseudomallei outside the Northern Territory
- investigating the cost-effectiveness of new treatments for malaria when associated diagnostic testing is required (e.g., testing for G6PD deficiency prior to malaria treatment)
- early detection of Ross River virus and Barmah Forest outbreaks
- assessment of the capabilities of current malaria rapid diagnostic tests in Africa by monitoring for the presence of hrp2-deletions in *Plasmodium falciparum*

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#### Pathogenesis, Host-Pathogen interactions and Innate Immunity

- using molecular and structural biology and genetics to identify potential drug targets
- developing and characterising mouse models to gain new insights into the factors that regulate viral and bacterial infections
- isolation and genetic characterisation of new arthropod-borne viruses
- identifying regulators of immune responses during infection
- understanding the molecular basis of pathogenesis
- using CRISPR to address virulence in human helminth infections
- mechanistic studies of tropical infectious disease immune dysregulation

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#### Diagnosis

- developing and commercialising rapid, cost-effective and non-invasive point-of-care (POC) diagnostic tools
  - working with agencies and pharma companies, such as the WHO, Foundation for Innovative New Diagnostics, Merck Global Health and Australian Army Malaria Institute to improve the quality of diagnostic tools used for clinical diagnosis of malaria
  - developing new diagnostics for Strongyloides stercoralis with national partners in Strongyloides Australia
  - identifying rare and emerging parasitic zoonosis in Australia
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## Preclinical models and human challenge studies

- human malaria challenge studies
  - mouse and non-human primate models
  - pre-clinical model of tuberculosis pathology and rare patient samples
  - toxicology expertise
  - human clinical trials
  - experimental human hookworm challenge studies
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### Some examples of successful translation of research include:

- Infectious diseases physician and Professor of mathematical and statistical modelling of disease transmission, Emma McBryde (AITHM/JCU) has supported a number of countries to develop their national TB programs, including allocation of TB resources using transmission dynamic and health economic models. This includes: Papua New Guinea (PNG), the Philippines, Fiji, Pakistan, Bhutan, Mongolia and Bulgaria.
- A/Prof Bridget Barber (QIMR Berghofer) leads a team that has performed Phase I testing of 6 new anti-malaria drugs in the past 10 years and enabled new insights into the pathogenesis of malaria and host immunity.
- Dr Katja Fischer (QIMR Berghofer) has made outstanding contributions to research on scabies. In 2023, Dr Fischer's most recent project is developing a Point-of Care diagnostic test for scabies which is funded by the DIORAPTE Foundation (NL).
- Prof Scott Ritchie (JCU) played a lead role in the Bill and Melinda Gates Foundation-funded Eliminate Dengue program that used Wolbachia carrying mosquitoes to eradicate dengue from Far North Queensland.
- A/Prof Stephan Karl (AITHM/PNG Institute of Medical Research) built the entomology section of the PNGIMR to over 50 staff. He co-leads large-scale investments (incl. Department of Foreign Affairs and Trade >AU\$ 9m and National Institute of Allergy and Infectious Diseases >AU\$5m) to build vector surveillance and control capacity and conduct implementation research in PNG. His research on long-lasting insecticidal nets for malaria prevention (Nat. Comm, 2021) has changed regional policy and global vector control guidelines.
- A/Prof Daniel Watterson (UQ) identified a new target, NSI, for flavivirus, and showed for the first time that NS1 antibody has a broad range of protection against multiple flaviviruses, including dengue, Zika and West Nile.
- Prof Tom Burkot (AITHM/JCU) leads DFAT-funded \$5m PacMOSSI program. He is a Fellow of the American Society of Tropical Medicine and Hygiene, and holds positions on the Malaria Policy Advisory Committee and the Malaria Elimination Oversight Committee of the WHO Global Malaria Programme, the Aedes albopictus Torres Strait Programme Technical Advisory Group, the Indo-Pacific Initiative Advisory Group of the Innovative Vector Control Consortium, and is on the Management Board of Building Out Vector Borne Diseases in Sub-Saharan Africa.
- Prof Michelle Gatton (QUT) developed an online semi-real-time outbreak detection tool for Ross River virus and Barmah Forest virus to assist Queensland Health and local governments within Queensland to rapidly identify increased transmission of both viruses. Prof Gatton also provides expert advice to the WHO Global Malaria Programme to inform policy on malaria diagnostics, and surveillance of malaria.
- Prof Antje Blumenthal (UQ) in collaboration with Metro South Health Clinical Tuberculosis Services and international collaborators is developing a comprehensive platform for pre-clinical evaluation of TB drug and vaccine candidates.
- Prof Colleen Lau's (UQ) clinical travel medicine research has influenced Australian and international guidelines for clinical practice, including vaccine schedules, intradermal vaccinations, and malaria prophylaxis. Studies on the efficacy of fractional dosing of the Japanese encephalitis vaccine has been used by ATAGI to inform vaccination strategies for the recent outbreak in Australia. Further, since 2014, Prof Colleen Lau (UQ) has led operational research projects on lymphatic filariasis elimination, leptospirosis, and arboviruses in the Pacific Islands.
- JCU's A/Prof Patrick Schaeffer has developed a novel TT-lock Immuno-PCR platform and demonstrated its application in the diagnosis of melioidosis as well as a sensitive assay to detect the presence of the influenza nucleoprotein.
- A/Prof Greg Devine (QIMR Berghofer) leads a research program to characterise, monitor and manipulate the entomological determinants of arbovirus and malaria transmission in Australia and globally. He steers the Mosquito and Arbovirus Research Committee which helps local and state government prioritise, fund and conduct research relevant to operational disease control.
- Dr Paul Giacomini and Distinguished Prof Alex Loukas (AITHM/JCU) lead the world in experimental human hookworm challenge models and clinical trials on experimental worm infections, which has included securing \$5m from the US Defense Department DARPA program.
- A/Prof Roslyn Hickson (AITHM/JCU) leads a joint program with CSIRO on emerging infectious diseases, including wildlife disease, zoonotic spillover, and vector-borne diseases. Their work encompasses 'omics' based approaches to understand and characterise high-risk human-animal interfaces to understanding transmission risks and informing policy and practice.
- A/Prof Paul Horwood (JCU/AITHM) is a member of the Human Animal Spillover and Emerging Diseases Scanning (HASEDS) national working group responsible for reporting emerging disease threats directly to the Australian Chief Veterinary Officer, Chief Medical Officer, and Chief Environmental Biosecurity Officer.
- A/Prof Catherine Rush (AITHM/JCU) leads studies into TB and drug resistant TB (DR-TB) susceptibility and resilience in rural PNG, including the characterisation of gastrointestinal parasite and bio-smoke induced immune dysregulation.
- A/Prof Jeffrey Warner (AITHM/JCU) established the molecular epidemiology of melioidosis in PNG plus factors that enable persistence of Burkholderia pseudomallei in the North QLD environment.

