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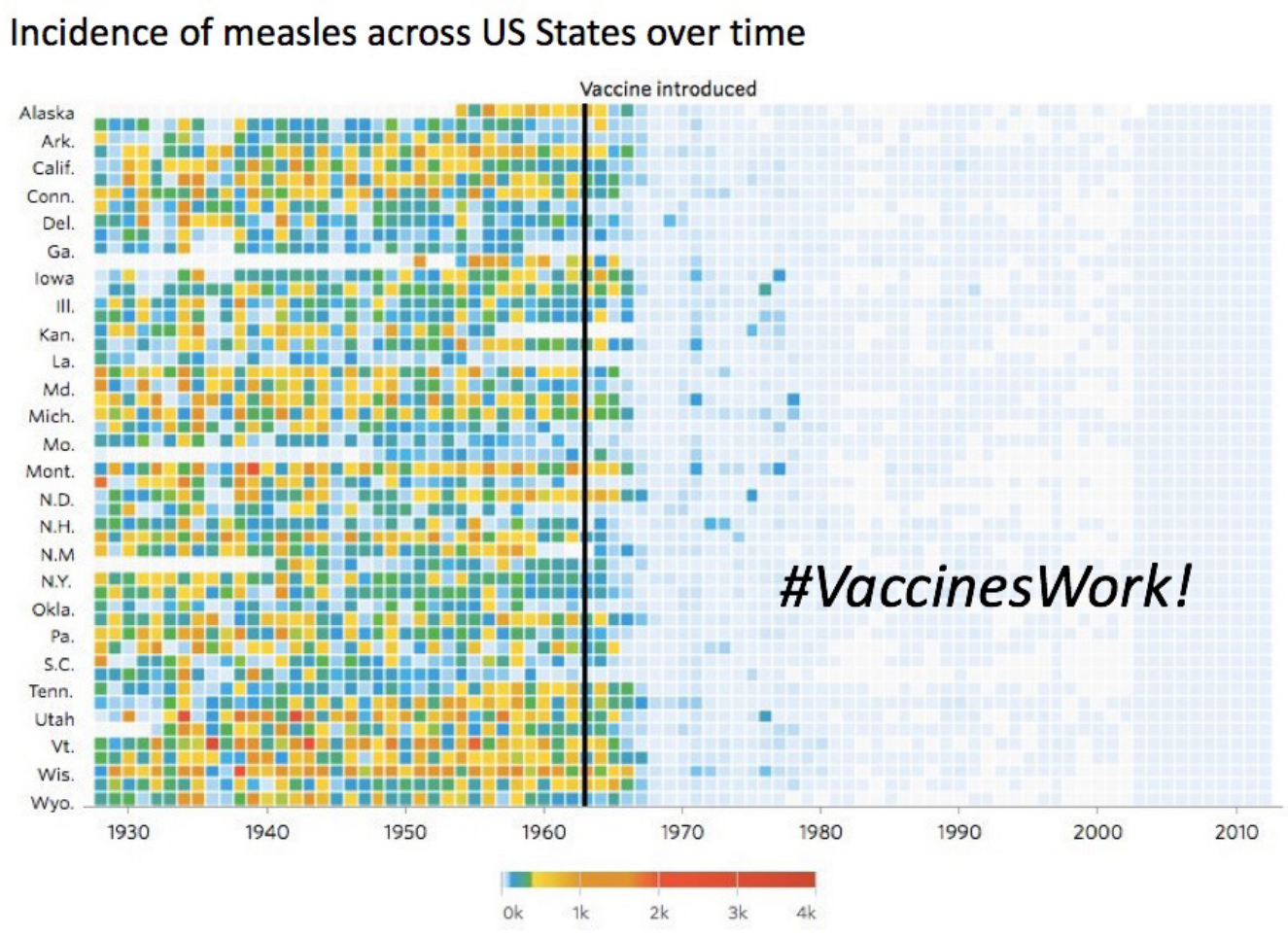
Vaccines@UQ Symposium



Location

Auditorium
Queensland Biosciences Precinct
Level 3, Building 80,
306 Carmody Rd, St Lucia

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Vaccines@UQ

Monday 25 November 2019

Location **Auditorium** **Queensland Biosciences Precinct, Building 80, UQ St Lucia Campus**

