The Australian Society for Medical Research

The Queensland Committee of the ASMR are proud to present the

2018 QUEENSLAND HEALTH & MEDICAL RESEARCH AWARDS

The Queensland Health & Medical Research Awards are sponsored by the Queensland Government

Queensland Government

asmr Australian Society for Medical Research

public, political, scientific advocacy since 1991

The Health and Medical Research Workforce...

the essential ingredient to a thriving Australia

The current state of the health and medical research workforce

Between 2013 and 2016 the NHMRC supported workforce declined by

16.2%

At the end of 2016, 1 in 4 Australian researchers did not have job security for 2017

Investing in health and medical research, through the National Health and Medical Research Council (NHMRC), will drive economic growth, reduce healthcare costs and enable Australians to prosper...

ASMR's vision for the future

Incrementally increasing investment into NHMRC to reach 3% of total health expenditure by 2025/26 will generate $58 billion in health and economic benefits

Investing in the health and medical research workforce...

Every $1 invested into the NHMRC supported workforce returns $3.20 in health and economic benefits

Increasing the NHMRC supported workforce by 40% could lead to net gains of $35 billion

$35 billion

Ongoing expansion to the science and innovation economy

In an ageing population, investment into health and medical research will underpin a healthier, more productive Australia, reducing the projected spend on health and aged care

Foreword

Queensland Health is once again proud to support the ASMR 2018 Queensland Health and Medical Research Awards. Health research and innovation is pivotal in finding new and better healthcare options that will ultimately improve health outcomes for Queenslanders.

The important role research and innovation has to play in the health system was recognised again by Queensland Health with the release of a new Queensland Health strategy to support the field: Queensland Advancing Health Research 2026.

The Strategy sets the goal of healthier Queenslanders through research informed healthcare, which will be pursued by actions across five key objectives. These objectives include building Queensland Health's research leaders and culture; strengthening collaboration across the Queensland research community; supporting discoveries in high impact fields and translating cutting-edge research into better health outcomes. The Strategy is accompanied by an additional $10 million investment in health research by Queensland Health over the next four years.

The ASMR Queensland Health and Medical Research Awards showcase the impressive breadth and depth of health and medical research in Queensland. Congratulations to all the award finalists and a sincere thank you to the broader health and medical research community for the valuable contribution you make to improving Queensland's healthcare.

Michael Walsh
Director-General, Queensland Health

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Queensland Health Medical Research Awards Seminar Schedule

8:00 am	**Opening Remarks** Dr Lena Von Schuckmann (ASMR QLD Convenor)
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9:00 – 9:45 am	**Mid-Career Researcher Presentations** **Chair:** Dr Srilakshmi Srinivasan Dr Muhammad Shiddiky – Page 17 Dr Michael Smout – Page 19 Dr Conan Wang – Page 21
9:45 – 10:15 am	*Morning tea*
10:15 – 11:00 am	**Early-Career Researcher Presentations** **Chair:** Ms Yu Hung Dr Kyohei Nakamura – Page 25 Dr Kirsty Short – Page 27 Dr Tania Rivera Hernandez – Page 29
11:05 – 11:50 am	**Postgraduate Researcher Presentations** **Chair:** Ms Sandra Brosda Ms Katie Lineburg – Page 33 Dr Philip Mosley – Page 35 Dr Kosala Weerakoon – Page 37
11:50 am	**Closing Remarks** Dr Lena Von Schuckmann **(**ASMR QLD Convenor)
12:00 pm	*Lunch and Judges Meeting*

ASMR Medallist 2018 – Professor Hope Jahren

Professor of Social Geobiology,
University of Oslo

The ASMR Gala Dinner will feature a talk from the 2018 ASMR Medallist, who we are delighted to announce is Professor Hope Jahren. Professor Hope Jahren is an American geochemist, geobiologist and best-selling author.

She has been named one of Time magazine's 100 most influential people (2016) and one of Popular Science's "Brilliant 10" young scientists (2005). Professor Jahren has also been awarded three Fulbright Scholarships, and currently holds the J. Tuzo Wilson professorship at the University of Oslo in Norway.

Responsible for the first extraction and analysis of DNA found in paleosol and the first discovery of stable isotopes existing in a multicellular organism's DNA, she is in fact an 'Isotope detective".

Spanning disciplinary boundaries, her research uses stable isotope to answer some of the world's biggest science questions, including how prehistoric forests can inform us about climate change, how understanding the isotopic composition of plants can tell us about where our food comes from, and how much food, in particular sugar, we are consuming.

We're sure Professor Jahren's ideas will captivate Gala Dinner audiences around the country, and we warmly invite you along to discover how we might transform our societal structures to set Australia on the path towards a healthier, more prosperous future.

Medical Research: Bringing Health to Life

ASMR Research Fund

You can help build strength in Australia's Health and Medical Research Sector

The Australian Society for Medical Research is the peak body representing and supporting Australian Health and Medical Researchers. Supporting and encouraging early career researchers is an essential element in building and maintaining the Health and Medical Research sector in Australia.

In order to facilitate and promote learning and collaboration in early career researchers, the **ASMR offers two Research Awards each year**, enabling early career researchers to travel to another laboratory either within Australia (Domestic Research Award) or overseas (International Research Award) to learn and diversify their skills and networks.