- UniSC's A/Prof Joanne Macdonald has developed a rapid genetic detection platform for tropical diseases, including Hendra and Nipah viruses, dengue, malaria, and anti-microbial resistance, in collaboration with A/Prof Greg Divine, Dr Leon Hugo, A/Prof Bridget Barber, and Prof Andreas Suhrbier (QIMR-Berghofer); A/Prof David Whiley, Dr Jody Peters and Prof Roy Hall (UQ); and Dr Andrew van den Hurk (Forensic and Scientific Services, Queensland Health). Significant funding has been leveraged from the Bill and Melinda Gates Foundation, the National Foundation of Medical Research Innovation, the DMTC medical countermeasures program, and industry partner BioCifer Pty Ltd.
- Prof Colleen Lau's (UQ) research on lymphatic filariasis has contributed to the global evidence base for improving surveillance strategies for elimination programs, including the use of spatial epidemiology to identify hotspots, and evaluation of new diagnostics and molecular xenomonitoring.
- Prof Christian Engwerda and Bridget Barber (QIMR Berghofer) and Prof Denise Doolan (UQ) are using controlled human infection models to understand induction of protection against malaria to discover new host-directed therapeutics.
- Dr Martina Jelocnik (UniSC) leads research into the molecular epidemiology, control and diagnosis of One Health chlamydia, with a special focus on the zoonotic pathogen *Chlamydia psittaci*. She also works on the development of rapid isothermal assays that can be deployed at the Point-of-Care for detection of chlamydia and other pathogens.
- Prof Nigel McMillian (Menzies Health Institute Queensland; MHIQ at Griffith University; GU) was the first to show that human papillomavirus (HPV)-driven cancer can be eliminated completely using CRISPR, through showing that CRISPR/Cas9-loaded stealth liposomes effectively clear established HPV16-driven tumours in syngeneic mice.
- Prof Rajiv Khanna AO (QIMR Berghofer) successfully completed Phase I clinical trial on adoptive immunotherapy for drug-resistant CMV infection in solid organ transplant patients and developed the research behind the QuantiFERON-CMV, a whole blood interferon-gamma release assay to monitor changes in cell-mediated immunity to CMV marketed by Qiagen. Prof Khanna is currently conducting a Phase I clinical trial of "off-the-shelf" allogeneic virus-specific T cell therapies for treatment or prevention of virus-associated complication in adult solid organ transplant recipients and pediatric stem cell transplant recipients. Prof Khanna is also extending clinical testing of allogeneic CMV-specific T cell therapy for recurrent and primary glioblastoma/astrocytoma grade IV.
- Prof Rajiv Khanna AO and A/Prof Corey Smith's (QIMR Berghofer) work in epitope mapping, cell-mediated immune responses and development of cellular therapies for transplant patients and has generated more than \$90m in commercial revenue since 2018.
- A/Prof Annika Antonsson (QIMR Berghofer) works on risk factors for HPV-driven oropharyngeal cancers and oral HPV infection in the general population. Her work has the potential to identify people at risk of developing oropharyngeal cancer and early detection of HPV-driven oropharyngeal cancers (Int J Cancer. 2023).
- Prof Maher Gandhi (Mater Research Institute-UQ; Princess Alexandra Hospital) and Dr Colm Keane UQ; Princess Alexandra Hospital) showed for the first time that Epstein-Barr virus (EBV)-associated primary central nervous system lymphoma (PCNSL) in the immunosuppressed is immunobiologically distinct from EBV2- HIV2- PCNSL, and, despite expressing an immunogenic virus, retains the ability to present EBV (Blood, 2021). Based on this research, they tested several patients with a combination of ibrutinib and EBV-specific T cells (Am. J. Transplant., 2021), which led to MRFF funding for an early phase clinical trial led by the Australian Leukemia and Lymphoma Group (ALLG) and a second MRFF grant to expand the research via another Phase 1 clinical trial.

## Virus associated diseases and cancers

Queensland is internationally recognised for its world-class research and development in virus associated diseases and cancer, with Prof Ian Frazer and the late Dr Jian Zhou developing the basic technology behind the human papillomavirus vaccine against cervical cancer, Gardasil®. Prof Rajiv Khanna (QIMR Berghofer) is a world leader in the development of novel immunotherapeutic strategies for the treatment of virus-associated cancers and post-transplant infectious complications and is currently involved in a clinical trial evaluating cellular immunotherapy to prevent viral complications (specifically, Cytomegalovirus (CMV), Epstein-Barr Virus (EBV), BK virus and adenovirus) in children undergoing stem cell transplants. Furthermore, QIMR Berghofer houses Q-Gen Cell Therapeutics, a fully integrated GMP standard manufacturing facility for translating clinical research to the bedside.

### Examples of world-leading research that has or will lead to changes in clinical practice:

- Distinguished Prof Alex Loukas (AITHM/JCU) and collaborators from the US, Thailand and the UK and the Netherlands successfully used the gene-editing tool CRISPR/Cas9 to limit the impact of parasitic worms responsible for schistosomiasis and for liver fluke infection, which can cause a diverse spectrum of human disease including bile duct cancer.
- A/Prof Corey Smith (QIMR Berghofer) led the development of the first TGA licenced manufacturing process for T cell immunotherapy production in Australia for a Phase I/II trial in EBV-associated diseases.
- Prof Denise Doolan (UQ) is deciphering the role of EBV in risk of EBV-associated cancers and developing a novel diagnostic platform for EBV infection-related cancers and expanding that to EBV-associated autoimmune diseases (Multiple Sclerosis).

## Acute and chronic respiratory infections

Queensland researchers and academic clinicians are international leaders in the area of acute and chronic respiratory infections, specifically in the areas of (i) chronic infections in Cystic Fibrosis (CF) and Bronchiectasis (both in the paediatric and adult settings); (ii) pediatric respiratory infections, including clinical management of cough, bronchiectasis and pneumonia; and (iii) potential vaccine and therapeutic strategies for the control of the Respiratory Syncytial Virus (RSV), a major cause of hospitalisation of children with respiratory infections and (iv) acute respiratory infections in primary care. Profs Scott Bell and Claire Wainwright are ranked as the #5 and #9 experts globally and #2 and #5 experts nationally for CF (Expertscape, Aug 2023). Prof Anne Chang is ranked #2 globally for cough and #3 globally (and #1 nationally) for bronchiectasis, with Prof Keith Grimwood ranked as #2 nationally for bronchiectasis (Expertscape, Aug 2023).

## Examples of world-leading research that has or will lead to changes in clinical practice:

- \$15m in investment was secured to establish the Queensland Cystic Fibrosis Research Program, which includes ~A\$9m from US-based Cystic Fibrosis Foundation and \$2.1m from MRFF. The Program is co-led by Profs Peter Sly, Claire Wainwright and Scott Bell across CHQ and The Prince Charles Hospital (TPCH), and is focused towards tackling premature loss of lung function, progressive lung disease and antibiotic resistance in CF. This includes Prof Wainwright and Prof Rachel Thomson leading a global adaptive clinical trial - the Finding the Optimal Regimen for Mycobacterium abscessus Treatment (FORMAaT), a world first study to produce high quality evidence for the treatment of Mycobacterium abscessus complex—a group of drug-resistant, non-tuberculous mycobacteria.
- Queensland researchers, Profs Lidia Morawska (QUT), Claire Wainwright (CHQ/UQ), Scott Bell (TRI/UQ), Keith Grimwood (GU/Gold Coast University Hospital) and Drs Luke Knibbs (UQ) and Timothy Kidd (UQ) were awarded the 2018 Eureka Prize for Infectious Diseases Research. This was in recognition of the team uncovering the process by which the deadly pathogens causing airway infections are transmitted between CF patients.
- A/Prof Simon Phipps is an expert in the preclinical modelling of acute lower respiratory infections (ALRI) and has identified numerous immune-mediated pathways that drive severe disease and the development of chronic respiratory diseases. He has discovered that a healthy infant gut microbiome limits ALRI severity and is working with industry to improve the composition of infant formula (via the use of synbiotics) to promote infant growth and immune development.
- Prof Rachel Thomson (UQ, TPCH, Princess Alexandra Hospital (PAH), Gallipoli Medical Research Institute) chairs the American Thoracic Society's Assembly on Pulmonary Infections and Tuberculosis—a global collaborative of over 2,800 clinicians, scientists, and public health practitioners focused on all aspects of pulmonary infections and host defense.
- The Prince Charles Hospital's (TPCH) Adult Cystic Fibrosis Centre is leading the worldwide trial of a breakthrough drug CFTR (cystic fibrosis transmembrane conductance regulator) that has the potential to revolutionise care worldwide by targeting the cause for the first time rather than managing symptoms.
- Prof Claire Wainwright (Children's Health Queensland; CHQ/UQ) was a key contributor to the international clinical trial that led to Orkambi® being listed on the PBS in October 2018.
- Prof Anne Chang's respiratory research (cough, asthma, pneumonia, bronchitis) has been incorporated into 27 national/international treatment guidelines. She also diagnostically categorised a new infection-related condition, protracted bacterial bronchitis (PBB) in 2006, which globally changed the way chronic wet cough is treated and led the world's first guideline on the management of chronic cough in children. She was the sole Australian in the 2006 American College of Chest Physician's Cough Guidelines.
- Prof Peter Sly (UQ) is internationally recognised in the area of environmental child health. He is the Director of the Children's Health and Environment Program (CHEP), former Director of the WHO

Collaborating Centre for Children's Health and Environment Program, former chair and current Emeritus member of the Pacific Basin Consortium (PBC) and is an advisor to the WHO Department of Public Health, Environmental and Social Determinants of Disease.