Time	Presentation
2.00pm	Coffee and tea available on arrival
2.20pm	**Welcome** Prof. Ian Henderson, Co-Chair of the Symposium *Deputy Director (Research) - Institute of Molecular Biosciences, The University of Queensland*
2.30pm	**Group A Streptococcus vaccines - animal models and adjuvants** Prof. Mark Walker, *Australian Infectious Diseases Research Centre, School of Chemistry and Molecular Biosciences, The University of Queensland*
3.00pm	**Animal tick vaccines- realisTICK progress and challenges** Prof. Ala Tabor, *QAAFI, The University of Queensland*
3.30pm	**Harnessing the Therapeutic Potential of Interleukin-22 in Neonatal Respiratory Viral Infection** Dr Sumaira Hasnain, *Goup Leader - Mater Research Institute, The University of Queensland*
4.00pm	**KEYNOTE PRESENTATION: Features of protective antibody responses to *Salmonella*** Prof. Adam Cunningham, *University of Birmingham*

Tuesday 26 November 2019

Location **Auditorium** **Queensland Biosciences Precinct, Building 80, UQ St Lucia Campus**

Time	Presentation
8.30am	Coffee and tea available on arrival
9.00am	**Welcome** Prof. Paul Young, Co-Chair of the Symposium *Head of School of Chemistry and Molecular Biosciences, The University of Queensland*
9.10am	**KEYNOTE PRESENTATION: Enhancing group A streptococcal vaccine design through global population genomics and nonhuman primate infection studies** Dr Mark Davies, *Doherty Institute, University of Melbourne*
10.00am	**The development of single-dose vaccine technologies for large animals** Prof. Timothy Mahony, *QAAFI, The University of Queensland*
10.30am	**Defined Semisynthetic Platforms for Producing Potent Semisynthetic Protein-TLR2 Agonist Fusion Vaccines** Dr Peter Michael Moyle, *Senior Lecturer - School of Pharmacy, The University of Queensland*
11-11.30am	Break for morning tea
11.30am	**Evaluation of a novel chimeric dengue vaccine candidate delivered to the skin by high-density microarray patches in an infectious challenge mouse model** Dr David Muller, *School of Chemistry and Molecular Biosciences, The University of Queensland*
12.00pm	**Self-assembling and self-adjuvanting lipopeptide nanoparticulate vaccine candidates for the induction of protective immune responses** Prof. Istvan Toth, *School of Chemistry and Molecular Biosciences, The University of Queensland*
12.30pm	**Vaccine development for gonococcal superbugs** A/Prof. Kate Seib, *Research Leader & Associate Director (Research) - Institute for Glycomics, Griffith University*
1-1.30pm	Break for lunch
2.00pm	**Rapid response pipeline for stabilised subunit vaccines** Dr Keith Chappell, *School of Chemistry and Molecular Biosciences, The University of Queensland*
2.30pm	**The *Chlamydia* epidemic: What do we need from a vaccine?** Prof. Kenneth Beagley, *Biomedical Sciences, Queensland University of Technology*
3.00pm	**Sementis Copenhagen Vector, a new vaccinia-based vaccine platform; application to ZIKA/CHIK vaccine development** Prof. Andreas Suhrbier, *QIMR Berghofer Medical Research Institute*
3.30pm	**Vaccine delivery to the skin: benefits and challenges** Dr Angus Forster, *Chief Development and Operating Officer, Vaxxas Pty Ltd*
4-4.30pm	Break for afternoon tea

Vaccines@UQ

2019 Skerman Lecture

The annual Skerman Lecture recognises the contribution of Professor Victor Bruce Darlington Skerman in the development of Microbiology at The University of Queensland. Professor Skerman was Head of the Department of Microbiology from 1962 to 1981, having been appointed Foundation Chair of Microbiology in 1961. He had broad interests in microbial physiology, ecology and diversity, but is best known and recognised for his international reform of bacterial systematics and nomenclature.

This year's lecture, **Novel technologies for discovery, design and development of new and effective vaccines**, will be presented by Professor Mariagrazia Pizza, Senior Scientific Director, Bacterial Vaccines at GSK VACCINES.