The ASMR Research Awards are made possible by the generosity of ASMR members who make donations to the ASMR Research Fund.

The ASMR Research Fund was established by ASMR with the sole purpose of providing research awards to ASMR members, in particular early career members.

Without continued generosity, ASMR would not be able to continue to build strength and expertise in Australian Health and Medical Researchers via its support of early career researchers with the ASMR Research Awards.

If you would like to make a contribution to the ASMR Research Fund, and support the development of Australian Health and Medical Researchers, please follow link below.

https://asmr.org.au/research-awards/

Note: all donations to the ASMR Research Fund are tax deductible

Clinical Researcher Award Finalists

PROF JOHN FRASER

Department of Intensive Care
Critical Care Research Group
The Prince Charles Hospital, Brisbane.

When is a dead heart truly dead?

Prof Fraser founded the Critical Care Research Group (CCRG) in 2004 - a multi-disciplinary research collaborative encompassing local, state, national and international levels to improve outcomes for patients living with cardiovascular disease. As a part of his development of this collaborative research initiative, in 2014 he and his team were awarded an international Centre for Research Excellence (CRE) (one of only six clinical CREs) in Australia, looking at the development and utilisation of bionic hearts and lungs. This CRE has become an international network, with collaborations between Australia (Sydney, Melbourne and Brisbane), New Zealand, China, Japan, Taiwan, Malaysia, United Kingdom, United States, Kenya, South Africa, Brazil, Germany, Italy, France, and Ireland. He has published 300+ peer-reviewed papers, co-authored the first textbook on mechanical and circulatory support, and has been invited to speak as a keynote and sessional speaker at over 200 events both nationally and internationally. Since its inception, Professor Fraser and the CCRG have attracted more than $40M AUD in grants and industry funding.

Scientific Abstract:

Background: Heart transplantation (HTx) is the only cure for end-stage heart failure (HF), a condition that in Australia causes 1 death every 2.5 hrs. Globally, < 1 in 4 hearts that are offered up for donation are transplanted. The unmet need of donor hearts is compromised by these 'wasted hearts' - reducing quality of life etc. Waitlist numbers and deaths on waitlists are increasing, and underrepresent the actual demand for donor hearts. Current practices limit donor sources to brain dead (BD) donors. These practices are inefficient, and 80% of hearts are unused due to excessive travel and ischaemic times, cardiac injury, and stringent donor criteria. Kidney/lung donor pools have vastly increased through use of 'donation after circulatory death' (DCD) donors. The use of DCD donors for HTx is gaining attention, however a poor mechanistic understanding hinders their widespread use clinically, thus they are an under-utilised and poorly defined source of donor hearts.
Aims/Methods: This project aims to increase the donor heart pool by; 1) optimising BD hearts and characterising DCD donor hearts for HTx and 2) extending organ preservation via hypothermic ex vivo perfusion (HEVP). A large ovine model of heart transplant in BD and DCD donors will be used, combining clinical and basic research techniques to determine the efficacy of DCD donor hearts and HEVP using BD and DCD hearts in HTx settings. We intend to show that we can increase donor heart availability by optimising BD hearts, using DCD donor hearts, and extending organ preservation using HEVP - all 3 options being non-inferior to current clinical protocols using BD donors and cold static storage.
Conclusions/Outcome: If successful, HEVP organ preservation using BD and DCD hearts will be therapeutically advantageous to overcome Australia's tyranny of distance. These studies will contribute to improving current HTx protocols to extend donor pools and reduce waiting times and deaths of HF patients.

DR LISA GILLINDER

Mater Advanced Epilepsy Unit
Mater Centre for Neurosciences

Defining the clinical phenotype of neuronal autoantibody associated epilepsy

Dr Gillinder has a joint clinical appointment as an Epileptologist at the Mater Advanced Epilepsy Unit, and Neurologist / Epileptologist at the Princess Alexandra Hospital in Brisbane. Dr Gillinder is the first person to undertake a surgical epilepsy fellowship in Queensland and the first person to be trained in Stereo-electroencephalograph (SEEG) within Australia. She is now one of only 3 epileptologists in Australia qualified in SEEG. She completed her Physicians examinations while concurrently completing a research higher degree at the University of Queensland, studying the quantification of myocardial steatosis using Magnetic resonance spectroscopy. Dr Gillinder's current research focus is to define the clinical features associated with chronic autoimmune epilepsy. She is the first to describe an association between neuronal autoantibodies and perisylvian epilepsy. This work offers potential new treatment options for this unique epilepsy subtype, which is often refractory to conventional therapies.