- Profs Matt Sweet and Peter Sly and their teams (UQ) have discovered that immune cells from people with CF are defective in zinc-mediated killing of bacteria. This information is being used to design strategies that restore this immune response in people with CF to reduce bacterial infections.
- Research by Prof Lydia Morawska (QUT), an internationally renowned aerosol physicist, led to the World Health Organisation changing their stance on COVID-19 being transmitted through the air as an aerosol.
- Bond University's A/Prof Mark Jones and Emeritus Prof Mieke van Driel (UQ) are the coordinating editors of the NHMRC funded Cochrane Acute Respiratory Infections Collaborative Group since 2001, which was established to conduct Cochrane systematic reviews of the evidence for treatment and prevention of acute respiratory infections which have been essential underpinnings for antibiotic guidelines in Australia and internationally.
- Prof Bell (UQ/TPCH/Translational Research Institute) was one of two selected from a pool of experts worldwide, to assess the global health and economic challenges of CF over the next three decades and to provide the blueprint for care going forward.
- Dr Tim Wells (UQ), Prof Daniel Chambers (TPCH, UQ) and Dr Daniel Smith (TPCH, UQ) are pioneering a new treatment for drug-resistant bacterial infections, that fights infection through blocking antibodies in chronic airway pathogens in CF, bronchiectasis and post lung transplant. The experimental treatment, which involves a technique called "plasmapheresis", was used to successfully treat an untreatable infection in a CF patient that underwent a double lung transplant.
- An experimental Alzheimer's disease treatment, repositioned as an anti-infective agent, is proving effective at treating some of the most persistent, life-threatening antibiotic-resistant bacteria. Profs Mark von Itzstein (Institute for Glycomics, GU), Mark Walker (UQ) and their teams, in collaboration with researchers from the University of Melbourne, have discovered that the drug called PBT2 is effective at disrupting and killing a class of drug resistant bacteria – known as Gram-negative bacteria – that cause infections such as pneumonia, bloodstream infections and meningitis.
- Dr Hillary Vanderven (AITHM/JCU) along with collaborators from Myrio Therapeutics, CSIRO, University of Melbourne and Monash are developing and testing new antibody-based therapies to treat severe influenza virus infections.

## Pathogenesis and Immunity

Queensland researchers are global leaders in unveiling the mechanisms of action of how pathogens induce disease in humans. This includes identifying and validating potential therapeutic targets that can be progressed into formal drug discovery programs.

- Distinguished Prof Alex Loukas (AITHM/JCU) and colleagues have developed a human challenge model for hookworm infection and showed its utility for testing new vaccines (Lancet Infect Dis., 2021) and as a therapeutic modality for treating inflammatory conditions (Nature Comms, 2023).



- Prof Suresh Mahalingam (MHIQ, GU) studies how mosquito-transmitted alphaviruses cause disease, particularly arthritic disease. The team focuses on two major viruses: 1) Ross River virus, and 2) Chikungunya virus, which is a globally distributed pathogen that causes debilitating febrile arthritic disease. Prof Mahalingam's team has made numerous insights into mechanisms of alphavirus disease, a number of which have led to new approaches to drug and vaccine development (Lancet Infect Dis, 2017). Prof Mahalingam, in collaboration with researchers from University of Tartu and University of Glasgow developed a suite of molecular tools for basic and applied COVID-19 research (PLoS Biology, 2021).
- Prof Alexander Khromykh (UQ) invented circular polymerase extension reaction (CPEP) methodology for rapid generation of infectious cDNAs for a range of positive strand RNA viruses, which Prof Khromykh recently applied to SARS-CoV-2 (Nat. Comm., 2021), to discover Zika virus transmission determinant (Nat. Comm., 2020), and to co-invent a new vaccine platform based on insect-specific flaviviruses (Sci. Translat. Med., 2019, patent).
- Prof Mark Walker (UQ) and the team discovered a variety of *Streptococcus pyogenes* bacteria that had acquired "superantigen" toxins that allowed the bacterium to better colonise its host. They showed that removing these the toxin genes from the clones causing scarlet fever reduced colonisation in an animal model of infection (Nat. Comms, 2020).
- A/Prof Bridget Barber and Prof Christian Engwerda (QIMR Berghofer) and Dr Michelle Boyle (now Burnet Institute) are testing a small molecule inhibitor of human cytokine signaling pathways that acts synergistically with anti-parasitic drugs to improve parasite clearance and enhance anti-parasitic immunity. This Phase Ib controlled human malaria infection study is being conducted in collaboration with the Sunshine Coast University (UniSC) Clinical Trials Unit.
- Prof Ian Henderson (UQ) was part of an international team that discovered the cellular machinery responsible for exporting lipids to the outer membrane of Gram-negative bacteria, with previous work from his team showing that mutation of the genes involved in lipid transport renders bacteria unable to cause disease (Nature Microbio, 2019).
- Prof Paul Young (UQ) and team identified a flavivirus protein (virus group including dengue, West Nile, Japanese encephalitis viruses etc.) that operates as a viral toxin, responsible for the vascular leak characteristic of severe disease in dengue patients, and CNS involvement of WNV. They have gone on to show that this protein is a viable target for drug design and development (a patented target).
- Profs Matt Sweet and Mark Schembri (UQ) and their teams discovered that *uropathogenic Escherichia coli* (UPEC), the major cause of UTIs, has a two-pronged strategy to survive the body's immune response. They showed that compared to non-pathogenic bacteria, UPEC can evade the zinc toxicity response of macrophages, but these bacteria also show enhanced resistance to the toxic effects of the zinc (PNAS, 2019).
- A/Prof James Fraser (UQ) and team solved the first crystal structure of a fungal ADS lyase from *Cryptococcus neoformans*, which revealed features that could be exploited in antifungal drug design (JBC, 2017).
- A/Prof Mohammad Katouli and team (UniSC) have identified specific *E. coli* strains that have a better ability to colonize the gut epithelium, translocate and survive in mesenteric lymph nodes before entering the blood to cause septicemia. Their research has identified the molecular mechanism by which these bacteria translocate efficiently and are currently focused on the use of probiotics to prevent development of gut-associated septicemia.
- Prof Johnson Mak (Institute for Glycomics, GU) is leading an NIH-funded study of how HIV-1 interacts with vaginal microbes and their role in HIV-1 infection and transmission (Cell Reports, 2022).
- Dr Daniel Rawle and Andreas Suhrbier (QIMR Berghofer) have, using the Institute's state of the art PC3 facility, characterised a new mouse model of Japanese encephalitis (JEV), which includes the new Australian outbreak genotype 4 virus. A recently awarded MRFF grant seeks to work with Southern RNA to develop a new JEV RNA vaccine.
- Profs Mark Walker and Mark Schembri (UQ) led a study on the four main bacteria that cause sepsis to find common responses and identify potential new targets for antibiotics that target all sepsis-causing bacteria (Nat. Comm., 2023). Prof Walker is also a co-lead of a genomic surveillance program tracking Strep A bacteria, which discovered a new variant in Australia (Nat. Comm., 2023).
- Prof Antje Blumenthal (UQ) and team were the first to discover that small molecule inhibitors of the transcription factor that controls key virulence genes in *Listeria monocytogenes*, a common food-borne pathogen, enable host macrophages to eliminate the pathogen in processes that no longer require the help of T cells. This has implications for developing strategies for treating potentially fatal *Listeria* infections in vulnerable individuals with compromised immune systems (PLOS Pathogens, 2022).

