

The Australian Society for Medical Research



The Queensland branch of the ASMR are proud
to present the

2016 HEALTH & MEDICAL RESEARCH AWARDS

Queensland Health and Medical Research
Awards are proudly supported by the
Queensland Government





Safeguarding the future of Australian health & medical research

The Australian Society for Medical Research

- The Australian Society for Medical Research (ASMR) is the peak professional body representing Australian health and medical research
- The society was founded in 1961 by a group of clinician researchers to advocate for the best interests of Australian health and medical research
- Through direct and affiliate members, the ASMR has grown to represent more than 24,000 people actively involved in health and medical research
- The ASMR has no political alignments, regularly meeting with Federal MPs in Canberra and around Australia to present an evidence-based case on the benefits of health & medical research

Australian health & medical research is **poised to address future health challenges**

- Australia is an ageing population. By 2050, almost a quarter of the population will be over the age of 65^{1,2}
- The burden of diseases associated with ageing is also increasing, and is predicted to consume Federal budgets¹⁻³
- Government health expenditure is projected to increase from \$2800/person in 2014-15 to \$6,000/person in 2054-55²
- Health system expenditure is anticipated to grow from \$113 billion in 2012 to \$255-324 billion in 2054-55^{2,4}
- The last 10 years of NHMRC funded medical research has saved almost \$6 billion to the health system due to increased well being⁵

Health & medical research is **one of Australia's economic pillars**

- Every \$1 invested in Australian health and medical research returns an average of \$2.17 in health and economic benefits³
- The last decade of NHMRC funded medical research has led to savings of \$385 million in productivity, from avoided deaths and illnesses, and other indirect costs⁵
- Over the last decade, the largest increase in real exports has been in medical instruments, and medicinal and pharmaceutical products — a direct outcome of investment into health and medical research⁶
- Independent modelling demonstrates that lifting the investment into NHMRC to represent 3% of total health expenditure will lead to health and economic savings⁴
- More importantly, investment into health and medical research underpins a healthier, more productive Australian workforce

ASMRs 2016 **pre-budget submission** to Treasury

- ASMR seeks an immediate injection of \$300 million into the NHMRC Medical Research Endowment Account in the 2016 Federal Budget (this will represent 1% of total health expenditure)
 - To help mitigate Australia's
 - unstable research ecosystem and prevent squandering its opportunity to capitalise on years of investment into our highly qualified and talented workforce -the enabler of research capacity and improved health.
 - best and brightest being lost; our most valuable and irreplaceable asset – expert people
- Incrementally increase NHMRC investment into health and medical research to reflect 3% of total health expenditure by 2023⁴

1. Australian Government, The Treasury 2010. *Australia to 2050: future challenges — The 2010 Intergenerational Report*. www.treasury.gov.au/gtr/2010/default.asp
 2. Australian Government, The Treasury 2015. *2015 Intergenerational Report: Australia in 2055*. www.treasury.gov.au/PublicationsAndMedia/Publications/2015/2015-Intergenerational-Report
 3. Access Economics. *Exceptional returns: The Value of Investing in Health R&D in Australia II*, 2008. www.asmr.org.au/Publications.html
 4. Deloitte Access Economics. *Extrapolated returns on investment in NHMRC medical research*, 2012. www.asmr.org.au/Publications.html
 5. Deloitte Access Economics. *Returns on NHMRC funded Research and Development*, 2011. www.asmr.org.au/Publications.html
 6. Prime Minister's Manufacturing Taskforce. *Report of the Non-Government Members*, 2012. www.innovation.gov.au/industry/manufacturing/Taskforce/Documents/SmarterManufacturing.pdf



Queensland Health is proud to again support the Australian Society for Medical Research (ASMR) Queensland Health and Medical Research Awards. I would like to congratulate all applicants and recipients for 2016. These awards provide an important opportunity to recognise the exceptional scientific contributions of Queensland's health and medical researchers.

The Health and Medical Research Unit within the Clinical Excellence Division is providing a place for fertile interaction where leadership, research excellence and improvement in health and medicine are key objectives.

We at Queensland Health are investing heavily in innovation, science and tackling the challenges of this century and the next by supporting a diverse range of health and medical research by clinical practitioners and other health specialists.

These range from indigenous health initiatives to identifying new cancer markers; from early familial recognition of mental health psychosis to changing the eating habits of pregnant women prone to diabetes; from deep brain stimulation for epilepsy to improving transplant outcomes.

And there's no doubt we have had some extraordinary commercial successes. Spinifex, Q Sera, immune therapy in bone marrow transplants, Q PHARM malaria treatments are all examples of discoveries and ideas developed here at home that have attracted global investment.

As noted astronomer, writer and scientist, Dr. Carl Sagan says, "somewhere, something incredible is waiting to be known." And within the exciting research talent celebrated tonight we can see that Queensland's young researchers have their eyes wide open to dramatic, life changing possibilities.

Congratulations and thank you to all applicants and finalists. I look forward to seeing the positive impact of your research for patients in Queensland, across Australia and ultimately the world.

Michael Walsh

Director-General, Queensland Health

2016 ASMR Queensland Health and Medical Research Award Finalists:

Postgraduate Student Researcher:

Faith Brennan, School of Biomedical Sciences, UQ
Kai Tang, IHBI, QUT
Sarah Walton, School of Biomedical Sciences, UQ
Haolu Wang, School of Medicine, UQ
Aleena Wojcieszek, Mater Research Institute, UQ
Arabella Young, QIMR Berghofer Medical Research Institute

Postdoctoral Researcher:

Dr Mark Adams, QUT, TRI
Dr Brooke Coombes, School of Biomedical Sciences, UQ
Dr Zeinab Khalil, Institute for Molecular Bioscience, UQ
Dr Indira Prasadam, IHBI, QUT

Senior Researcher:

Dr Michelle Lupton, QIMR Berghofer Medical Research Institute
Dr Michele Teng, QIMR Berghofer Medical Research Institute
Dr Makrina Totsika, IHBI, QUT

Clinical Researcher:

Prof Louise Cullen, QUT, Metro North Queensland Health
Dr Jonathon Fanning, School of Medicine, UQ
Dr W. Phillip Law, UQ, TRI



ASMR Medallist 2016 – Professor Theodore Berger



Theodore (Ted) Berger is Professor of Biomedical Engineering at the Viterbi School of Engineering at the University of Southern California. He could be described as a 'neuroprosthetics pioneer', leading a multi-disciplinary collaboration to develop a microchip-based neural prosthesis for the hippocampus, a region of the brain responsible for long-term memory. Damage to the hippocampus is frequently associated with epilepsy, stroke, and dementia (Alzheimer's Disease), and is thought to underlie the memory deficits characteristic of these neurological conditions.