Scientific Abstract:

Epilepsy affects more than 250,000 Australians, with many of these being refractory to conventional therapies. This is a very costly condition to treat and it causes significant psychosocial burden. Our current research into a unique epilepsy subgroup is addressing this important health issue. This study will define the clinical phenotype associated with neuronal autoantibodies in chronic refractory epilepsy. This involves a multimodality approach to diagnosis that will test the hypothesis that these antibodies are associated with a definable clinical phenotype, which can be used to generate diagnostic criteria similar to what exists for autoimmune encephalitis. Patients will undergo thorough clinical evaluation guided by the stereo-electroencephalography methodology aimed at localisation of the epileptogenic zone. This involves evaluation of seizure semiology, epilepsy risk factors, medical background, neuropsychiatric and neuropsychological assessments. Prolonged electroencephalographic (EEG) recordings will be used to define the electroclinical features of these epilepsies and advanced neuroimaging techniques will be used to evaluate for inflammatory abnormalities in these cases. Ethical approval has been granted. Our pilot study found that these antibodies are associated with perisylvian network epilepsies, as defined by seizure semiology and unique EEG changes. We also found an association with certain epilepsy risk factors, and a very high prevalence of mental health disorders in this population. Most importantly, we demonstrated a clear response to immunotherapy, with many of these refractory patients becoming seizure free. If our hypothesis is correct and we can confirm our preliminary findings in a large cohort, this will change the clinical approach to chronic epilepsy. Once these patients are clinically recognisable as a distinct subgroup they can be more easily identified and will therefore receive more appropriate treatment. This will also lead directly to randomised trials to determine which immunotherapies are most effective. This work will potentially result in a cure for this epilepsy subgroup.

DR PATRICK HARRIS

UQ Centre for Clinical Research
Department of Microbiology, Pathology QLD, RBWH
Infection Management Services, PA Hospital

An international randomised trial of carbapenem-sparing therapy for bacteraemia caused by ceftriaxone non-susceptible Escherichia coli or Klebsiella pneumoniae

Dr Patrick Harris is an Infectious Disease Physician at the Princess Alexandra Hospital, a Medical Microbiologist at Pathology Queensland, and Postgraduate Research Fellow at The University of Queensland Centre for Clinical Research. He completed his medical degree at University College London in 2001. Following initial postgraduate training in the UK he worked as a clinical lecturer at the College of Medicine in Malawi, prior to specialist training in infectious diseases and microbiology in Australia and Singapore. He has published more than 45 peer-reviewed articles, many as first author. He completed his PhD in 2018 under the supervision of Prof. David Paterson at UQ. His research interests include clinical trials of new treatment strategies for antibiotic resistant bacteria and the application of genomics to clinical microbiology.

Scientific Abstract:

Background: Extended-spectrum β-lactamases (ESBLs) increasingly mediate resistance to third-generation cephalosporins (3GCs) in Escherichia coli and Klebsiella pneumoniae. Bloodstream infections (BSI) caused by ESBL-producers are usually treated with carbapenems, yet overuse may select for carbapenem resistance. We aimed to test whether piperacillin-tazobactam ("carbapenem-sparing" therapy) is non-inferior to meropenem (a carbapenem) in patients with these infections.
Methods: We enrolled hospitalised patients from 32 sites in 9 countries from February 2014 to July 2017. Adult patients were eligible if they had at least one positive blood culture with E. coli or Klebsiella spp. testing non-susceptible to 3GCs, but piperacillin-tazobactam susceptible. Patients were randomised 1:1 to piperacillin-tazobactam 4.5g 6-hourly or meropenem 1g 8-hourly for a minimum of 4 days, with total duration determined by the treating clinician. The primary outcome was all-cause mortality at 30 days post randomisation. A non-inferiority margin of 5% was used.
Results: A total of 391 patients were included, from 1,646 screened. Of these, 379 were randomized appropriately, received at least one dose of study drug and were included in the modified intention to treat (mITT) population. One patient was lost to follow-up. A total of 23/187 (12.3%) patients randomised to piperacillin-tazobactam met the primary outcome of mortality at 30 days, compared with 7/191 (3.7%) randomised to meropenem (risk difference 8.6%, 95% CI 3.4% to 14.5%; RR 3.4, 95% CI 1.5 to 7.6; P =0.002). Effects were consistent in an analysis of the per-protocol population. There were no significant differences in subsequent infections with carbapenem resistant organisms between treatment arms.
Conclusions: The use of piperacillin-tazobactam as definitive therapy for BSI caused by E. coli or K. pneumoniae with non-susceptibility to 3GCs was inferior to meropenem and should be avoided in this context. These results have significant implications for selecting optimal treatment of these organisms and will change clinical practice.

Queensland Health
Health and Medical Research

Health and Medical Research, within the Preventive Health Unit, Health Service and Clinical Innovation Division, Department of Health, provides leadership for Queensland Health in the advancement of Queensland Health's research expertise and translation of research outcomes to better healthcare for Queenslanders.

Health and Medical Research inputs into national initiatives to advance research (e.g. National Health and Medical Research Council projects to increase clinical trials) and coordinates Queensland Health's input into State Government initiatives (e.g. Queensland's Science and Innovation Action Plan and projects led by the Department of Science, Information Technology and Innovation).

Health and Medical Research oversees state-wide policy for research ethics review and governance, supports researchers through a fellowship program, and provides assistance with knowledge transfer and realising the health, commercial and social benefits of research outcomes. It is also responsible for services such as the provision and monitoring of approvals for using confidential health information for research under the *Public Health Act 2005 (Qld).*

For more information visit www.health.qld.gov.au/ohmr/default.asp.