## Prevention and control

Queensland is home to world-leading clinician researchers in infection prevention and control, including non-pharmaceutical interventions. Profs Amanda Ullman (UQ/Children's Health Queensland; CHQ) and Claire Rickard (UQ/Royal Brisbane & Women's Hospital; RBWH) and are the #1 and #2 experts globally for Vascular Access Devices, and #5 and #1 experts globally for Occlusive Dressings and Catheter-Related Infections (Expertscape, Aug 2023). Prof Glasziou has been named in Clarivate's Highly Cited Researchers list three times over the last five years. Queensland University of Technology (QUT) researchers and engineers are working closely with RBWH academic clinicians on virus and bacterial reduction on surfaces and with TPCH academic clinicians and Stryker on antibacterial technology for use for use on surgical implants and equipment.

### Examples of world-leading research that has or will lead to changes in clinical practice:

- Prof Claire Rickard (UQ) and Geoff Playford (PAH) conducted a landmark clinical trial to identify the optimal duration of infusion set use to prevent life-threatening catheter-related bloodstream infections (6007 patients across 10 Australian hospitals) (The Lancet, 2021).
- Prof Paul Glasziou (Bond University) is co-founder of a global collaboration established to use, improve & evaluate effective Behavioural, Environmental, Social and Systems Interventions (BESSI) to reduce viral transmission for future epidemic and pandemic preparedness.

- Prof Sophia Couzo (JCU) instigated and led the development of seminal clinical practice guidelines, including leading the 3rd edition of the National Guide to a Preventive health Assessment for Aboriginal and Torres Strait Islander Peoples for the NACCHO in partnership with the RACGP.
- Prof Prasad Yarlagadda (UniSC) is leading world-class research into virus and bacteria reduction on surfaces with Profs Kirsten Spann (QUT) and Michael Schuetz (QUT/Royal Brisbane and Women's Hospital; RBWH) (ACS Biomater Sci Eng, 2020) and antibacterial technology for use with titanium for both orthopaedic implants and other surgical equipment with Prof Ross Crawford (QUT/TPCH) and the international medical technologies company, Stryker.
- Dr Johanna Kenyon (QUT) pioneered the approach to characterising immunogenic surface polysaccharides produced by *Acinetobacter baumannii*; research that informs development of vaccine and phage therapies. She also developed an internationally-adopted polysaccharide typing system that contributed to transforming the approach to trace local and global outbreaks.
- A/Prof Yoni Nazarathy (UQ) and international colleagues have developed Safe Blues – an App that provides real time population-level estimates of the level of physical proximity and near-future projections of the epidemic (Patterns, 2021).
- A/Prof Clair Sullivan and Dr Magid Fahim (UQ) played key roles in Digital Metro North's response to COVID-19, developing an App which digitised the paper capture of arrival cards into the State. This information could then be readily reused to help health services plan to look after these individuals by knowing how many people there were, where they were and how long they were going to be in self-quarantine for.
- Researchers from the Queensland Alliance for Environmental Health Sciences (QAEHS, UQ), CSIRO and Monash University have successfully designed and validated novel passive sampling techniques which have been effectively deployed in upstream sewage networks in QLD to monitor the transmission of COVID-19 across different areas within the wastewater catchment.
- Prof Michael Monteiro (UQ) and team have developed, in collaboration with Boeing Pty Ltd and the University of Melbourne, a new anti-viral polymer coating which is highly effective against all COVID-19 variants and other viruses tested (e.g., Influenza A). The polymer coating has been tested on the International Space Station (ISS) and will be tested again in November 2023. The work has resulted in two publications and 5 patent families.
- Prof Colleen Lau (UQ) and her team led the development of a COVID-19 Real-time Information System for Preparedness and Epidemic Response (CRISPER) for Australia, which included a suite of interactive tools, maps and apps to optimise information sharing and decision making for the individuals, clinicians, and public health decision makers.
- Prof Colleen Lau (UQ), A/Prof Kirsty Short (UQ) and their teams led the development of a CoRiCal (COVID Risk Calculator) – decision support tools to help individuals and clinicians weigh up the risks versus benefits of the COVID-19 vaccines.
- Australian Red Cross Lifeblood (Prof Robert Flower, Dr Elvina Viennet and Dr Eileen Roulis) in collaboration with Dr Helen Faddy (UniSC) and others work on a myriad of infectious diseases, including those considered emerging, and their impact on blood transfusion safety, with an overall aim to improve the safety of the blood supply in Queensland and nationally.



## Rural and remote communities

Queensland researchers and academic clinicians are internationally recognised for their research and clinical trials in infectious disease elimination and clinical management in rural and remote Indigenous communities, specifically in paediatric and young adult populations. Prof James Ward (UQ) and A/Prof David Whiley (UQ/ Pathology Queensland) have a large program of research focused around eliminating sexually transmissible infections and reducing the risk of blood-borne viruses in remote Indigenous communities in the NT, WA and far north QLD. Prof Emma McBryde (AITHM/ JCU) is one of Australia's most renowned infectious disease modellers and Infectious diseases physician working in Northern Australian Indigenous communities, and the Torres Strait Islands. Prof McBryde is developing evidence-based systems approach to reducing the rate of methicillin-resistant staphylococcus aureus in remote and very remote areas of Northern Australia.

Prof Anders Cervin (RBWH/UQ) leads a program of research, collaborating with Profs Kirsten Spann (QUT), Flavia Huygens (QUT) and Dr Seweryn Bialasiewicz (UQ/Pathology Queensland) to identify alternative strategies to prevent and treat recurrent middle ear infection, which is especially prevalent in Indigenous children. Lastly, Prof Anne Chang (CHQ/Menzies/QUT) established the first international collaborative team investigating respiratory illness in Indigenous children.

### Examples of world-leading research that has or will lead to changes in clinical practice:

- Prof James Ward (UQ) established the ATLAS Indigenous Primary Care Surveillance and Research Network, which currently represents >40 Aboriginal Community Controlled Health Organisations (ACCHOs) and Indigenous communities nationally, including urban (10%), regional (25%) and remote (64%) areas. The key objective of the ATLAS Network is to collect de-identified surveillance data from ACCHOs and other primary health care providers across Australia to track and interpret patterns of infectious disease, including STI and BBV testing and treatment. The vision is to deliver the largest integrated Indigenous primary care surveillance network in Australia, increasing the capacity of Indigenous primary health care services to provide high quality, evidence-based, best practice clinical care. To date, data have

been analysed for >145,000 individuals aged ≥15 years attending medical consultations at ACCHOs between January 2016 and December 2022 - with the databank containing >6 million records for these individuals.