His laboratory, over the last 25 years, has been dedicated to understanding the mechanisms underlying neuronal integration, and has applied its findings to generate many applications of the discoveries. In particular, applying non-linear systems analytic procedures to the experimental study and mathematical modeling of synaptic and network dynamics of the hippocampus. These studies are now classic in demonstrating how engineering approaches can be brought to bear on fundamental problems in the neurosciences, and are the basis for a two-decades long series of advances in nonlinear modeling methodologies for the nervous system.

Professor Berger was named as one of "The 100 Leading Global Thinkers of 2013" by Foreign Policy Magazine. He is that rare embodiment of bold vision, brilliance, courage and tenacity; the attributes which expand the boundaries of science and create the future. *He and his trans-disciplinary colleagues have developed a brain prosthesis designed to help people suffering from memory loss. The device implanted into the brain has performed well in animal tests and is currently being evaluated in human patients.*

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The Australian Society for Medical Research

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.

<http://asmrfiles.org.au/research/>

Note all donations to the ASMR Research Fund are tax deductible

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FAITH BRENNAN

School of Biomedical Sciences

The University of Queensland

Improving outcomes from spinal cord injuries



Rugby league fans watched in horror as Newcastle Knights rising star Alex McKinnon suffered a spinal cord injury as a result of a tackle gone wrong. While McKinnon has since made steady progress in his rehabilitation, a major factor that impedes recovery after neurotrauma is an excessive acute inflammatory response triggered by the spinal cord injury. Research conducted by Faith Brennan and colleagues at the University of Queensland reveals that the transfusion of a blood product, known as intravenous immunoglobulin (IVIg), can attenuate this harmful inflammatory response and improve functional recovery in an animal model of spinal cord injury. The protective effects of IVIg on spinal tissue could also be detected non-invasively through advanced magnetic resonance imaging techniques. The findings indicate that IVIg is a promising candidate for spinal cord injury clinical trials.

Scientific Abstract:

Traumatic spinal cord injury (SCI) leads to neural cell death and disruption of the blood-spinal cord barrier, which activates complement and allows circulating immune cells to enter the spinal cord parenchyma. This inflammatory response contributes to secondary injury and impairs neurological recovery. The aim of this study was to determine whether intravenous immunoglobulin (IVIg) therapy, which is already FDA approved for treating a variety of autoimmune conditions, can counteract neuroinflammation in experimental SCI. C57BL6/J mice were subjected to severe contusive SCI, then administered either IVIg (up to 2 g/kg, 0.4cc, i.v.), vehicle, or albumin (protein loading control) at 1 hour post-SCI. Recovery of locomotor function was monitored for 5 weeks post-injury using the Basso Mouse Scale (BMS). Non-invasive MRI and diffusion tensor imaging (DTI) were used to assess lesion development in live mice at 1, 7 and 35 days post-SCI. ELISA and routine histological techniques were used to compare complement activation and tissue pathology between experimental groups post-mortem. We report that IVIg improves functional and histopathological outcomes and attenuates macrophage infiltration and complement activation in experimental contusive SCI. Importantly, the therapeutic benefits of IVIg on tissue sparing were detectable through non-invasive imaging, with IVIg treatment counteracting the trauma-induced changes in MRI and DTI indices in spinal white matter tracts. Imaging data was significantly correlated with the functional recovery of individual mice, and also accurately predicted the degree of myelin preservation. The findings of this study highlight the prospect of using IVIg as an anti-inflammatory treatment for SCI patients, and the potential of imaging techniques to assess intervention strategies in preclinical models. The ability to non-invasively detect treatment effects in live animals is a major step forward to accelerate the translation of promising therapeutic interventions into the clinic.

KAI TANG

Institute of Health and Biomedical Innovation

Queensland University of Technology

Dissecting the prostate cancer stem cell niche inside the bone marrow



Prostate cancer frequently metastasizes to the bone, which becomes incurable. Although ample evidences support the idea that tumour metastasis originates from a rare population of cancer cells known as “cancer stem cells”; however, how they manage to survive and grow in the bone is still largely unknown. In this study, I have demonstrated, for the first time, that the bone cells and fat cells within the bone marrow actively promote the expansion of prostate cancer stem cells. More importantly, by interrupting the interaction between prostate cancer cells and bone/fat cells, I have developed approaches that can effectively inhibit the growth of the prostate cancer stem cells population. Therefore, my work may offer both prognostic and therapeutic opportunities in the treatment of metastatic prostate cancer.

Scientific Abstract:

Ample evidence supports that prostate tumour metastasis originates from a rare population of cancer cells, known as cancer stem cells (CSCs). Prostate CSCs share many similarities with normal stem cells, including the dependency on a stem cell niche. Prostate CSCs that disseminate into the bone marrow are believed to manipulate the hematopoietic stem cell (HSC) niche to initially maintain a quiescent state before producing a new niche to support the development of bone metastasis. Therefore, a better understanding of the bone marrow stem cell niche and its role in supporting bone metastasis may aid the development of effective treatments. The aim of my study was to investigate the role of osteoblasts and adipocytes, two major cellular components of the bone marrow, in the formation of a CSC-specific niche during the development of prostate tumor bone metastasis. Here, I demonstrated, for the first time, the role of angiopoietin-1 (Ang-1)/Tie-2 and cholecystokinin (CCK)/CCKBR signalling pathways in the maintenance of prostate CSC within the bone marrow stem cell niche. I have discovered that prostate cancer (PCa) cells not only express both Tie-2 and CCKBR, but also respond to the stimulation of their ligands, Ang-1 and CCK, leading to induction of quiescence and CSC self-renewal respectively. More importantly, I found that inactivation of Tie-2 or CCKBR with specific inhibitors significantly suppress both the expression of CSC markers and the self-renewal ability of the CSCs. Overall, my project has successfully uncovered in the key signalling pathways responsible for promoting prostate CSC self-renewal and the development of bone metastasis. Therefore, further preclinical studies that target these pathways (i.e. Ang-1/Tie-2 and CCK/CCKBR) may result in the development of effective treatments against this most deadly form of prostate cancer.