Queensland Government

Mid-Career Researcher Award Finalists

DR MUHAMMAD SHIDDIKY

School of Environment and Science and
Queensland Micro and Nanotechnology Centre
Griffith University

Highly Porous Superparamagnetic Nanoparticles Based Molecular Diagnostics

Muhammad J. A. Shiddiky is a Senior Lecturer and NHMRC Career Development Fellow in the School of Environment and Science & Queensland Micro- and Nanotechnology Centre at Griffith University. He obtained his Ph.D. degree from Pusan National University (PNU), South Korea in 2007. Following his Ph.D. research, he was a Postdoctoral Fellow at Monash University and ARC DECRA Fellow at the University of Queensland. His research career has been dedicated to understanding microfluidics, electrochemistry, nanotechnology and surface chemistry based phenomenon for the developments of new technologies and devices that enable biological activities to be measured and manipulated. He has published over 100 high impact papers on topics in biosensors, molecular diagnostics and translational research. He is one of the recipients of an ARC DECRA, an NHMRC CDF, an UQ Postdoctoral Research Fellowship, an UQ ECR Fellowship, and a Graduate Student Award for PhD research excellence. He has licenced two patents.

Scientific Abstract:
Circulating biomarkers in accessible bodily fluids have been shown to have a clear association with a range of pathological conditions. However their detection in these samples represents a major challenge mainly due to the complex nature of the samples and low concentration of the target biomarkers. Most current diagnostic methods use expensive extraction kits, and rely on sophisticated instrumentation, limiting their use in developing countries and other resource poor settings.
The proposed solution is based on a new class of multifunctional metal (gold or platinum)-loaded, highly porous, superparamagnetic nanoparticles. The particles were initially modified with specific bio-recognition probes, dispersed in analyte fluids where they work ask as 'dispersible nanocarriers' to bind specific targets. The gold or platinum loaded on the porous framework of the particles allows the direct attachment of a larger number of bio-recognition probes via gold or platinum-biomolecules affinity interactions which can significantly enhance the capture efficiency. The magnetic property of the particles allows magnetic mixing, purification, and collection which can improve assay performance by reducing the matrix effects of the samples, as non-target species can be removed via magnetic purification steps. Their peroxidase-like activity could be adapted to an ELISA-based sensing protocol where the oxidation of TMB in the presence of H2O2 could be mimicked to generate coloured complexes for naked-eye observation and UV-vis or electrochemical detection. The method has successfully been tested for the analysis of exosomes, autoantibodies and exosomal micro-RNA in a small cohort of clinical samples. The clinical applicability of the method has been tested in detecting exosomes, autoantibodies and exosomal micro-RNA in a small cohort of samples obtained from patients with epithelial ovarian cancer high-grade serous subtype. We envisage that our assay could find a wide range of applications in developing low-cost and simple sensing approaches in the fields of medicine and biotechnology.

DR MICHAEL SMOUT

Australian Institute for Tropical Health and Medicine and
Centre for Biodiscovery & Molecular Development of Therapeutics
James Cook University

Saving diabetic feet with supercharged wound healing

Michael started science with an undergraduate degree at the University of Queensland. His research career started with melanoma mutations and viral infections, but his passion for nearly two decades has been parasitic worms. Exploring worm vaccines both in Brisbane and the USA was followed by delving into the cancerous Thai liver-worm parasite. After graduating from his PhD in 2010 at the Queensland Institute of Medical Research (QIMR) in Brisbane he migrated north to join James Cook University and is now part of the AITHM/CBMDT research hubs. The move has expanded his love of parasitic worms to all things venomous in the tropics, including the deadly big box jelly, scorpions, and sea snakes. Currently he is developing the worm spit compound, granulin, as a wound healing stimulant to help the million people around the world that suffer from devastating non-healing chronic wounds.

Scientific Abstract:

Diabetics, the elderly, and smokers often suffer from chronic wounds that don't heal and 10% of patients will require an amputation. Diabetics are especially at risk and twelve Australians every day lose a limb to diabetes. A treatment that stimulates wound healing is desperately needed – shorter, or avoided hospital stays would benefit the 1.7 million Australian diabetic patients and ballooning healthcare costs of the Australian Government (currently AUD$3.7 billion/year for diabetes). We believe we have the answer from a surprising source – the secretions from a parasitic liver worm. Parasitic worms are large, invasive pathogens. To combat the pathology they induce, worms evolved strategies to promote wound repair in infected hosts. We identified the granulin growth factor protein, named Ov-GRN-1, as the parasitic wound healing protein. Recently we have synthetically created a range of Ov-GRN-1 derived 23-35 amino-acid peptides as potential wound healing treatments (Patent# PCT/AU2017/050959). Currently, we are running a range of cell and animal based tests to develop our treatment. Initially we screened peptides with human fibroblasts and 200 nanomolar concentration in complete growth media was sufficient to stimulate significant proliferation. Subsequent experiments demonstrate our optimal peptide significantly improves mouse wound healing 43% relative to control peptides. Furthermore, this experiment almost doubled the healing capability of our positive control Regranex (22%), the only FDA approved biological product for chronic wounds. We are the first to develop a minimised peptide version of the granulin protein that can be easily synthesised and scaled up for low cost, clean and safe production. We believe we have a unique product that can help heal the million patients worldwide who currently suffer from the plague of chronic wounds.