- Prof Anne Chang (CHQ/Menzies/QUT) has been CIA on 2 NHMRC CREs in respiratory health of Aboriginal and Torres Strait Islander children, with her research focused on improving the respiratory health of children living in the Torres Strait region of northern Australia.
- Dr Michelle Redman-MacLaren (JCU) is a public health researcher who facilitates qualitative and mixed methods research working with Indigenous peoples, especially Pacific Islander and Aboriginal and Torres Strait Islander peoples, to improve sexual and reproductive health, reduce transmission of infectious diseases and strengthen health systems. Her NHMRC-funded PhD research was focused on HIV prevention with women in Papua New Guinea.
- Research by Prof Cervin and colleagues has led to the identification of a number of bacterial strains that have the capability of interfering with the pathogenic bacteria common in chronic sinusitis as well as in recurrent ear disease. The team are now in the process of setting up clinical trials to test the effect of friendly bacteria on bacterial colonisation in the ears and sinuses, and should it be successful, it would be a paradigm shift in the way we treat upper airway infections and reduce the need for antibiotics.
- Prof Darren Gray and Dr Catherine Gordon (QIMR Berghofer) in collaboration with Strongyloides Australia are working on developing new diagnostics for Strongyloides stercoralis in remote communities, and community-led interventions to prevent infection.
- Prof McBryde has worked as Senior TB physician for Torres and Cape Hospital and Health Service and in this capacity has overseen research to inform practice changes, including diagnostic pathways for tuberculosis, and changes to alert systems for severe presentations in remote clinics. Prof McBryde also uses a combination of mathematics, in-silico simulation and medicine, to develop infectious disease modelling tools to inform government on COVID-19.

## 2. Diagnostics

### Development and optimisation Clinical translation Genomics and biobanking

Queensland is well known for the development and commercialisation of infectious disease diagnostic tests.

Examples include:

- Prof Flavia Huygens (QUT) co-founded Microbio, a biotechnology start-up company that uses bioinformatics, genomics and molecular microbiology for pathogen detection with a specific, sensitive and fast test - InfectID, which uses real-time PCR followed by high-resolution melt-curve analysis to identify pathogen species directly from whole blood without the need to pre-culture.
- Biocifer was established in 2016 to develop and commercialise a highly sensitive molecular genetics diagnostic platform, designed to be deployed in-lab, in-field and at the point of care to rapidly improve the speed of disease and pathogen detection – based on the research by A/Prof Joanne Macdonald (UniSC).
- Immunexpress is developing and commercialising SeptiCyte® technology to accurately rule-in or rule-out sepsis in patients suspected of infection. Immunexpress is a privately-owned company with offices in Seattle, USA, and Brisbane. Immunexpress' products are based on patented host immune response technologies validated in large human clinical trials around the globe.
- AnteoTech was established in 2000 as a raw materials diagnostic business, which in 2018 started developing in-house diagnostic tests. In March 2021, Anteotech obtained a CE mark approval for its portable antigen rapid test for Sars-Cov-2, with the company supplying raw material (AnteoBind™) for Ellume's home-based test. The company is currently working with several InVivo

Diagnostic and Global Life Science companies that are currently using or evaluating AnteoBind™ for incorporation into their next generation assay development.

- Prof Paul Young (UQ) and team identified the dengue virus protein NS1 as a diagnostic biomarker in the 1990s and worked with the local Brisbane diagnostics company Panbio (now part of Abbott) to develop and commercialize the assay. A diagnostic test for early detection of dengue in infected patients was released on to the market in 2006. The basis of this test (now in a lateral flow format) is now the global standard for early dengue diagnosis.
- Distinguished Prof Alex Loukas (AITHM/JCU) and colleagues were funded by Austrade and Merck Global Health to use immunomics approaches to discover and develop point-of-care diagnostic tests for urogenital schistosomiasis (Lancet Microbe, 2021).

More information about Queensland's diagnostic capabilities is located throughout this document.



# 3. Drugs

## Discovery and development

Queensland has a global reputation for its antimicrobial, antiviral and antiparasitic discovery and advanced drug development capabilities, infrastructure, and expertise. In addition to a wealth of drug discovery research throughout the university sector, the State houses state-of-the-art drug discovery research institutes - the Institute for Molecular Bioscience (IMB; UQ), Griffith Institute for Drug Discovery (GRIDD; GU), Institute for Glycomics (GU) and the Centre for Molecular Therapeutics (JCU). In addition, Queensland is home to Compounds Australia, the national compound management facility (GU), which curates ~1.5 million compounds and partners with ~45 national and international members. Compounds Australia also stores NatureBank (GU), Australia's largest natural product screening library of >125,000 extracts and fractions derived from a collection of >30,000 archived biota samples. Queensland provides unprecedented access to native flora and fauna from the Australian iconic Great Barrier Reef and ancient rainforests (AITHM, JCU).

Queensland hosts the Community for Open Antimicrobial Drug Discovery (CO-ADD; an open screening platform for antimicrobials, with comprehensive collections of multi-drug resistant clinical isolates), the Queensland Emory Drug Discovery Initiative (a joint drug development initiative between UQ and Emory University), and the Fraunhofer International Consortium for Anti-Infective Research, iCAIR® (an international partnership between the Institute for Glycomics (GU), and Germany's Fraunhofer Institute for Toxicology and Experimental Medicine, the Institute for Clinical Biochemistry at the Hannover Medical School, and Helmholtz Centre for Infection Research, focused on the discovery and development of drugs, vaccines, and advanced preclinical development services to combat respiratory infections).

QIMR Berghofer, GU (Institute for Glycomics), UQ (SCMB, IMB, TRI), and JCU (AITHM) have the capacity to perform candidate testing in PC<sub>3</sub> containment facilities. The QIMR Berghofer facility has attracted significant industry funded research, including from Biocifer, BTG, Zucero and InterK, GSK, Valneva, Leo Pharma, and the AITHM facility is rated the best small animal PC<sub>3</sub> facility in the nation by regulatory authorities (Office of the Gene Technology Regulator).

### Some examples of successful translation of discovery research include:

- Distinguished Prof Alex Loukas' (AITHM/JCU) discovery of proteins extracted from hookworm saliva, can prevent the development of symptoms associated with a range of inflammatory diseases. This research has been licensed into a start-up company, Macrobiome Therapeutics Pty. Ltd.
- Inflazome Ltd, a company founded on UQ (Profs Matt Cooper, Kate Schroder, and Avril Robertson) and Trinity College Dublin research, which is developing treatments by inhibiting the inflammasome, was acquired by Roche for an upfront payment of ~A\$617m plus additional milestone payments – making it one of the largest Biotech deals in Australian history.

- UQ researchers (led by Prof Mark Blaskovich) have secured up to ~A\$17.1m (dependent on meeting development milestones) from Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) to accelerate the development of Octapeptin engineered peptides aim to replace last-resort polymyxin antibiotics – this is the first Australian project in the CARB-X portfolio.
- Profs Antje Blumenthal, David Fairlie and Rob Capon (UQ) and their teams combine expertise in organic and medicinal chemistry, microbiology, molecular and cellular biology to refine and characterise new natural product inspired antimicrobial leads against drug-sensitive and multi-drug resistant tuberculosis (AAC 2019, Microbiology Spectrum 2023).
- A/Prof Lara Herrero (Institute for Glycomics, GU) discovered a potential new treatment strategy for viral arthritis caused by mosquito-borne alphavirus infections, including the debilitating Ross River virus and chikungunya virus, by repurposing the currently TGA/FDA approved glycotherapeutic Pentosan polysulfate, which was licensed to Paradigm Biopharma and has successfully completed phase II clinical trials. Under the TGA's Special Access Scheme, the repurposed drug Zilosul® was made available to physicians to treat patients with chronic arthritis caused by viruses.
- A research team led by Prof Mark von Itzstein AO (Institute for Glycomics, GU) has partnered with Hong Kong listed China Grand Pharma's newly established Australian company Grand Medical Ltd to develop a new drug for Human Parainfluenza Virus.
- Distinguished Prof Vicky Avery's team (GU) were the recipients of the world's leading NFP malaria drug development organisation, Medicines for Malaria venture (MMV), International Drug Discovery Project of the Year 2007 for innovative use of technology to identify new anti-malarials, and again in 2013 for their contribution to the clinical candidate, MMV390048, the first Plasmodium phosphatidylinositol 4-kinase inhibitor to reach clinical development as a new antimalarial.
- A research team led by Prof Mark von Itzstein (Institute for Glycomics, GU) and the Australian National University have co-developed a new experimental drug to treat sepsis that was licensed to China Grand Pharma's Australian-based subsidiary, Grand Medical Ltd, and has successfully completed a Phase 1a clinical trial in healthy volunteers, and is now undergoing a Phase 1b clinical trial in sepsis patients.
- Researchers at the Centre for Immunology and Infection Control (QUT), GRIDD (GU), ARC Industry Transformation Centre for Fragment Based Design (Monash) and La Trobe Institute for Molecular Science (LTU) are co-developing new experimental drugs to treat infections by multidrug resistant bacteria that inhibit a bacterial enzyme involved in protein folding. Industry partners include Vernalis Research, a HITGEN company.