SARAH WALTON

School of Biomedical Sciences

The University of Queensland

Prenatal hypoxia increases susceptibility to renal and cardiovascular impairments in mouse offspring



What nourishes us in the womb and as infants can profoundly affect our health in later life. Maternal ill health, environmental disadvantage and malnutrition can impair optimal development of organs such as the heart and kidney, meaning these organs may not be robust enough to support a person throughout their lifespan. This likely contributes to high rates of chronic disease in Australia. We have used mice to study how reduced oxygen supply during pregnancy, the most common pregnancy complication, affects kidney and cardiovascular health in later life. These mice are born with smaller, underdeveloped kidneys and develop signs of cardiovascular and kidney disease in adulthood. When fed a diet high in salt, the symptoms of cardiovascular and kidney disease worsens significantly. This suggests that although prenatal disadvantage such as low oxygen supply may be unavoidable, consuming a healthy postnatal diet may prevent or at least limit poor health outcomes.

Scientific Abstract:

In Australia, chronic kidney disease and cardiovascular disease are prominent public health issues. Both are linked to abnormal kidney development, notably reduced nephron number, which may result from *in utero* perturbations. We evaluated the impact of prenatal hypoxia on renal and cardiovascular development and function in the mouse, and whether high salt intake could exacerbate functional impairments.

Pregnant CD1 mice were housed in a hypoxic chamber (12.0% O₂) environment from embryonic day 14.5 to 19.5 (birth). Offspring consumed control (0.2% NaCl) or high-salt diets (5% NaCl) from 10 weeks to 12 months of age. Renal function was examined via 24h metabolic cages and blood pressure was measured by radiotelemetry. Mesenteric arteries were collected for pressurised *in vitro* myography studies, and kidneys were used to determine nephron number by unbiased stereology and subsequently evaluated by an expert pathologist.

Male hypoxia-exposed offspring presented with elevated urinary albumin excretion at 12 months of age. This was associated with a 25% reduction in nephron endowment, significant glomerular hypertrophy and glomerulosclerosis compared to male control offspring. These histopathological changes were exacerbated by the high-salt diet. In contrast, female hypoxia-exposed offspring had normal nephron endowment and no overt signs of renal impairment or histopathology. Male and female hypoxia-exposed offspring both presented with ~14mmHg increase in mean arterial pressure and mild vascular endothelial dysfunction. Consumption of a high-salt diet in both sexes led to marked mesenteric vascular stiffening in hypoxia-exposed offspring.

In summary, prenatal hypoxia perturbed kidney development, impaired renal function and increased susceptibility to salt-induced renal injury in male offspring. Both sexes developed signs of cardiovascular disease in adulthood. This suggests that female offspring are afforded some renoprotection from hypoxia *in utero* however this protection does not extend to the cardiovascular system.

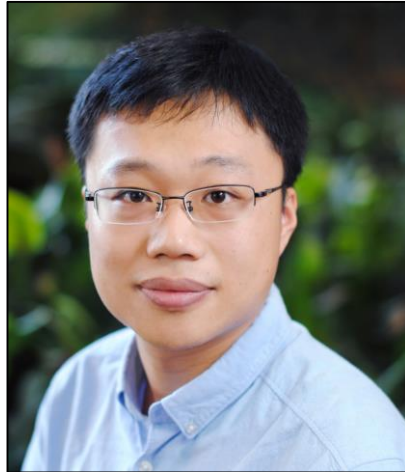


HAOLU WANG

School of Medicine

The University of Queensland

Characterizing and predicting the in vivo kinetics of therapeutic mesenchymal stem cells



Cell therapy has emerged as an evolutionary therapeutic force especially for diseases not curable by traditional therapeutics. However, the success of many cell therapies has been grossly impeded by the poorly-understood cell-tissue interactions and ill-defined cell kinetics in the body. Mesenchymal stem cell (*MSC*) is one of the most promising and widely used therapeutic cells. In this study, we visualized and quantified therapeutic *MSCs* in mouse organs, and characterized their kinetics by a physiologically-based kinetic model. Using this newly developed model, the behaviour of therapeutic *MSCs* could be accurately predicted in patients with different diseases and different routes of administration from external datasets. This is the first study provides the optimized dosage, route of administration, and targeting strategies for *MSC*-based therapy to achieve the maximum effectiveness with the lowest risk. In addition, this model can be easily applied to other types of therapeutic cells for designing standardized treatment protocols.

Scientific Abstract:

Cell therapy has emerged as an evolutionary therapeutic force especially for diseases not curable by traditional therapeutics. However, the success of many cell therapies has been grossly impeded by the poorly-understood cell-tissue interactions and ill-defined cell pharmacokinetics in the body. Mesenchymal stem cell (MSC) is one of the most promising and widely used therapeutic cells for many debilitating diseases including liver cirrhosis, diabetes, spinal cord injury and myocardial infarction. In this study, we first visualized the mouse organ disposition and cell-tissue interactions of green fluorescent protein-expressing MSCs after intravenous injection by high resolution intravital microscopy, and then elucidated the concentration-time profiles of the administered cells in organs using flow cytometry. Based on these findings, we developed the first physiologically-based kinetic model of therapeutic MSCs. The utility of this model was examined across species and administration routes by extrapolation of this model to rats and humans, as well as to intra-hepatic arterial injection. The clinical application of this model was also tested with data obtained from stem cell-based therapies to patients with liver cirrhosis. Our model successfully characterized the *in vivo* kinetics of therapeutic MSCs. Sensitivity analysis revealed that the targeting efficiency of therapeutic MSCs is determined by the lung retention and interaction between MSCs and target organs, including cell arrest, depletion and release. Model validations with multiple external datasets indicated its accurate inter-route and inter-species predictive capability in both normal and disease states. This is the first study provides the optimized dosage, route of administration, and targeting strategies for MSC-based therapy to achieve the maximum effectiveness with the lowest risk. By adapting specific parameters, this model can be easily applied to other types of therapeutic cells for designing standardized treatment protocols.

ALEENA WOJCIESZEK

Mater Research Institute

The University of Queensland

Care in subsequent pregnancies following stillbirth: an international survey of patients



Stillbirth affects more than two million families globally every year. Most parents will conceive again soon after stillbirth. These parents are far more likely to have another stillbirth in the next pregnancy. The next pregnancy after stillbirth is also a very anxious time for parents, as they worry about whether their baby will survive. Yet, there is little research on best practice care in pregnancies after stillbirth. In this study we asked parents from 40 countries about the care they received during pregnancies following stillbirth. We found that parents often had extra antenatal visits and scans, but they rarely had extra emotional support. Also, many parents felt their care providers did not always give them quality, respectful care, such as listening to them and spending enough time with them. This is the first international study of its kind and can inform international best practice care for pregnancies following stillbirth.