DR CONAN WANG

Institute for Molecular Bioscience
The University of Queensland

Unlocking Future Therapeutics with Constrained Peptides

Conan Wang obtained his PhD in biological sciences from the University of Queensland, Australia, in 2009. Dr Wang was awarded an NHMRC Early Career Fellowship and undertook postdoctoral studies at Hong Kong University of Science and Technology, Hong Kong, and Griffith University in Brisbane, Australia. He returned to the University of Queensland in 2013 to continue his research work and is currently a research officer at the Institute for Molecular Bioscience. His research is focused on the design and characterization of therapeutically-active peptides.

Scientific Abstract:

Bioactive peptides have great potential as drug leadsfor a wide variety of diseases, including cardiovascular disease, metabolic disease, pain and cancer, because they can bind to their targets with exquisite specificity. However, turning them into drugs has been a considerable challenge because of their typically poor metabolic stability. Through the course of my career, I have been investigating approaches for designing peptide therapeutics and overcoming their limitations. One approach is called molecular grafting and involves fusing a bioactive peptide lead onto a stable scaffold to improve its stability and expand its functionality. I will show using a specific example of how this approach can be used to design stable therapeutics for the treatment of multiple sclerosis by pre-conditioning the immune system to prevent disease onset. Designed peptides showed exceptional stability. One in particular significantly reduced the development of the disease in a mouse model of multiple sclerosis. Histological analysis confirmed reduced inflammation and demyelination. I have also developed a novel strategy for improving oral bioavailability of peptides, providing a way to overcome one of the main challenges limiting translation of peptide leads into drugs. High oral bioavailability increases patient compliance, leads to safe dosage levels and minimizes unwanted side-effects. Using my approach, I designed several peptides that showed high permeability, significantly beyond what is typically expected for peptides, in in vitro and in vivo models.Broadly, my contribution to medical research is in investigating novel approaches for designing therapeutic agents; and so, one could perhaps say that I am forging keys that hopefully unlock new medicines for the benefit of human health.

2018 ASMR MRW® Gala Dinner

ASMR Medical Research Week® 1st – 9th of June 2017

Featuring the ASMR Medalist 2018, The Lab Girl **Professor Hope Jahren** and presentation of the prestigious Queensland Health & Medical Research Awards supported by **QLD government**.

Presenting 2018 ASMR Medalist
Professor Hope Jahren – Biology Institute at the University of Oslo
Best selling author **"The Lab Girl"** and 2016 TIME magazine's **100 most influential people**

Location:	**Hillstone Golf Club St Lucia**
Date:	**1st June 2018**
Time:	**From 18:30 PM**
Tickets:	**$130 and $95 for students**

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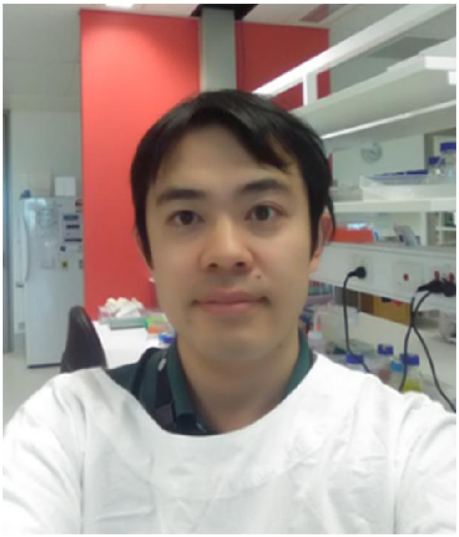
Ph: (02) 9230 0333, Fax: (02) 9230 0339 Email: asmr@alwaysonline.net.au Website: www.asmr.org.au Snr Executive Officer: Catherine West

Early-Career Researcher Award Finalists

DR KYOHEI NAKAMURA

QIMR Berghofer Medical Research Institute

Interleukin-18 as a potential Achilles' heel of multiple myeloma



Dr. Nakamura is a Senior Research Officer at the Immunology in Cancer and Infection laboratory, the QIMR Berghofer (QIMRB) Medical Research Institute. He received his medical degree from Tohoku University, Sendai Japan in 2008. He received clinical training in Haematology and Rheumatology, and obtained board certification in Internal Medicine and Rheumatology in 2014. During his clinical training, he studied innate immunity focused on NK cell and inflammation biology, and completed his Ph.D. in 2014. Since he joined the QIMRB in 2015, his research has been focused on immunopathology of blood cancers, especially multiple myeloma. His key research questions are: 1) How do malignant myeloma cells create immunosuppressive microenvironment in the bone marrow, 2) how do anti-myeloma drugs change the myeloma immune environment, and 3) Can the bone marrow milieu be a potential therapeutic target in multiple myeloma?