- Prof Paul Young's team in the School of Chemistry & Molecular Biosciences (SCMB) at UQ identified the secreted dengue viral protein, NS1 as a viral toxin responsible for the severe pathology seen in some infected patients. Re-purposing of drug candidates and monoclonal antibody therapies are being trialled to treat these severe disease manifestations.
- Prof Ian Henderson's team in the IMB at UQ discovered antibody dependent enhancement of bacterial infections in HIV positive individuals and in patients with urosepsis and respiratory infections. This resulted in the first successful use of plasmapheresis for the treatment of infection in patients and resulted in clinical improvement in all patients treated.
- Under the leadership of Prof Nigel McMillian and in collaboration with the US research institute, City of Hope, researchers have developed a potential world-first COVID-19 antiviral therapy that was shown to reduce viral load in SARS CoV2-infected mice by 99.9 per cent.
- Prof Katherine Andrews and A/Prof Tina Skinner-Adams (GU) have identified a novel slow action activity for the malaria drug proguanil in partnership with CSIRO and the Medicines for Malaria Venture, contributing to understanding how this drug may work clinically.
- A/Prof Vito Ferro and team in SCMB at UQ have identified heparan sulphate (HS) mimetics as powerful antiviral agents. The angiogenesis and metastasis HS mimetic inhibitor PG545 is being re-purposed as a potent antiviral agent against a range of viruses including dengue virus and SARS-CoV-2.
- Research under the leadership of Prof Antje Blumenthal (UQ) in collaboration with intensive care specialists A/Prof Jeremy Cohen (RBWH) and Dr James Walsham (PAH) has identified that new drug candidates developed for cancer treatments may be repurposed for ameliorating damaging inflammation and cytokine storm in sepsis, without compromising the immune system's ability to control the underlying bacterial infection (Blood Advances 2017).
- A/Prof Markus Muttenthaler (UQ) and collaborators identified a strong association between the presence of gastrointestinal biofilms and irritable bowel syndrome and inflammatory bowel disease (Gastroenterology, 2021). They are currently pursuing nature-derived antibiofilm peptides as an oral treatment.

## Optimisation and stewardship

Queensland clinician researchers are international leaders in optimising antibiotic dosing in critically ill patients and antibiotic use in the primary care setting. Globally, Profs Jason Roberts and Jeff Lipman are ranked as the #1 and #3 experts in 'anti-bacterial agents' (Expertscope, Aug 2023).

## Optimising antibiotic dosing in critically ill patients

### Examples of world-leading research that has led to changes to clinical practice:

- Research led by Profs Jason Roberts and Jeff Lipman (UQ and RBWH) has led to the launch of universal Therapeutic Drug Monitoring guidelines (developed by 16 antibiotic experts across 11 countries) to optimise the concentrations of antibiotic and antifungal medications given to severely ill patients in hospital. This has led to the DIRECT study, which explores the combination of rapid diagnostics and dosing software to minimise the time to maximally effective antibiotic therapy in adults and children—a collaboration across TPCH, PAH, RBWH and QCH (Dr Adam Irwin and Prof Jason Roberts).
- Profs Jason Roberts and Jeff Lipman conducted the Defining Antibiotic Levels in Intensive care patients (DALI) study, which involved 384 patients across 68 hospitals and showed on a large scale that current beta-lactam antibiotic dosing in critically ill patients does not consistently achieve therapeutic drug exposures. Their data suggested that infected critically ill patients may have adverse outcomes as a result of inadequate antibiotic exposure and that a paradigm change to more personalised antibiotic dosing may be necessary to improve outcomes for these most seriously ill patients.
- UQ graduate, Dr Robert McLeay founded the Brisbane-based company, DoseMe, in 2012 to develop an App to support medical practitioners to provide precise and personalised drug dosing to their patients. Today it is a NASDAQ-listed Tabula Rasa HealthCare solution.
- Prof Jeff Lipman's research has been instrumental in changing antibiotic prescribing habits worldwide for critically ill patients - first with aminoglycosides (he conducted the first and still largest clinical trial to show single daily dosing to be more effective and safer than multiple daily dosing) and more recently with beta-lactam antibiotics – where Profs Lipman, Roberts and Paterson are leading a multi-centred Phase 3 study (BLING III) that compares the effect on 90-day mortality of -lactam antibiotics administered via continuous versus intermittent infusion in 7,000 critically ill patients with sepsis - the largest clinical trial investigating antibiotic dosing in serious infections.
- Dr Patrick Harris (UQ/Pathology QLD) and Prof David Paterson conducted the world's largest trial on antibiotics for extended-spectrum beta-lactamase producing bacterial infections (the "MERINO trial"), involving 30 hospitals across 9 countries – it was voted the trial most likely to change clinical practice by attendees of the 2018 Infectious Disease Society of America annual meeting.
- Prof Peter Timms, Dr Samuel Phillips (UniSC) and collaborators from the University of Melbourne conducted a world first RCT on the treatment of rectal Chlamydia trachomatis infections, testing the efficacy of Doxycycline and Azithromycin (New England Journal of Medicine, 2021).

## Antibiotic use in the primary care setting

Prof Paul Glasziou is internationally recognised for his research in evidence-based practice and led two NHMRC CREs in minimising antibiotic resistance in the community (2012 - 2017 and 2018 – 2024; \$2.4M each) with the late Prof Chris Del Mar. The outputs from the first CRE include generating new knowledge about effective interventions that GPs can adopt to reduce their prescribing of antibiotics for acute respiratory infections. This research has influenced policy in Government (e.g. Australian Strategic and Technical Advisory Group on Antimicrobial Resistance), Australian Commission on Safety and Quality in Health Care; and professional bodies (e.g. Royal Australian College of GPs). The second CRE established a national antibiotic stewardship in primary care research group (ANZ-GRIN) with over 43 members nationally, including from 10 from Queensland (Bond, UQ, and JCU), with links to the European General Practice Research in Infectious Diseases network (GRIN). A/Prof Geoff Spurling (Inala Indigenous Health Service/UQ) and the late Prof Chris Del Mar provided the research evidence to support delayed antibiotic prescription for respiratory tract infections as a way to address adverse reactions, cost, and antibacterial resistance (Cochrane Reviews, 2017).

Profs David Paterson, Mark Schembri, A/Prof Scott Beatson, Dr Patrick Harris and colleagues have also secured an MRFF (\$1.2m; 2018) grant to undertake a randomised clinical trial of a multimodal intervention to reduce antimicrobial use in residential aged care facilities.