Scientific Abstract:

Background: The risk of stillbirth and other pregnancy complications is increased for parents with a previous stillbirth. Pregnancies subsequent to stillbirth are also laden with anxiety, fear, and other complex emotional responses. While it is clear that parents require specialised clinical care and emotional support in pregnancies subsequent to stillbirth, there is little evidence to inform the management of these pregnancies. This study investigated the frequency of additional care, and parents' perceptions of quality, respectful care, in pregnancies subsequent to stillbirth.

Methods: Data were obtained from a multi-language, web-based survey of parents. Data were analysed using descriptive statistics and stratified by geographical region. Subgroup analyses explored variation in care by gestational age at index stillbirth.

Results: A total of 2,716 parents from 40 high- and middle-income countries responded. Additional antenatal care visits and ultrasound scans were provided for 67% and 70% of all parents, respectively, although there was wide variation across geographical regions. Care specifically addressing psychosocial needs was less frequently provided, such as specialist antenatal classes for bereaved parents (3%), visits to a bereavement counsellor (10%), and access to named care provider's phone number (27%). Compared to parents whose stillbirth occurred at 29 weeks' gestation or less, parents whose stillbirth occurred at 30 weeks' gestation or greater were more likely to receive various measures of care in the subsequent pregnancy, particularly the option for early delivery after 37 weeks. Only around half (47-63%) of all parents felt that elements of quality, respectful care were consistently applied, such as listening to parents, spending enough time with parents, and involving parents in decision-making.

Conclusions: Care in pregnancies subsequent to stillbirth appears inconsistent. Greater attention is required to providing thoughtful, empathic, and collaborative care in all pregnancies following stillbirth. Training for health professionals providing care in pregnancies subsequent to stillbirth is needed.



ARABELLA YOUNG

QIMR Berghofer Medical Research Institute

Targeting immunosuppressive adenosine to enhance anti-tumour immunity



Cancer immunotherapies are currently revolutionising treatment options for cancer patients. In contrast to conventional therapies, immunotherapy strengthens a patient's own immune response towards aberrant cancer cells, providing long-term protection against a range of tumour types. However, within the tumour microenvironment, multiple immunosuppressive mechanisms exist to prevent an effective immune reaction. Therefore, identifying alternate therapeutic targets and synergistic combinatorial approaches is required to further improve clinical responses. Notably, production of the immunosuppressive metabolite adenosine is increased within the tumour microenvironment. This inhibits tumour cell killing performed by immune cells leading to disease progression. As therapies targeting both adenosine generation and signalling are currently undergoing early phase clinical trials in cancer, we assessed whether co-targeting multiple parts of the adenosine pathway improved therapeutic benefit. Here, we identified that co-blockade of adenosine-related molecules limits tumour initiation, growth and metastasis, providing important considerations for optimal activity as these therapies move forward to clinical utility.

Scientific Abstract:

Adenosine is a potent immunosuppressor, which hampers an effective immune reaction towards cancer cells within the tumour microenvironment. In particular, adenosine inhibits tumour cell killing performed by cytotoxic lymphocytes and enhances proliferation of immunosuppressive cell types. Preclinical studies have identified that blockade of CD73 (the ectonucleotidase that generates adenosine) and antagonism of A2A adenosine receptor (A2AR) signalling heightens anti-tumour immune responses. However, it is yet to be established as to whether targeting both stages of the adenosinergic pathway in combination further enhances anti-tumour efficacy. To determine whether co-targeting CD73 and the A2AR would provide improved tumour control or show redundancy we developed double-deficient mice. In response to AT-3 mammary carcinoma and SM1WT1 melanoma, A2AR and CD73 double-knockout mice displayed significantly improved primary tumour control compared to wild type mice or single gene-deficient controls, indicative of their non-redundant functions. Mechanistically, loss of A2AR signalling increased CD8⁺ T cell infiltration, which was imperative for tumour control. Additionally, A2AR-deficient mice increased CD73 expression on host cells infiltrating the tumour, representing an escape mechanism inhibited in double-knockout mice. Following, we assessed the therapeutic efficacy of A2AR antagonism alongside anti-CD73 in experimental and spontaneous metastases models. When given concurrently, these therapies reduced metastatic burden and enhanced survival benefit. In particular, anti-CD73 therapeutic activity was mediated by Fc receptor engagement, indicative of the multi-functionality of CD73, alongside adenosine production. Similarly, these *in vivo* findings were paralleled in mixed lymphocyte reactions utilizing human anti-CD73. Adenosine-related therapies are currently entering phase 1 clinical trials in oncology. Understanding optimal treatment regimes, cancer types and combinations to achieve maximal benefit for cancer patients will be important for the clinical success of adenosinergic therapies. This study illustrates the importance of targeting multiple parts of the adenosinergic pathway in combination, revealing its multi-faceted impact on tumour initiation, growth and metastatic progression.

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.





The Australian Society for Medical Research

Queensland Health & Medical Research Awards 2016 Finalist Seminars

Proudly supported by the Queensland Government

Postdoctoral Researcher Award Finalists (9:30-10:30am)

Dr Mark Adams (QUT, TRI) 9:30-09:45
 Dr Brooke Coombes (School of Biomedical Sciences, UQ) 9:45-10:00
 Dr Zeinab Khalil (Institute for Molecular Bioscience, UQ) 10:00-10:15
 Dr Indira Prasadam (Institute of Health and Biomedical Innovation, QUT) 10:15-10:30

Senior Researcher Award Finalists (10:45-11:30am)

Dr Michelle Lupton (QIMR Berghofer Medical Research Institute) 10:45-11:00
 Dr Michele Teng (QIMR Berghofer Medical Research Institute) 11:00-11:15
 Dr Makrina Totsika (Institute of Health and Biomedical Innovation, QUT) 11:15-11:30

Clinical Researcher Award Finalists (11:30am-12:15pm)

Prof. Louise Cullen (QUT, Metro North Queensland Health) 11:30-11:45
 Dr Jonathon Fanning (School of Medicine, UQ) 11:45-12:00
 Dr W Phillip Law (UQ, Translational Research Institute) 12:00-12:15

Venue: The University of Queensland, St Lucia (Hawken Engineering Building, Room S201)
Date: Monday 30th May 2016
Time: 9:30 am

Postgraduate Student Award Finalists (9:45am-12:00pm)

Faith Brennan (School of Biomedical Sciences, UQ) 9:45-10:00
 Kai Tang (Institute of Health and Biomedical Innovation, QUT) 10:00-10:15
 Sarah Walton (School of Biomedical Sciences, UQ) 10:15-10:30
 Haolu Wang (School of Medicine, UQ) 11:15-11:30
 Aleena Wojcieszek (Mater Research Institute, UQ) 11:30-11:45
 Arabella Young (QIMR Berghofer Medical Research Institute) 11:45-12:00