Tuesday 26 November 2019

Location **Auditorium** **Queensland Biosciences Precinct, Building 80, UQ St Lucia Campus**

Time	Presentation
4.30pm	**Novel technologies for discovery, design and development of new and effective vaccines** Prof. Mariagrazia Pizza, Senior Scientific Director, Bacterial Vaccines GSK VACCINES Vaccines have had a major impact on human health over the past two centuries, allowing for the control and elimination of many infectious diseases. Most of the vaccines available today, although very effective, have been developed using conventional approaches. Important discoveries in the field of chemistry, microbiology and immunology and the development of new and sophisticated technologies have provided alternatives to the design of improved vaccines or of novel vaccines against infections for which preventive measures do not exist. **Meet the speaker** Prof. Mariagrazia Pizza received her degree in Chemistry and Pharmaceutical Technologies at the University of Naples, Italy. After a fellowship at the EMBO laboratories in Heidelberg, Germany, Mariagrazia moved to Siena, where she is currently Senior Scientific Director for Bacterial Vaccines at GSK Vaccines. She has led many bacterial projects and contributed to the discovery of a pertussis vaccine based on a genetically detoxified toxin, shown to be able to protect children from disease and to the discovery of new vaccine antigens by genome mining (reverse vaccinology), which are the basis of a new MenB vaccine now licensed in more than 38 countries worldwide. She has received many scientific awards, is fellow of Academic Societies and EMBO, and Honorary Visiting Professor at the University of Leicester. She has over 200 publications in international peer-reviewed journals and is co-inventor of many patents.
5.30-6.30pm	Networking and refreshments to follow

Vaccines@UQ Symposium

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Vaccines@UQ
Presentation Abstracts

Professor Kenneth Beagley

Professor of Immunology
School of Biomedical Sciences
Institute of Health and Biomedical Innovation

The *Chlamydia* epidemic: What do we need from a vaccine?

Chlamydial infections are increasing globally, with more than 130 million new infections annually. Both females and males are infected and more than 60 % of infections are asymptomatic and therefore untreated as most countries do not actively screen for *Chlamydia*. Treatment costs, including infertility treatments, impose a substantial health burden on the community, due mainly to the reproductive tract inflammation caused by chronic untreated infection in females. To date, there is no human chlamydia vaccine and animal studies have failed to demonstrate that vaccination can elicit sterilising immunity. We will present data to show that, in animal models, through appropriate choice of adjuvant and immunisation route, vaccination can (i) reduce the magnitude and duration of infection (ii) reduce the infection-associated inflammatory damage to both female and male reproductive tract tissues and (iii) that vaccination of both females and males can synergise to prevent infections. We will also present modelling studies to suggest that such vaccines, even in the absence of sterilising immunity, could have a major impact on the incidence of infection within both human and koala populations.

Dr Keith Chappell

School of Chemistry and Molecular Biosciences
The University of Queensland

Rapid response pipeline for stabilised subunit vaccines

The University of Queensland has recently received $14.7M in funding from the Coalition for Epidemic Preparedness Innovations (CEPI) to establish a rapid response vaccine pipeline. This project brings together a highly skilled team from some of Australia's leading scientific organizations and world-class facilities. The ambitious goal of this project is to establish a holistic and robust pipeline that can facilitate the completion of pre-clinical development within a 16 week window and subsequent human phase I trials and large scale vaccine manufacture (>200,000 doses) within a further 10 weeks. Vaccine produced through this pipeline will therefore be available for rapid deployment and provide the best possible opportunity to counter emerging viral epidemics. This timeline is made possible by UQ's broadly applicable platform technology (molecular clamp), which facilitates the expression and purification of recombinant viral glycoproteins in subunit form without loss of native antigenicity.

Professor Adam Cunningham

Institute of Immunology and Immunotherapy
University of Birmingham

Features of protective antibody responses to *Salmonella*

Antibodies to the Gram-negative bacterial surface induced after natural infection or vaccination save hundreds of thousands of lives each year. Despite the importance of antibodies in protection, we have little understanding of what makes one antibody protective yet another not. Moreover, we do not fully understand how antibodies work in vivo to enable killing of Gram-negative bacteria nor what protection "looks like". In this talk, I will present recent work from our lab that addresses these fundamental questions. These studies focus on how IgG induced to the porin protein OmpD from *Salmonella* Typhimurium targets the bacterial cell surface. They provide insights into the host factors that are required to successfully limit infection and the features of the pathogen that act to counter these. Collectively, these help identify ways to improve the design of novel vaccines and immune therapeutics against Gram-negative bacteria.