## Antimicrobial resistance

QLD houses a highly collaborative infectious disease ecosystem that spans universities, research institutes, hospitals, Pathology Queensland and Forensic and Scientific Services, with strong links between researchers and clinicians (medical, nursing and pharmacy) in paediatrics and adults. Scientists and academic clinicians are world leaders in antimicrobial resistance, infection prevention and control and the rapid diagnosis and treatment of sepsis. The UQ Institute for Molecular Bioscience Centre for Superbug Solutions leads a large research program encompassing antibiotic discovery (led by Prof Mark Blaskovich, who runs the Community for Open Antimicrobial Drug Discovery screening program) and the genetics/genomics of antibiotic resistant bacterial pathogens (led by Profs Ian Henderson, Mark Walker, Waldemar Völlmer and Mark Schembri). Through Queensland Genomics, the clinical utility of Whole Genome Sequencing to control hospital-acquired infections has been demonstrated across 3 tertiary and 2 regional hospitals, with the goal of expanding genomics analysis as a state-wide service through Pathology Queensland.

### Examples of world-leading research that has or will lead to changes in clinical practice:

- Prof Michael Jennings (Institute for Glycomics, GU) is using high-throughput screening to identify existing safe and approved drugs with novel antimicrobial activity to combat antimicrobial resistant pathogens.
- Research under the leadership of Prof Mark Schembri (UQ) led to the discovery of how bacteria share antibiotic-resistance genes using a genetic screening system to identify the components required for the transfer of an antibiotic resistance plasmid from one bacterial cell to another (Nat Micro, 2020).
- A/Prof Scott Beatson and Dr Brian Forde (UQ) leads a team that regularly reports the genome analyses of antibiotic resistant

bacteria to the major tertiary hospitals in Brisbane (PAH, RBWH and CHQ) as part of Queensland Genomics. He was also part of the collaborative team, led by Dr Patrick Harris, that demonstrated the clinical utility of Whole Genome Sequencing and metagenomics in solving a persistent outbreak of carbapenem-resistant *Acinetobacter baumannii* in RBWH's intensive care unit (Microb Genom, 2021).

- The Queensland Paediatric Sepsis Program, co-led by Dr Adam Irwin (UQ/CHQ) and A/Prof Paula Lister (CHQ), was awarded the Global Sepsis Alliance award in 2020.
- Prof Bala Venkatesh (PAH/Wesley/UQ) was the lead investigator on the largest septic shock clinical trial (ADRENAL trial) to date with >3000 patients (NEJM, 2018).
- A/Prof Makrina Totsika's (QUT) approach of inhibiting bacterial virulence factors, including adhesins that allow bacteria to colonise surfaces, has shown promise for changing the way we prevent and treat bacterial infections. Her team is developing pathoblocker drugs that can replace antibiotics or restore their action against drug resistant bacteria and antibiotic-resilient bacterial biofilms.
- A/Prof Paul Horwood (JCU/AITHM) is leading an NHMRC-funded project to determine the factors that facilitate the spread and persistence of methicillin resistant *Staphylococcus aureus* (MRSA) in PNG.
- A/Prof Catherine Rush (AITHM/JCU) is investigating the immunological mechanisms that induce de-novo *Mycobacterium tuberculosis* mutagenesis associated with DR-TB.
- Dr Jake O'Brien (QAEHS, UQ) secured an NHMRC Investigator grant to develop a national wastewater surveillance program for monitoring antimicrobial resistance in the general population.
- Prof Matt Sweet's team and collaborating research groups at UQ discovered a molecular pathway that enables immune cells to both kill bacteria and switch off destructive inflammation (PNAS, 2023). This information is being harnessed for the development of mRNA-based therapeutics as host-directed therapies to combat antimicrobial-resistant bacterial pathogens.
- Profs Rob Parton, Matt Sweet and teams at UQ discovered that organelles called lipid droplets enable immune cells to kill bacteria (Science, 2020). This information has been used to design pharmacological approaches for clearing infections caused by antimicrobial-resistant bacterial pathogens.
- Profs Mark Blaskovich, Rob Capon and Ian Henderson and Dr Mark Butler (UQ) have been monitoring the clinical pipeline for more than a decade. Their latest paper (J. Antibiotics, 2023) found 62 new antibiotics in development, with 34 of those based on structures not previously used as antibiotics.
- Prof Blaskovich and Dr Alysha Elliott (UQ) are investigating the potential of metal compounds to be developed into antifungal drugs, finding one in five metal compounds displayed antifungal properties (JACS Au, 2022)
- Prof Blaskovich and his team have also taken over the SPARK database (Shared Platform for Antibiotic Research and Knowledge) from the Pew Charitable Trusts, which captures information from companies and researchers that have retired from antibiotic discovery to provide a single source of antibiotic-related data that would otherwise be difficult to access. SPARK has information from around 160,000 compounds.

# 4. Vaccines

## Vaccine development

Queensland is a global leader in the development of vaccine candidates, including the HPV vaccine, Gardasil®. Internationally recognised for our fight against tropical diseases (predominately malaria and tuberculosis (TB)), neglected tropical diseases (Zika, Chikungunya and Dengue), Streptococcus Group A and STIs (gonococcal and chlamydia), our researchers have identified, designed and are advancing vaccine candidates through preclinical and clinical stages of development.

### Some examples of successful translation of discovery research towards the clinic include:

- Under the leadership of Prof Michael Good and A/Prof Danielle Stanisc, GU researchers are developing the malaria vaccine candidate PlasProtect™ which has successfully completed the world's first clinical trial of a whole parasite blood-stage malaria parasite vaccine and recently completed a Phase 1b challenge study.
- A/Prof David Harrich's (QIMR Berghofer) has developed a novel in vitro production system for making dengue defective interfering particles (DIPs) and demonstrated potent inhibition of all dengue virus serotypes using DIP technology – securing him an Innovator Award from the Wellcome Trust.
- UQ's Dr David Muller and Prof Paul Young have successfully explored, in preclinical studies the delivery of multiple virus vaccines, dengue, Zika, polio, measles/rubella and SARS-CoV-2 to the skin via Vaxxas' high-density microarray patch. The potent production of protective immune responses has been demonstrated for each, with a SARS-CoV-2 candidate vaccine progressing to human Phase 1 clinical trials this year.
- Prof Michael Good AO, A/Prof Danielle Stanisc and their team have developed a new vaccine in pre-clinical studies to treat human babesiosis, a tick-transmitted disease closely related to malaria. The research team have developed a whole parasite Babesia vaccine that acts as a universal vaccine, inducing immunity against different human Babesia species.
- Profs Kate Seib and Michael Jennings (Institute for Glycomics, GU) entered into a deal with LimmaTech Biologics (Switzerland) to co-develop and commercialise a vaccine candidate to prevent gonorrhoea.
- Prof Michael Good AO, A/Prof Manisha Pandey and their research team at the Institute for Glycomics have developed a Streptococcus A vaccine candidate, which is currently in a Phase I clinical trial in Canada. Concurrent trials in Australia are planned to commence 2024.
- UQ's Prof Denise Doolan is advancing the development of a malaria vaccine designed to induce effective T cell responses, and that has promise for protection against multiple species of Plasmodium parasites.
- Prof Mark Walker (UQ), Dr Tania Rivera Hernandez and collaborators at Emory University have used a non-human primate model to demonstrate efficacy of an experimental vaccine against Group A Streptococcus pharyngeal infection.
- QUT's Prof Ken Beagley and Prof Peter Timms (now UniSC) co-led the development of a vaccine for Chlamydia in the koala. Prof Peter Timms and Dr Samuel Phillips (UniSC) have now advanced this vaccine which is now being used extensively by wildlife hospitals and local councils across the country. Prof Beagley is part of an international research team that has been awarded up to \$A14 million from the National Institutes of Health (NIH) to test identified human chlamydia vaccine candidates.
- A/Prof Andreas Kupz (AITHM/JCU) has led the development of an improved BCG TB vaccine candidate (through genetically enhancing the currently available BCG vaccine) designed to expand protection in adults. The vaccine candidate has been selected by the Bill and Melinda Gates Foundation Collaboration for TB Vaccine Discovery consortium (CTVD; <https://www.ctvd.co/Pages/default.aspx>) for direct comparison with 5 other advanced TB vaccine candidates in three pre-clinical animal models to shortlist 1-2 candidates for stage-gated clinical trials. The team are also seeking to develop PNG as a clinical trial site for the global TB vaccine effort.
- Prof Alex Loukas (AITHM/JCU) co-led the development of a phase 1 clinical trial for a hookworm vaccine using irradiated parasites that was developed and tested for safety and efficacy in a clinical trial in Queensland (Lancet Infect Dis, 2021). The team also secured funding from the NIH (National Cancer Institute) to develop subunit vaccines for liver fluke infection which is a WHO group 1 carcinogen and the major cause of bile duct cancer in South East Asia where the infection is endemic.
- Prof Suresh Mahalingam (MHIQ, GU) has joined forces with scientists from Indian Immunologicals Limited, a leading vaccines manufacturing company based in Hyderabad, India to develop a live attenuated SARS-CoV-2 vaccine using the latest codon de-optimisation technology.
- A/Prof Catherine Rush (AITHM/JCU) is studying the host factors that are associated with vaccine success in TB endemic communities in rural PNG.
- Prof Rajiv Khanna AO (QIMR Berghofer) has led the development of prophylactic vaccines for Epstein-Barr virus and Cytomegalovirus. These vaccines are currently being developed in collaboration with Atara Biotherapeutics and Dynavax Technologies respectively. Both these vaccines are based on a novel multi-epitope patented technology.
- Dr Jody Peters and Prof Roy Hall (UQ) have developed a novel chimeric vaccine against the 2022 Australian outbreak strain of Japanese encephalitis virus and with Prof Andreas Suhrbier (QIMR Berghofer) and Dr Peter Kirkland (EMAI, NSW) have demonstrated protection of mice and pigs against virus challenge. They also used a similar vaccine design against West Nile virus and with Dr Sally Isberg (CCR, Darwin) demonstrated protection of saltwater crocodiles against skin lesions caused by infection with this virus.