Venue: Translational Research Institute, Woolloongabba (Level 2 Auditorium)
Date: Wednesday 1st June 2016
Time: 09:45 am

Proudly supported by:

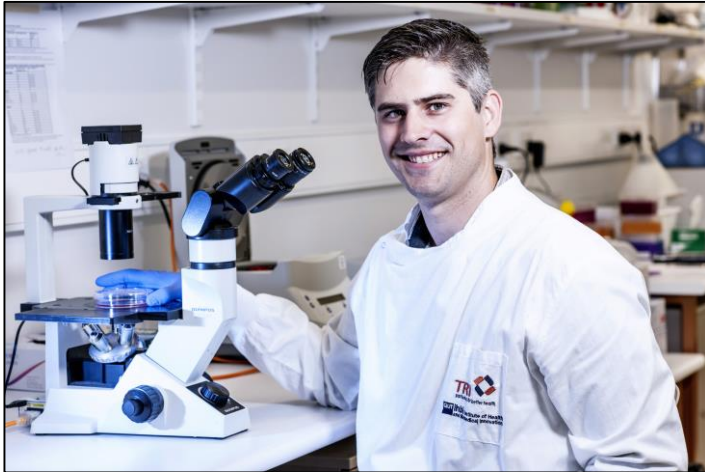


DR MARK ADAMS

Translational Research Institute

Queensland University of Technology

CDCA3 is a potential target to enhance non-small cell lung cancer cell sensitivity to cisplatin



Lung cancer is responsible for the most cancer-related deaths worldwide and has a poor survival rate. The most common type of lung cancer is non-small cell lung cancer (NSCLC). A commonly used drug to treat NSCLC is cisplatin. However, cancer cells develop mechanisms to cope with cisplatin leading to resistance to this therapy in patients.

We have focused on identifying novel molecules that might prove useful in preventing cisplatin resistance. Accordingly, we have identified the molecule cell division cycle associated protein 3 (CDCA3) which functions normally to permit controlled growth. We have identified that levels of CDCA3 are increased in NSCLC and that cancer cells lacking the CDCA3 molecule are more sensitive to cisplatin than control cells.

We have identified that CDCA3 is a novel factor mediating NSCLC. Strategies to target and suppress the levels of this molecule may benefit patient outcome by preventing cisplatin resistance.

Scientific Abstract:

Lung cancer is the leading cause of cancer-related mortality worldwide with an Australian 5 year survival rate of 14%. Non-small cell lung cancer (NSCLC) is the most commonly diagnosed form of lung cancer. Cisplatin-based regimens are currently the most effective chemotherapy for NSCLC. However, chemoresistance poses a major therapeutic problem. New and reliable strategies are required to avoid drug resistance in NSCLC.

Cell division cycle associated 3 (CDCA3) is a key regulator of the cell cycle. Herein, we describe CDCA3 as a novel target to delay or prevent cisplatin resistance in NSCLC. CDCA3 transcripts and protein levels are markedly elevated in NSCLC patient tissue and highly expressed in tumour cells relative to proximal normal cells. Depletion of CDCA3 *in vitro* markedly impairs proliferation in nine NSCLC cell lines by inducing a mitotic cell cycle arrest, ultimately resulting in p21-dependent cellular senescence. Importantly, silencing of CDCA3 also greatly sensitises NSCLC cell lines to cisplatin. In line with these *in vitro* data, NSCLC patients that have elevated levels of CDCA3 and treated with cisplatin have a poorer outcome than patients with reduced levels of the protein. To aid patient response to cisplatin, we have been looking at the possibility of using strategies to suppress CDCA3 expression in tumour cells. Accordingly, we identified that in response to cisplatin, CDCA3 is phosphorylated (S⁸⁷ and S²²²) via casein kinase 2 (CK2) in NSCLC cells, which prevents degradation of the CDCA3 protein. Interestingly, the CK2 inhibitor CX-4945 reduces CDCA3 protein levels in cisplatin treated NSCLC cells.

Our data highlight CDCA3 as a novel factor in mediating NSCLC. We propose that preventing cisplatin-induced CDCA3 phosphorylation by targeting CK2 is a worthwhile and novel strategy in treating NSCLC. This novel strategy may be useful in treating NSCLC and may ultimately benefit patient outcome by preventing cisplatin resistance.



DR BROOKE COOMBS

School of Biomedical Sciences

The University of Queensland

Corticosteroid injection, physiotherapy, or both for treatment of tennis elbow



Corticosteroid injection is widely used for treatment of tendon pain such as tennis elbow, despite evidence that it delays recovery when compared to a wait and see approach or physiotherapy. A randomised control trial of 165 patients with chronic tennis elbow was conducted to test whether a combination of corticosteroid injection and physiotherapy is superior to corticosteroid injection alone. Contrary to our hypothesis, results revealed that adding physiotherapy to corticosteroid injection provided no long-term benefit. More than half of all patients treated with a single corticosteroid injection experienced a recurrence, a substantially greater proportion than the placebo group. In clinically relevant terms, for every 2 to 3 patients treated with corticosteroid (versus placebo) injection, one person experienced recurrence during the year. These findings are relevant to clinicians and policy makers, providing strong evidence that corticosteroid injection should not be considered as a first-line treatment for tennis elbow.

Scientific Abstract:

Importance: Corticosteroid injection and physiotherapy, common treatments for lateral epicondylalgia (tennis elbow), are frequently combined in clinical practice. However, evidence on their combined efficacy is lacking.

Objective: To investigate the effectiveness of corticosteroid injection, multimodal physiotherapy, or both in patients with unilateral tennis elbow.

Design, Setting, and Patients: A 2x2 factorial, randomised, injection-blinded, placebo controlled trial was conducted at a single university research center and 16 primary care settings in Brisbane, Australia. A total of 165 patients aged 18 years or older with unilateral tennis elbow of longer than 6 weeks' duration were recruited.

Interventions: Corticosteroid injection (n=43), placebo injection (n=41), corticosteroid injection plus physiotherapy (n=40), or placebo injection plus physiotherapy (n=41).

Measures: The 2 primary outcomes were 1-year global rating of change scores for complete recovery or much improvement and 1-year recurrence (defined as complete recovery or much improvement at 4 or 8 weeks, but not later) analysed on an intention-to-treat basis ($P < .01$).