Vaccines@UQ
Presentation Abstracts

Dr Mark Davies
Dohert - Sanger Senior Research Fellow
Peter Doherty Institute for Infection and Immunity
The University of Melbourne

Enhancing group A streptococcal vaccine design through global population genomics and nonhuman primate infection studies

The development of a group A streptococcal (GAS) vaccine has been hindered by a number of hurdles including the high serotypic diversity of the pathogen, autoimmune complications following repeated GAS infections, and the lack of non-murine models to validate proposed GAS vaccine formulations. To overcome these hurdles, we generated a global GAS genome database to unravel the evolutionary dynamics of this major human pathogen. This database of 2,083 genomes were obtained from 22 countries, with a focus on sampling from streptococcal endemic settings. We identified a core panel of pre-clinical GAS vaccine antigens that would provide theoretical global coverage on the basis of >99% antigen carriage and <2% sequence heterogeneity. Using this platform, 5 conserved antigens (arginine deiminase [ADI], C5a peptidase [SCPA], streptolysin O [SLO], interleukin-8 [IL-8] protease [SpyCEP], and trigger factor [TF]), that have not been linked to autoimmune complications yet are highly conserved within a global context, were investigated as a putative multi-component vaccine formulation. We developed a non-human primate (NHP) infection model of GAS pharyngitis and evaluated the protective efficacy of the 5 conserved antigen formulation termed 'Combo5'. Antibody responses against all Combo5 antigens were detected in NHP serum, and immunised NHPs showed a reduced pharyngitis and tonsillitis compared to controls. Within an evolving global bacterial pathogen such as GAS, we have identified a number of proposed pre-clinical GAS vaccine antigens that fulfil the criteria for a global vaccine and provide protection from pharyngitis in a NHP model. Our work establishes a technical and experimental framework for the development of a global GAS vaccine.

Dr Angus Forster
Chief Development and Operating Officer
Vaxxas Pty Ltd

Vaccine delivery to the skin: benefits and challenges

Needle free vaccination continues to be a field of significant academic and commercial R&D, with technologies often directed toward less invasive administration of vaccines into the skin. Vaxxas is developing a High-Density Micro-Array Patch (HD-MAP) for targeted vaccine delivery to the abundant immune cells in the epidermis and dermis. This technology offers potential benefits of simplicity of vaccination, removal of needles, improved thermostability and enhanced immune responses. We have recently conducted a phase I clinical trial using the HD-MAP with a monovalent influenza vaccine. This was the first clinical evaluation of the vaccine dose-sparing potential of this type of delivery technology. 2.5 µg of A/Singapore/GP1908/2015 (H1N1) HA administered by HD-MAP induced haemagglutination inhibition (HAI) and microneutralization titres that were not significantly different to those induced by 15 µg HA given by intramuscular injection. HD-MAP delivery of 15 µg and 10 µg HA resulted in a faster increase in HAI responses than IM. The vaccine HD-MAP was stable for 12-months when stored at 40 °C, opening the potential for storage outside the cold-chain. Alongside the need to demonstrate performance in the clinic and for product stability, Vaxxas has focused on addressing the significant challenges of product and process scale-up and cost.

Dr. Sumaira Z. Hasnain
Group Leader
Mater Research Institute-The University of Queensland

Harnessing the Therapeutic Potential of Interleukin-22 in Neonatal Respiratory Viral Infection

Respiratory Syncytial Virus (RSV) causes the most common respiratory infection in children. To date, no vaccine has been proved to be safe and effective in the control of RSV. Viruses, like RSV, must utilise the host cellular machinery, including the Endoplasmic Reticulum (ER) to produce viral proteins for replication. Infected host cells mounts defence against viruses by generating oxidative stress and ER stress. We discovered that IL-22 is a potent ER stress suppressor and aimed to explore the role of IL-22 in neonatal viral infection. Using a preclinical model of RSV, Pneumovirus (PVM) infection in neonatal mice and mice were treated with anti-IL-22 antibody, or recombinant-IL-22 (rIL-22). We also treated human rhinovirus and RSV infected HeLa and primary human bronchial epithelial cells with IL-22. rIL-22 treatment increased viral load in HeLa cells infected with human Respiratory Syncytial Virus and Human Rhinovirus in vitro which was associated with decreased expression of ER stress markers. In the high-dose PVM infection model, rIL-22 administration led to ~80% mortality. In the absence of IL-22 (IL-22 neutralisation or using IL-22ra-deficient mice) there was a reduction in PVM load and lung injury. RNA-seq analysis conducted on sorted lung epithelial revealed that genes involved in protein processing in ER related to antigen processing/presentation were upregulated in epithelial cells in the absence of IL-22. We demonstrate a direct role of IL-22 in modulating MHC class I/II expression. Locally elevated IL-22 during respiratory viral infection could increase viral replication by promoting epithelial specific viral protein synthesis via dampening the stress pathways. Blocking endogenous IL-22 limits viral replication and immunopathology by promoting viral antigen processing/presentation and can be therapeutically manipulated at appropriate times to help limit respiratory viral infection.