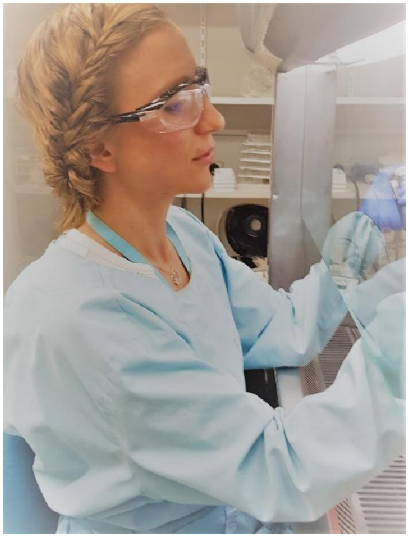
Scientific Abstract:

Multiple myeloma is a type of blood cancer in the bone marrow (BM), characterized by monoclonal antibody production, bone destruction, and kidney injury. Despite recent advances of new anti-myeloma therapies, primary and acquired resistance remains major barriers to a cure. An in-depth understanding of the myeloma microenvironment might bring clue for better control of myeloma, as myeloma cells highly depends on the BM niche for their survival, proliferation and therapy-resistance. Given that myeloma progression is tightly associated with destruction of the normal BM architecture, we hypothesize that the myeloma-induced tissue injury is a key driver for inflammation and immunosuppression in the BM niche. Using a preclinical Vk*MYC myeloma model, a global transcriptome analysis of the immune microenvironment in 73 patients, and a retrospective analysis of BM cytokine levels and prognosis in 152 patients, we showed that the inflammasome-mediated cytokine IL-18 critically drove myeloma progression. Mechanistically, IL-18 in the myeloma niche conferred potent immunosuppressive activities to BM immature myeloid cells, leading to generation of an immunosuppressive milieu. Strikingly, we found that high levels of BM IL-18 at diagnosis predicted poor prognosis, independently of age, clinical stages, or high-risk cytogenetics. Furthermore, our preclinical studies showed that therapeutic blockade of IL-18 could augment efficacies of anti-myeloma drug, bortezomib. Overall, these results indicate that dysregulated IL-18 is a key regulator for the vicious cycle of inflammation and immunosuppression in the myeloma milieu. Now our research aims to obtain in-depth molecular mechanisms of myeloma-associated inflammation and to develop effective anti-myeloma therapies by targeting the inflammatory niche. Since immunotherapies have shown promising efficacies in myeloma patients in recent clinical trials, our research will provide essential information to overcome immunosuppression and to bring a cure for patients.

DR KIRSTY SHORT

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

Understanding the long term effects of obesity on our susceptibility to the flu



Dr. Kirsty Short is a UQ Development /ARC DECRA research fellow. She completed a PhD in 2013 at the Department of Microbiology and Immunology at the University of Melbourne. In 2013 she was also awarded an NHMRC CJ Martin Early Career Fellowship to go to the Netherlands to work in the Department of Virosciences at Erasmus Medical Centre. She returned to Australia at the end of 2015 to work at the University of Queensland. In 2017 she established her own independent research group studying influenza virus pathogenesis. Her group works on many different aspects of the flu including how the flu virus affects different animal species, investigating the role of the immune system in severe flu infections and the interactions between the flu and chronic medical conditions such as diabetes and obesity.

Scientific Abstract:

Obesity significantly increases the risk of death following an influenza virus infection. Consistent with these clinical observations, we and others have shown that mice with diet-induced obesity develop much more severe influenza than their lean-fed counterparts. Traditionally, it has been assumed that this increased susceptibility can be reversed by weight loss. However, this remains to be tested experimentally. Here, a novel mouse model was developed to study the long-term effects of obesity on anti-viral immunity. Four week old C57BL/6 mice were fed a high fat or lean diet for 10 weeks. After 10 weeks, mice fed a high fat diet had a significantly higher total body weight and percentage body fat compared to mice fed the lean diet. Obese mice were then swapped to a lean diet for 10 weeks. After 10 weeks on the lean diet, mice that were previously obese (PO) had an equivalent body weight and percentage body fat to mice that received the lean diet for the entirety of the 20 week treatment period. However, upon infection with influenza virus (A/Auckland/09(H1N1)), PO mice displayed increased viral replication, inflammation, body weight loss and pulmonary dysfunction compared to lean fed mice. The inflammatory cells in the lungs of PO mice also had an altered metabolic state compared to those of lean fed mice. We therefore propose that obesity can have long-term effects on the metabolism of innate inflammatory cells such that they are impaired in their anti-viral response. The current obesity epidemic represents one of the biggest health crises of the 21st century. Understanding the long-term effects that obesity has on the immune response to influenza virus will help pave the way for the development of novel therapeutics to improve the health of the billions of people who are, or previously have been, obese.

DR TANIA RIVERA HERNANDEZ

Australian Infectious Diseases Research Centre and SCMB
The University of Queensland

An experimental group A Streptococcus vaccine that reduces pharyngitis and tonsillitis in a non-human primate model

As a teenager growing up in Mexico I had a strong interest in science particularly biology, mathematics and physics. That led me to find a degree that would combine all those fields, which was an engineering degree in biotechnology. Early on during my degree I became fascinated with vaccines as one of the most powerful tools in public health and an incredible scientific development. After finishing my engineering degree in Mexico, I moved to Australia to pursue a PhD on vaccine development. In my PhD I worked in a vaccine platform that could be tailored to different infectious diseases, amongst them group A Streptococcus (GAS). I have since been working on GAS vaccine development and am currently focusing on the establishment of a nonhuman primate model to assess vaccine efficacy. I hope that my current work in the field will contribute to accelerate the successful development of a GAS vaccine.