Results: Corticosteroid injection resulted in lower complete recovery or much improvement at 1 year vs placebo injection (83% vs 96%, $P = .01$) and greater 1-year recurrence (54% vs 12%; $P < .001$). The physiotherapy and no physiotherapy groups did not differ on 1-year ratings of complete recovery or much improvement (91% vs 88%, $P = .56$) or recurrence (29% vs 38%; $P = .25$).

Conclusion and Relevance: Among patients with chronic tennis elbow, the use of corticosteroid injection versus placebo injection resulted in worse clinical outcomes after 1 year, and physiotherapy did not result in any significant long term differences. Prior to use, clinicians should counsel patients regarding the likelihood of short term benefit and long term delay in recovery after a single corticosteroid injection for tennis elbow. Clinical guidelines should recommend corticosteroid injection not be considered as a first line intervention for tennis elbow.



DR ZEINAB KHALIL

Institute of Molecular Bioscience

The University of Queensland

Wollamide-D: A potent anti-mycobacterial cyclic hexapeptide drug lead



Tuberculosis (TB) remains one of the most enduring infectious disease challenges facing global healthcare. Nine million people develop TB and 1.5 million die per year. The combination of multi-drug resistance (MDR), co-morbidity with HIV-AIDS, and a lack of investment in anti-infective drug discovery has resulted in access to clinically useful TB antibiotics being severely limited.

We recently identified a novel drug family, the wollamides, isolated from bacteria in Australian soils. The wollamides exhibited potent anti-TB activity. Based on this very promising discovery, a library of 50 wollamide analogues was synthesized and tested in assays against clinically relevant TB strains. This proved the anti-TB activity of a lead drug candidate wollamide-D. Of great significance, these studies demonstrated that wollamide-D has bactericidal activity of comparable potency to commercially available anti-TB drugs and has low toxicity and suitable bioavailability to be a viable therapeutic option.

Scientific Abstract:

During an investigation into *Streptomyces* nov. sp. from Australian soils, a novel class of cyclic hexapeptide, the wollamides was isolated. The wollamides exhibit growth inhibitory activity against Gram-positive bacteria (IC_{50} 0.6 – 7 μ M), and were non-cytotoxic to mammalian cells (IC_{50} >30 μ M). More significantly, wollamides-A and B exhibited anti-mycobacterial activity (IC_{50} 0.52 and 0.48 μ M) against BCG - a model organism for *Mycobacterium tuberculosis* (Mtb). Of particular note, addition of wollamide-B (2 and 20 μ M) to BCG infected macrophages, the major host cell for mycobacteria, significantly reduced the number of viable intracellular BCG colony forming units (CFU) 6 days after infection (41-64%), with microscopic observation of the macrophage cultures revealing no cytotoxic effects.

A library of 50 synthetic wollamide analogues was synthesised and tested in (i) cytotoxicity assays targeting a range of human cancer cell lines. The analogues did not exhibit any cytotoxicity (IC_{50} >30 μ M) (ii) Mtb assays against clinically relevant strains proved the antitubercular activity of three analogues wollamide-B (D-Ornithine, D-Orn), C (D-Arginine, D-Arg) and D (D-Lysine, D-Lys). This demonstrated that replacing the D-Orn with other basic amino acids enhanced the anti-tubercular properties of wollamides. It was observed that wollamide-D (D-Lys) showed more potent inhibitory activity (IC_{50} 0.07 – 0.54 μ M) against 5 Mtb strains. Testing against MDR-TB confirmed that wollamide-D was the most active analogue against MDR strain Mtb H37Rv (approx. 80% inhibition at 10 μ g/ml) and a clinical isolate of isoniazid resistant-Mtb (75% and 90% inhibition at 3 and 10 μ g/ml). Bioavailability studies for wollamide-D in rats showed good intravenous bioavailability with half-life of 1 hour, comparable to current therapeutics.

Of great significance, these studies demonstrated that wollamide-D has bactericidal activity of comparable potency to commercially available anti-TB drugs such as rifampicin and has low toxicity and suitable bioavailability to be a viable therapeutic option.



DR INDIRA PRASADAM

Institute of Health and Biomedical innovation

Queensland University of Technology

DMP1 is a novel cartilage related gene required for maintenance of cartilage phenotype and prevention of articular cartilage degeneration



Osteoarthritis (OA) is a painful disease affecting millions of people worldwide. It results from the cartilage breaking down at the joints and severely hampers a person's mobility. An aging population has seen a rise in OA and higher rates obesity and a lack of effective drugs has seen an ever increasing cost and burden due to OA. This study shows that OA-related tissue damage is caused by deficiency of a pathway that regulates cellular phosphate levels. The protein dentin matrix protein 1 (DMP1) was found to be important in maintaining joint health. Loss of DMP1 leads to OA-like symptoms in both humans and mice by activating a cascade of molecular events that result in the destruction of cartilage tissue. These are important findings and a major advance in OA disease research which can pave the way for future drugs targeting OA.

Scientific Abstract:

Cartilage matrix degradation is the major hallmark of osteoarthritis (OA), however, the molecular mechanisms that control this matrix loss is poorly understood. Dentin matrix acidic phosphoprotein (DMP1) is an extracellular matrix protein and a member of the small integrin binding ligand N-linked glycoprotein family. We have recently identified strong localization of DMP1 in the mature articular cartilage tissue by immunohistological (IHC) examinations of knee samples. This was a surprise finding since DMP1 is an acidic phosphoprotein and its expression has previously only been reported in bone, dentin and cementum, hard tissues in which the importance of DMP1 for mineralization is well established. DMP1's role in non-mineralized tissues, such as articular cartilage, is unknown. In this study we explored the impact of DMP1-deficiency (DMP1^{-/-}) on the biomechanical properties of cartilage and the OA development in a knockout mouse model and also *in vitro*, using cartilage cells. Human cartilage from normal knee joints expressed high levels of DMP1 mRNA and protein compared to OA cartilages. IHC analyses showed only a limited number of DMP1 positive cells in human and mouse OA cartilage compared to normal controls. To determine if loss of DMP1 contributed to OA progression, we evaluated the effects of DMP1 loss by siRNA treatment of cartilage cells called chondrocytes. RT-qPCR showed down-regulation of canonical cartilage genes (SOX9, COL2A1 and ACAN) and up-regulation of cartilage degrading genes (MMP-13, ADAMTS4), indicating the importance of DMP1 in cartilage maintenance. Next, we assessed how loss of DMP1 affected articular cartilage in DMP1^{-/-} mice and found that this resulted in spontaneous development of joint deformities and cartilage degeneration. In conclusion, DMP1 is important for maintenance of joint morphology and cartilage homeostasis. This discovery in future will take us a step closer to a ultimate goal of a more effective and much-needed new treatment for OA.