Vaccines@UQ
Presentation Abstracts

Professor Timothy Mahony

Queensland Alliance for Agriculture and Food Innovation
The University of Queensland

The development of single-dose vaccine technologies for large animals

Annual losses to the livestock sector from infectious and parasitic diseases are estimated to exceed $3.5B in Australia alone. More effective control of these diseases is one way to deliver the productivity gains required to meet the growing need for sustainable protein production to feed an expanding human population. While vaccination is a proven method for disease control, conventional delivery technologies can be problematic to apply in some animal production environments. As an example, the extensive beef production systems which dominate Northern Australia typically muster cattle once or twice annually, making the utilisation of multi-dose vaccines difficult. To address this issue, we have been developing single-dose vaccination technologies to improve disease control in these and other animal production environments. Here we will described some of the single-dose technologies we have been developing and testing in large animal studies. The future application of these technologies will also be discussed.

Dr Peter Michael Moyle

Senior Lecturer
School of Pharmacy
The University of Queensland

Defined Semisynthetic Platforms for Producing Potent Semisynthetic Protein-TLR2 Agonist Fusion Vaccines

Vaccines are one of the most effective means to prevent disease. However, vaccines against many important diseases have not been developed, in part, due to safety issues associated with the use of traditional vaccine approaches. Subunit approaches (e.g. protein antigens) are thus an important approach to develop new vaccines, however these antigens require delivery with safe and effective immunostimulatory agents to stimulate appropriate, protective immune responses. We have successfully developed an enzymatic platform, which enables the high yielding (~70-90% yield), rapid (< 4 h), and site-specific conjugation of lipopeptide TLR-2 agonists onto the N- or C-terminus of folded recombinant protein antigens, under conditions that successfully maintain their folding. Optimisation of reaction conditions, to provide access to product in minutes, with minimal enzyme requirements have been developed, along with scalable processes for product purification. These techniques have yielded TLR-2 agonist fusions with 7 out of 8 tested proteins (mainly folded proteins), and have yielded a vaccine that unlike an antigen/alum mixture, was able to protect against a subcutaneous group A streptococcus challenge. In addition, this vaccine was demonstrated to elicit a more balanced Th1/Th2-response in comparison to the Th2-biased response associated with alum, increasing the utility of this platform. With folded protein antigens representing most antigens reported in the literature, it is envisioned that this approach will provide a useful platform for the development of novel and improved vaccines.

Dr David Muller

Senior Research Fellow, Australian Infectious Diseases Research Centre
School of Chemistry and Molecular Biosciences
The University of Queensland

Evaluation of a novel chimeric dengue vaccine candidate delivered to the skin by high-density microarray patches in an infectious challenge mouse model

Globally, there are an estimated 390 million cases of dengue infections annually resulting in a yearly economic cost of US$6.9 billion. Vaccination against dengue virus is the most promising tool to control dengue infection, as there is currently no dengue specific antiviral treatment. The Binjari virus (BinJV), a new insect-specific flavivirus that is unable to replicate in vertebrate cells, has allowed the design of a novel vaccine candidate. By exchanging the structural prM and E proteins of BinJV with those of pathogenic vertebrate-infecting flaviviruses (VIFs) such as dengue, a chimeric virus was generated that is antigenically indistinguishable from the pathogenic VIF parental virus. Dengue 2 chimeras (BinJV/DV2-prME) were made by exchanging the structural proteins of BinJV with those of dengue 2. In this study, we administered BinJV/DV2-prME with a needle-free delivery system using high-density microarray patches (HD-MAP). The HD-MAP is a 1 cm2 based vaccine delivery device consisting of 5,000 projections each 250 µm in length, onto which the vaccine is dry-coated. When applied to the skin, it deposits vaccine directly dermal and epidermal layers of the skin with high densities of Antigen presenting cells. Immunisation via the HD-MAPs resulted in significantly enhanced IgG kinetics after a single dose when compared to those vaccinated intradermally. Using the AG129 dengue challenge mouse model, complete protection was observed from lethal dengue 2 D220 mouse-adapted virus challenge, without viral breakthrough and low levels of NS1 detected in mice receiving vaccine by the HD-MAP.