Scientific Abstract:

Pharyngitis caused by group A Streptococcus (GAS), but not asymptomatic GAS carriage, is a prerequisite for the autoimmune disease acute rheumatic fever (ARF). Repeated bouts of ARF may trigger rheumatic heart disease (RHD), a major cause of heart failure and stroke in developing countries accounting for 275,000 deaths annually. A vaccine that prevents pharyngitis would markedly reduce morbidity and mortality from ARF and RHD. Non-human primates (NHPs) have been utilized to model GAS diseases, and experimentally infected Rhesus macaques develop pharyngitis symptoms including erythema, hyperemic blood vessels, palatal petechiae and occlusion of the oropharyngeal space. Here we use a NHP model of GAS pharyngitis to evaluate the efficacy of an experimental vaccine (Combo5), specifically designed to exclude GAS components M protein and group A carbohydrate potentially linked to autoimmune complications. High-titer antigen-specific antibody responses were detected in NHP serum against all Combo5 antigens, and immunised NHPs showed a reduction in pharyngitis and tonsillitis symptoms compared to controls. Combo5 is the only pre-clinical GAS vaccine shown to provide protection against pharyngitis, warranting clinical development in humans. Our work establishes the NHP model as a gold standard for the assessment of GAS vaccines being developed for the prevention of ARF and RHD.

asmr Australian Society for Medical Research

Public, Political, Scientific Advocacy

Inspired Creativity
When Art Meets Science

Firkin Orator
Honour Harger
Executive Director ArtScience Museum, Singapore
Forging new synergies between art and science

Edwards Orator
Prof Paul Torzillo
Co-Director Healthhabitat & Clinical Professor, University of Sydney
Transforming health outcomes in remote and developing communities through intelligent housing design

Inside the Scientist's Studio

Prof Joseph Penninger, Scientific Director of the Institute of Molecular Biotechnology, Vienna
Delve into the life and mind of one of the world's great scientists

AUSTRALIAN SOCIETY FOR MEDICAL RESEARCH NATIONAL SCIENTIFIC CONFERENCE

NOVEMBER 21-23 2018

ELDER HALL MUSIC CONSERVATORIUM
ADELAIDE, SOUTH AUSTRALIA

Postgraduate Student Researcher Award Finalists

KATIE LINEBURG

QIMR Berghofer Medical Research Institute

HEMATOPOIETIC STEM CELLS AND THEIR PROGENITORS CRITICALLY REQUIRE AUTOPHAGY TO PROMOTE EARLY ENGRAFTMENT FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION

After finishing her Bachelor of Science at the University of Queensland in 2003, Katie commenced her scientific career in the field of neurodevelopment studying axon guidance during brain development. From here, she moved to the Eskitis Institute at Griffith University where she focused her work on the biology of adult stem cells, specifically the development, migration and phagocytic capacity of olfactory ensheathing cells. Katie then transitioned into the field of stem cell transplantation with a move to QIMR Berghofer where she went on to complete her PhD in 2018 on the role of autophagy, cytokine signals and ubiquitination in the complications associated with allogeneic stem cell transplantation. Her work on Autophagy in haematopoietic stem cells identified a critical requirement for this process in stem cell progenitors during the highly stressful and inflammatory setting of stem cell transplantation and the onset of graft-versus-host disease.

Scientific Abstract:

Hematopoietic Stem Cells (HSC) are critical for the success of stem cell transplantation. Autophagy is an intracellular process that has an established role in the long-term survival and function of HSCs. We investigated the contribution of autophagy to HSC in the setting of allogeneic transplantation, in which GVHD results in a T cell derived cytokine storm early post-transplant. Firstly, we demonstrate that TNF and IL-1□ synergistically promote autophagy in both HSC and progenitor populations in vitro. In vivo studies demonstrate that autophagy is increased in donor HSC and progenitor cells in the setting of GVHD compared to non-GVHD controls. Competitive transplant experiments of 1:1 Atg5-/- foetal liver (FL) with WT FL demonstrated that autophagy deficient cells display reduced capacity to reconstitute. In an MHC mismatch model of GVHD we demonstrated that while Atg5-/- cells are capable of engraftment they are overcome in the presence of alloreactive T cells and undergo primary graft failure by day 10 post-transplant while WT cells survive and engraft. We confirmed this early graft failure in a second model, using donor VAVcre Atg7fl/fl mice. The essential requirement for autophagy, specifically in early progenitors and HSC, was confirmed using LysMcre Atg7fl/fl mice. We demonstrate that autophagy is increased in the GVHD (T cell containing graft) setting and that without autophagy early myeloid precursors fail to provide short term reconstitution leading to primary graft failure and mortality. This primary graft failure can be rescued by the administration of cyclosporine, which works to dampen the T cell induced cytokine storm post-transplant. Thus intervention to increase autophagy in these cells post-transplant may improve engraftment in the clinic.