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Professor Theodore Berger



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Drs. Alison Anderson, Lotten Ragnarsson, Rebecca Watts, David Frazer, Xiahui Tan and Varinder Jeet
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DR MICHELLE LUPTON

QIMR Berghofer Medical Research Institute

Genes that effect risk of Alzheimer's are associated with reduced brain volumes before disease symptoms



In Alzheimer's disease (AD), MRI brain imaging shows reduced volumes of certain brain regions. Risk of having AD is partly influenced by genes, and I am interested in whether people who have genetic risk factors for AD have brain volume changes while they are still healthy. We found that older people with increased genetic risk of AD have reduced volumes in AD affected brain regions, and for some genetic variants this is apparent in healthy people. Because the disease process begins many years before symptoms, it is likely that early treatment of people who are a high risk will be a good strategy in preventing AD, before substantial brain damage. Knowing the effects of AD genetic risk variants will help identify targets for prevention therapy, and allow the identification of those most at risk of getting AD in the future.

Scientific Abstract:

Reduction in hippocampal and amygdala volume measured via structural MRI is an early marker of Alzheimer's disease (AD). The strongest identified genetic risk factor for AD is the APOE ϵ 4 allele.

Large scale genome wide association studies have identified an additional 19 common AD risk variants, and recent exome sequencing studies identified a rare risk variant in TREM2 with a large effect. Whether genetic risk factors for AD exert an effect on these subcortical structures independent of clinical status has not been fully investigated. I examined whether increased genetic risk for AD influences hippocampal and amygdala volumes in case-control and population cohorts at different ages, in 1674 older (aged >53yrs; 17% AD, 39% MCI) and 467 young (16-30 yrs) adults.

An AD polygenic risk score (PRS) combining a large number of common risk variants (excluding APOE), and a SNP in TREM2, were associated with reduced hippocampal volume in healthy older adults and those with mild cognitive impairment (MCI). APOE ϵ 4 was associated with reduced hippocampal and amygdala volume in those with AD and MCI, but was not associated in healthy older adults. No associations were found in young adults.

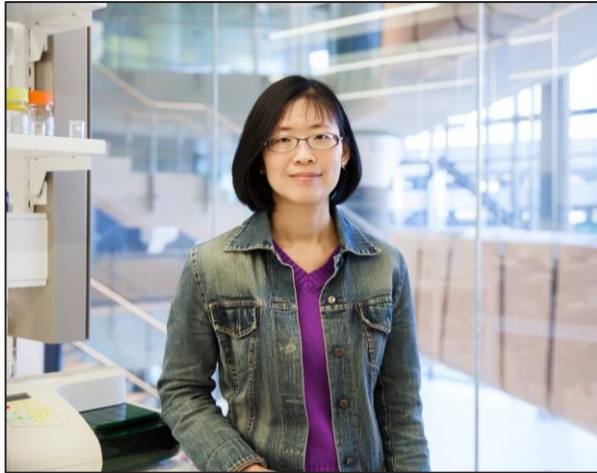
I have shown in a large sample that genetic risk for AD affects the hippocampus before the clinical symptoms of AD, reflecting a neurodegenerative effect prior to clinical manifestations in older adults. Early therapeutic intervention is likely to be the key to treating AD; the effects of AD genetic risk variants gives insight into early changes that are involved in predisposition to AD, and targets for prevention therapy. The use of genetic data and brain biomarkers will also identify those at high risk of AD or an early stage of disease enabling selection of individuals for drug trials and early intervention strategies.



DR MICHELE TENG

QIMR Berghofer Medical Research Institute


Superior power of neoadjuvant immunotherapy to eradicate metastatic disease



Cancer surgery is the most effective single modality for curing patients. Unfortunately, 50% of patients will relapse after surgery due to metastases and require further therapy. Immunotherapies such as Ipilimumab/Nivolumab have been revolutionary in causing long term tumour regression and potential cures in advanced cancers. We have data demonstrating immunotherapies given before surgery (neoadjuvant) is more effective in preventing metastases and we aim to understand the reason for its effectiveness.

Scientific Abstract:

Immunotherapy has recently entered a renaissance phase with the approval of multiple agents for the treatment of cancer. Immunotherapy stands ready to join traditional modalities, including surgery, chemotherapy, radiation, and hormone therapy, as a pillar of cancer treatment. Although immunotherapy has begun to have success in advanced cancer treatment, its scheduling and efficacy with conventional therapies such as surgery has not been systematically examined. Here, we have used two models of spontaneously metastatic breast cancers in mice, to illustrate the significantly greater therapeutic power of neoadjuvant, compared with adjuvant, immunotherapies in the context of primary tumor resection. Elevated and sustained peripheral tumor-specific immune responses underpinned the outcome, and blood sampling of tumor-specific CD8+ T cells immediately prior and post surgery may provide a predictor of outcome. These data now provide strong rationale to extensively test and compare neoadjuvant immunotherapy in humans.



DR MAKRINA TOTSIKA

**Institute of Health and Biomedical Innovation
Queensland University of Technology
*Preventing Bacteria from Sticking (Around)***



Antibiotic resistance -when bacteria change and antibiotics fail- is a looming public health crisis. Each year more than 700,000 people die from antibiotic-resistant infections with numbers predicted to skyrocket to 10 million annual deaths by 2050 if no action is taken. We desperately need new drugs to tackle multidrug resistant bacteria. A common cause of drug-resistant infections is *E. coli* ST131, a pandemic multidrug resistant organism that emerged in 2008. We published the first comprehensive investigation of ST131's genome and disease mechanisms. In follow-up studies we identified key ST131 factors that play a role in disease and tested novel drugs against them. This was the first time that a drug targeting bacterial adherence -the first step of infection- was successfully applied in treating mice with chronic ST131 infections and it could also prevent ST131 infections when antibiotics failed. We are now translating these findings into anti-adhesion antimicrobial therapies for humans.