## RNA Vaccines and Therapeutics

Queensland is at the forefront of RNA vaccine and therapeutic research and development, with UQ's BASE Facility the largest supplier of experimental mRNA vaccines and therapies in Australia. Further, in an historical \$280m partnership between Sanofi, Queensland Government, UQ and GU, a Translational Science Hub will be established at the soon to be built Translational Manufacturing Institute at TRI (TMI@TRI), which will link world-class researchers in Queensland with scientists at the Sanofi mRNA Centre of Excellence in France and the United States. This will create a unique global vaccines R&D network focused on mRNA technology and translational science, with the initial focus on the evaluation of a new generation of mRNA vaccines and the development of a world-first chlamydia vaccine.

### Some examples of successful translation of discovery research towards the clinic include:

- Dr Tim Mercer (UQ), Director of BASE, was awarded \$4.3m from the MRFF (2022) with collaborators towards the expansion of the BASE Facility to enable the manufacture and formulation of mRNA drug candidates for first-in-human clinical trials. To date, BASE has built over 50 experimental vaccines and therapies.
- Prof Mark Walker (UQ) is leading an international collaboration in partnership with Moderna to develop an mRNA vaccine for Step A which has received over \$8m in philanthropic funding from the Leducq Foundation (2023).
- Profs Nigel McMillan (MHIQ, GU) and Prof Kevin Morris (GU) have developed a first-in-class RNA nanoparticle drug against SARS-CoV-2 infection (Mol. Therapeutics, 2021), which has been licensed to Gene Company Pty Ltd (commercial partnership worth >\$135m) to further develop as a new treatment for SARS-CoV-2.
- Dr Adi Idris (QUT) and Prof Nigel McMillan (MHIQ, GU) developed and intranasal siRNA encapsulated LNP in vivo delivery system that is highly efficient at targeting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and respiratory syncytial virus (RSV) in infected mouse lungs (J. Microbio., Immunol. Infection, 2023).

## Platform and delivery technologies

Queensland researchers are global leaders in the development of vaccine platform and delivery technologies. This includes UQ's pioneering molecular-clamp vaccine technology that was used to develop a SARS-CoV-2 vaccine candidate in partnership with CEPI and CSL.

UQ's Rapid Response Vaccine Pipeline (RRVP), led by A/Prof Keith Chappell, includes all required aspects of vaccine development from an emergency response aspects of vaccine development from pre-clinical screening and animal testing right through to production of vaccine for use in phase I clinical trial testing. Key UQ capabilities enabling pandemic response extend to the rapid discovery of monoclonal antibodies, host-cell receptor identification, structural analysis and development of methods for assessment of virus neutralisation.

### Some examples of successful translation of discovery research towards the clinic include:

- Brisbane-based start-up company, Vaxxas, which is developing needle-free vaccine delivery technology ('Nanopatch') based on UQ research, has partnered with the US Government to support pandemic deployment of their high-density micro-array patch—a deal worth A\$30m.

- A/Prof Keith Chappell, A/Prof Dan Watterson and Prof Paul Young (UQ) co-developed the molecular clamp vaccine technology that underpinned UQ's COVID-19 vaccine program. The Molecular clamp platform has secured more than \$50m in funding support, with the upgraded second generation Clamp2 currently undergoing key proof of principle testing in a phase I clinical trial. The Clamp2 platform forms the basis of UQ's Rapid Response Vaccine Pipeline (RRVP), which seeks to address CEPI's 100 Days Mission <https://100days.cepi.net/> and has attracted venture capital support with the formation of a spin-out Vicebio Ltd <https://vicebio.com/>.
- Prof Roy Hall, Dr Jody Peters (UQ) have developed a chimeric flavivirus vaccine technology based on the novel insect-specific Binjari virus and with Prof Andreas Suhrbier (QIMR Berghofer) and Dr David Muller (UQ), have demonstrated protection against Zika, dengue, yellow fever and West Nile viruses using both injection and needle free delivery systems.
- QIMR Berghofer's Mosquito Control Laboratory and the UQ School of Public Health demonstrated that intradermal, reduced-dose administration of a registered Japanese encephalitis (JE) vaccine was as immunologically effective as conventional injection protocols. The results inform the ATAGI statement on JE vaccine use. Further trials are underway.
- Prof Bernd Rehm (GU) and his team developed a disruptive vaccine platform technology that uses reprogrammed E. coli to assemble antigen-coated biopolymer particles as safe and potent vaccines. This vaccine technology is versatile and allows for rapid response to new and emerging pathogens. Vaccines were stable at ambient temperature and can be cost-effectively mass produced using industrial biotechnology. Promising vaccine candidates were developed to induce protective immunity against parasites, bacterial and viral pathogens. This vaccine technology overcomes critical bottlenecks of existing technologies regarding the speed of response, manufacturability, functionality and stability.
- Prof Michael Good AO, A/Prof Manisha Pandey and their research team (Institute for Glycomics, GU) partnered with the Chinese pharmaceutical, Olymva, in a multi-million dollar deal, to further develop and commercialise their novel Streptococcus A vaccine delivery technology exclusively for Greater China.
- AIITHM/JCU Prof Alex Loukas (with Prof. Istvan Toth of UQ) leads the commercial development of mucosal delivery vaccine platform for gastrointestinal pathogens. The proprietary vaccine platform is based on peptide formulations that are 'self-adjuvanting' and induce potent mucosal immunity. The pre-clinical efficacy of such formulations is surprisingly high. The unique peptide formulations are amenable to facile GMP production based on existing synthetic peptide technologies.

## Concluding Remarks

Together we are greater than the sum of our parts. The Queensland research community is committed to working together to strengthen and coordinate Queensland's infectious disease research - building technical proficiency, capacity, structures and systems needed to deliver a discovery and translational development pipeline to tackle the most urgent local and global infectious disease challenges.