DR PHILIP MOSLEY

QIMR Berghofer Medical Research Institute

The Site of Stimulation Moderates Neuropsychiatric Symptoms after Subthalamic Deep Brain Stimulation for Parkinson's Disease

Dr Philip Mosley studied at the University of Oxford and obtained his medical degree in 2007. He moved to Australia in 2009 to complete his specialist training in psychiatry. He is a Fellow of the Royal Australian and New Zealand College of Psychiatry (RANZCP) and has completed an advanced certificate in Consultation-Liaison Psychiatry. As part of his training Dr Mosley completed a 2-year neuropsychiatry fellowship at the Royal Brisbane and Women's Hospital (RBWH) and the Asia-Pacific Centre for Neuromodulation (APCN) at the University of Queensland. Currently, Dr Mosley works as a member of the deep brain stimulation team at the APCN and as a clinical research fellow at the QIMR Berghofer Medical Research Institute. He runs a private neuropsychiatry practice and also provides a consultation-liaison psychiatry service to the neurology, medical and surgical wards at St Andrew's War Memorial Hospital. Dr Mosley is expected to complete his PhD in computational neuroscience and neuroimaging in 2019.

Scientific Abstract:

Deep brain stimulation (DBS) of the subthalamic nucleus for Parkinson's disease (PD) is an advanced therapy that addresses motor symptoms and improves quality of life. However, it has also been associated with damaging neuropsychiatric symptoms such as impulsivity and hypomania. A comprehensive analysis of neuropsychiatric outcomes with reference to the site of stimulation has not been undertaken.

We examined a consecutive sample of 64 persons with PD undertaking subthalamic DBS. Participants were assessed with a battery of neuropsychiatric instruments at baseline and at repeated postoperative intervals. A psychiatrist identified patients with clinically-significant symptoms due to stimulation. The site of the active electrode contact and a simulated volume of activated tissue were evaluated with reference to putative limbic, associative and motor subregions of the subthalamic nucleus. We studied anatomical correlates of longitudinal neuropsychiatric change and delineated specific subthalamic regions associated with neuropsychiatric impairment. We tested the ability of these data to predict clinically-significant symptoms.

Subthalamic stimulation within the right associative subregion was associated with neurocognitive disinhibition at 6-weeks ($p = 0.023$) and 13-weeks postoperatively ($p = 0.0017$). At 6-weeks, clinically-significant mood and behavioural changes were associated with the distance of the active contact to the right associative subregion ($p = 0.0026$) and stimulation within the right associative subregion ($p = 0.0009$). These findings were replicated at 13-weeks. Discrete clusters of subthalamic voxels associated with high and low likelihood of postoperative neuropsychiatric symptoms were identified in ventromedial and dorsolateral zones. When a classifier was trained on these data, clinically-significant symptoms were predicted with an accuracy of 79%. These data underscore the importance of accurate electrode targeting, contact selection and device programming to reduce postoperative neuropsychiatric impairment. The ability to predict neuropsychiatric symptoms based on subthalamic data may permit anticipation and prevention of these occurrences, improving safety and tolerability.

KOSALA WEERAKOON

QIMR Berghofer Medical Research Institute

A novel cell free DNA detection droplet digital PCR assay for the diagnosis of human schistosomiasis

Kosala graduated in Medicine from the University of Peradeniya, Sri Lanka in 2008. He then completed his Master of Philosophy degree on human rickettsial infections (2013), and Postgraduate Diploma in Applied Statistics (2010) from the same university. He has been working as a Lecturer in medical parasitology at the Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka since 2011 and is now doing his PhD at the University of Queensland, and QIMR Berghofer Medical Research Institute, Australia. Kosala has strong interest in tropical diseases involving clinical, laboratory and field research, particularly the diagnostics and epidemiology of infectious diseases. His current research focusses on development of advanced molecular diagnostic tools for accurate detection of human schistosomiasis and other intestinal parasitic infections, and also the stability and dynamics of parasite cell-free DNA within the mammalian host.

Scientific Abstract:

Schistosomiasis japonica remains a major public health and is of significant socio-economic concern in Southeast-Asia, particularly in the Philippines and in China. WHO aims to eliminate schistosomiasis as a public health problem by 2025 and accurate diagnostics will play a pivotal role in achieving this goal. Detection of schistosome DNA using molecular techniques represents a promising adjunct to currently available diagnostic tests. Parasite cell-free-DNA detection in human clinical samples is a recent valuable advance which provides significant benefits for accurate disease diagnosis.

We developed a novel ddPCR assay for the detection of schistosomiasis japonica with improved diagnostic sensitivity and specificity. The assay proved applicable for both SjC (Chinese) and SjP (Philippines) infections and was tested in a S. japonicum infection mouse model which detected both pre-patent and patent worm infections using serum, urine, faecal and salivary gland DNA. The target DNA copy numbers obtained in the assay showed a positive correlation with the infection burden assessed by traditional parasitological procedures. Following animal model testing, the assay was validated using clinical samples collected from 412 subjects resident in eighteen villages endemic for schistosomiasis japonica in the Northern Samar region of the Philippines. S. japonicum DNA present in stool, serum, urine and saliva was detected quantitatively with high sensitivity. The capability to diagnose the infection using non-invasively collected clinical samples with a higher level of sensitivity compared with traditional copro-microscopy, the capacity to quantify infection intensity, and the ability to detect an early infection have important public health implications for schistosomiasis control.

The novel ddPCR assay we developed and tested represents a valuable new tool for point-of-care diagnosis, the detection and surveillance of schistosomiasis, particularly in low prevalence and low intensity areas approaching elimination, and in evaluating the situation in those areas where emergence or re-emergence of the infection is a concern.

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