Vaccines@UQ
Presentation Abstracts

Professor Mariagrazia Pizza

Senior Scientific Director
Bacterial Vaccines
GSK Vaccines

Novel technologies for discovery, design and development of new and effective vaccines

Vaccines have had a major impact on human health over the past two centuries, allowing for the control and elimination of many infectious diseases. Most of the vaccines available today, although very effective, have been developed using conventional approaches. Important discoveries in the field of chemistry, microbiology and immunology and the development of new and sophisticated technologies have provided alternatives to the design of improved vaccines or of novel vaccines against infections for which preventive measures do not exist.

Associate Professor Kate L. Seib

Research Leader & Associate Director (Research)
Institute for Glycomics, Griffith University

Vaccine development for gonococcal superbugs

Neisseria gonorrhoeae is recognised by WHO and CDC as an urgent threat to global health due to the emergence of multi-drug resistant gonococcal strains. There are >106 million reported cases of gonorrhoea each year worldwide and there is currently no vaccine, and no new antibiotics or new vaccine candidates in late-stage development. However, the outer membrane vesicle (OMV) meningococcal B vaccine MeNZB, that was developed to protect against the closely related pathogen Neisseria meningitidis, was recently reported to be associated with reduced rates of gonorrhoea following a mass vaccination campaign in New Zealand. Our work is focused on identifying novel gonococcal vaccine target, as well as investigating the cross reactivity to N. gonorrhoeae of serum raised to the meningococcal B vaccine Bexsero, which contains the MeNZB OMV component plus three recombinant protein antigens. We have characterised several highly conserved and immunogenic gonococcal candidate vaccine antigens and shown that antibodies to these proteins are bactericidal and can block gonococcal infection of cervical and urethral epithelial cells. In addition, we have found that there is a high level of sequence identity between the MeNZB/Bexsero OMV antigens, and gonococcal proteins. NHBA is the only Bexsero recombinant antigen that is conserved and surfaced exposed in N. gonorrhoeae. Furthermore, we have found that Bexsero induces antibodies in humans that recognise and kill N. gonorrhoeae in vitro. Work is ongoing to identify the full set of gonococcal targets recognized by Bexsero-induced antibodies, and the functional activity of these antibodies against gonorrhoea.

Professor Andreas Suhrbier

Group Leader, Inflammation Biology
QIMR Berghofer Medical Research Institute

Sementis Copenhagen Vector, a new vaccinia-based vaccine platform; application to ZIKA/CHIK vaccine development

The “Sementis Copenhagen Vector” (SCV) system is a recently developed vaccinia-based, multiplication-defective, vaccine vector technology that allows manufacture in modified CHO cells avoiding the need for SPF chicken embryo fibroblasts. We recently described a single vector construct SCV vaccine that encodes the complete structural polyprotein cassettes of both Zika virus (ZIKV) and chikungunya virus (CHIKV) from different loci. A single vaccination of mice induced neutralizing antibodies and protection against CHIKV viremia and arthritis, and ZIKV viremia and foetal brain infection. Non-human primate studies show induction of neutralizing antibodies to all genotypes of CHIKV and ZIKV, and protection against ZIKV challenge. Phase I human trials are planned for 2020.

Vaccines@UQ
Presentation Abstracts

Professor Ala Tabor

Centre for Animal Science, Queensland Alliance for Agriculture and Food Innovation
The University of Queensland

Animal tick vaccines- realisTICK progress and challenges

With almost 900 species worldwide, ticks are mini-vampires that parasitise mammals, birds, reptiles, and amphibians, and are second to mosquitoes as disease vectors. The most significant species affecting livestock is the Rhipicephalus microplus species complex (cattle tick) with 80% of the world cattle populations at risk with an annual economic burden estimated at $US22-30b (2016). The Australian paralysis tick, Ixodes holocyclus, is indigenous to Australian wildlife and incidentally affects livestock, domestic pets and also humans. Approximately 100, 000 animals are affected each year along the east coast of Australia resulting in paralysis, expensive treatment costs, and intermittent mortalities. Australia leads the world in the development of anti-tick vaccines with the first tick vaccines commercialised in the 1990s (CSIRO-TickGARD; Cuba-GAVAC). TickGARD was discontinued in 2010 due to poor local and international adoption however provided the premise that a vaccination approach against ticks is feasible. UQ researchers have led successful 'omic' approaches to develop novel vaccines for both the cattle tick and the Australian paralysis tick with full patents lodged. A 'reverse vaccinology' approach identified several cattle tick vaccine candidates following ~15 years of research (antigen discovery, bioinformatics epitope predictions, in vitro immune screening, and in vitro tick feeding) and eight "proof of concept" cattle tick challenge trials (efficacies 66-90%). For the Australian paralysis tick, a large family of neurotoxins (holocyclotoxins/HTs) was identified from female adult tick salivary gland transcriptome data (Illumina HiSeq). Subsequently, a cocktail HT vaccine has protected dogs from I. holocyclus induced paralysis symptoms in a proof of concept trial. Challenges include the delivery of multiple antigens in a cost effective manner with consistently high efficacies. For cattle tick candidates, high host IgG responses do not always correlate to the ability to repel ticks in vaccination trials. The Australian paralysis tick is geographically limited with local commercial adoption of a vaccine contested by broad spectrum drugs delivered by large animal health companies internationally. Specific bioinformaTICK and screening approaches were successfully developed to identify novel vaccine candidates for the cattle tick and the Australian paralysis tick, and these approaches can be leveraged for vaccine development in related species.

Professor Istvan Toth

School of Chemistry and Molecular Biosciences
The University of Queensland

Self-assembling and self-adjuvanting lipopeptide nanoparticulate vaccine candidates for the induction of protective immune responses

The development of an effective vaccine for group A streptococci (GAS) has been challenged by the induced autoimmunity of epitopes derived from the C-repeat regions, unsuitable B-cell epitopes that have been shown to react with human heart tissue, and the minimal B-cell epitopes, which be-lieved to be safe, shows little or no immunogenicity unless bound to a delivery platform including the conjugation to an inbuilt adjuvant. Self-adjuvanting lipid core peptide (LCP) liposome systems where the antigen(s), carrier and adjuvant were within the same molecular entity has been developed. The LCP amphiphilic construct was incorporated into liposomes to produce particles with the desired size. The construct alone elicited high-levels of antibody titers comparable to that of the positive control (J14 + Complete Freund's adjuvant). The developed strategy to produce nanoparticles, consisting of a peripheral antigenic epitope layer conjugated to a dendrimer core, which is both self-adjuvanting and produces a strong immune response to the GAS M-protein, offers an attractive alternative to conventional vaccine approaches. The greatest advantage of this system being the generatation of protective immune response after oral administration. Our dendrimer-nanoparticles vaccine approach should be readily acquiescent to other pathogenic organisms in addition to GAS, and may prove particularly useful for the design of vaccines against infection deceases know to stimulate autoim-mune response in a host.

Professor Mark Walker

Australian Infectious Diseases Research Centre
School of Chemistry and Molecular Biosciences
The University of Queensland

Group A Streptococcus vaccines - animal models and adjuvants

Recent global advocacy efforts have highlighted the importance of the development of a vaccine against Group A *Streptococcus* (GAS). Combo5 is a non-M protein-based vaccine that provides protection against GAS skin infection in mice and reduces the severity of pharyngitis in non-human primates. However, Combo5 adjuvanted with Alum failed to protect against invasive GAS infection of mice. Here we show that formulation of Combo5 with adjuvants containing the saponin QS21 significantly improves protective efficacy, even though all 7 adjuvants tested generated high antigen-specific IgG antibody titres, including Alum. Detailed characterisation of Combo5 formulated with SMQ adjuvant containing QS21 showed significant differences compared to Alum in IgG subclasses generated following immunisation, and an absence of GAS opsonising antibodies. SMQ, but not Alum, generated strong IL-6, IFN-γ and TNF-α responses. This work highlights the importance of adjuvant selection for non-M protein-based GAS vaccines to optimise immune response and protective efficacy.