Scientific Abstract:

In April 2014 the World Health Organization (WHO) declared antimicrobial resistance a public health crisis, demanding global action. A recent UK report predicts that if no action is taken by 2050 more people will die per year from antibiotic resistant infections than cancer. New therapies to tackle multidrug resistant pathogens are sorely needed. *E. coli* sequence type 131 (ST131) is one of the top WHO-listed pathogens of international concern and the predominant cause of antibiotic-resistant urinary tract infections (UTIs) and life-threatening sepsis worldwide. We published the first genome sequence of *E. coli* ST131, revealing its extensive capacity for antibiotic resistance and virulence. We then mapped ST131's pathogenic trajectory during UTI in mice and showed that it can invade into bladder epithelial cells, forming intracellular biofilms that resist immune responses. We also found that ST131 can persist in the bladder of 40% of infected mice for long periods establishing chronic infection. In further studies we identified a key role for the FimH adhesin in ST131 pathogenesis *in vitro* and *in vivo*. Most clinical ST131 isolates encode the novel *fimH30* adhesin allele that is associated with fluoroquinolone co-resistance and a distinct pattern of expression. We delineated the unique molecular mechanisms regulating *fimH30* expression in these clinically predominant strains and its function. In further animal work, we demonstrated that inhibition of the FimH30 adhesin using a novel oral mannoside compound prevented acute UTI, unlike antibiotics, and dramatically reduced ST131 numbers in mice with chronic UTI. Our work showcases how detailed molecular understanding of a newly-emerged pandemic multidrug resistant pathogen, can lead to the timely development of effective therapies with distinct modes of action. We are now funded by the NHMRC to translate our findings into anti-adhesion therapies for common infections that have become refractory to most antibiotics.

PROFESSOR LOUISE CULLEN

QUT

Metro North Queensland Health

The economic impact of the Accelerated Chest Pain Risk Evaluation (ACRE) Project - a large scale implementation of the ADAPT Accelerated Diagnostic Protocol into clinical practice



Chest pain is a leading cause of presentation to hospital Emergency Departments, with lengthy investigations and treatments meaning many patients are admitted to hospital. The *Accelerated Chest Pain Risk Evaluation (ACRE)* project has demonstrated that a new, faster, method of investigating and treating unspecified chest pain in the Emergency Department is safe and effective at getting patients home sooner, frees up hospital beds, and saves millions in costs to the health system.

The ACRE project was conducted from October 2013 to August 2015, in 16 public hospital Emergency Departments around Queensland. Results show that patients' length of stay in the Emergency Department (the time spent in the Emergency Department before either being discharged home, or admitted to the hospital) decreased. Hospital admissions for chest pain fell by 13%, and patients who were admitted to hospital were able to safely return home six hours sooner than with standard treatment.

Scientific Abstract:

Introduction: Chest pain is a leading cause of presentation to Emergency Departments (EDs). Traditional guideline-recommended assessment strategies are lengthy, with many patients requiring admission to hospital. The Accelerated Chest Pain Risk Evaluation (ACRE) Project translated outcomes of the ADAPT trial into clinical practice to improve the efficiency whilst maintaining safety of the assessment of patients presenting to EDs with chest pain. It involved large scale clinical redesign across eligible Queensland Public Hospitals to implement the ADAPT accelerated diagnostic protocol (ADP).

Aims: To define economic benefits resulting from reductions in ED length of stay (LoS) and hospital admissions for possible cardiac chest pain patients presenting to Queensland Health EDs.

Method: The ADAPT ADP was implemented in 16 hospitals between October 2013 and August 2015. Pooled data from the 12 months pre-implementation at each site were compared to 16 months of pooled post-implementation data. Recently published local cost data for a possible cardiac chest pain cohort were applied to outcome measures of reduced ED LOS and reduced admissions.

Results: 5815 patients were managed on the ADP, accounting for 23.2% (95% CI: 22.7-23.8%) of possible cardiac chest pain presentations, closely matching ADAPT. Following implementation, median ED LoS for all patients presenting with possible cardiac chest pain decreased by 17 minutes (95% CI: 14.9-19.08 minutes) in the 25,024 patients, resulting in a release capacity of \$1.15m. Median total hospital LOS fell by 33.4% (404min; 95% CI: 370-437min) from 1210mins (IQR: 511-3494) to 806mins (IQR: 368-2300). Hospital admissions fell by 13.1% (95% CI: 12.3-13.9%) resulting in a release capacity of \$5.3m.

Conclusion: The ADAPT ADP when implemented into clinical practice can result in substantial cost reductions for the management of patients presenting to the ED with possible cardiac chest pain. Further strategies to safely and efficiently assess larger proportions of ED patients should be investigated.

DR JONATHON FANNING

School of Medicine

The University of Queensland

The emerging spectra of neurological injury in "lower-risk" patients undergoing transcatheter aortic valve implantation (TAVI)



Aortic stenosis (AS) is the most common heart valve disease in the Western World. Open-heart surgical aortic valve replacement (SAVR) is considered the 'gold-standard' treatment for AS. However, one-half of patients are rejected due to excessive surgical risk and are condemned to a rapid deterioration and poor prognosis, with mortality of 30% and 50% at 1 and 2 years, respectively, after symptom onset. Transcatheter aortic valve implantation (TAVI) is an innovative life-saving treatment that has substantially expanded therapeutic options in this group of patients. However, the possibility of brain injury from TAVI has raised serious concerns. Infact, using brain imaging, we have found that 60% of TAVI recipients suffer subclinical stroke. This innovative research, represents the most comprehensive neurological/cognitive assessment performed in this setting to date, and is the first to assess outcomes in a 'lower-risk' population.

Scientific Abstract:

Background: TAVI is associated with one of the highest incidences of stroke of any medical or surgical procedure. Clinically-apparent events represent only the 'tip-of-the-iceberg' of neurological injury. Comprehensively characterising the full burden of neurological injury is a pivotal first step to minimise the risk associated with the procedure and improve patient outcomes.

Methods: Forty-one patients undergoing TAVI with the Edwards SAPIEN-XTTM at The Prince Charles Hospital in Brisbane, Australia, were enrolled prospectively. Participants underwent brain MRI, including diffusion weighted imaging (DWI) sequences, pre-procedure, and 4 (\pm 2) days post-procedure. Standardised clinical assessment included serial completion of the National Institute of Health stroke scale (NIHSS), modified Rankin Score (mRS), Montreal Cognitive Assessment (MoCA), and Confusion Assessment Method (CAM), all administered at baseline, 4 (\pm 2) days post-procedure and again at six weeks.

Results: Mean (\pm standard error) participant age was 82.3 (\pm 1.1) years. Patients were of an intermediate surgical risk with a Society of Thoracic Surgeons (STS) score of 6.3 (\pm 0.09) and EuroSCORE II of 6.5 (\pm 1.1). MRI assessments identified 83 new DWI lesions (primary endpoint) in 19/31 patients (59.26%), a mean 2.6 (\pm 0.77) lesions/patient and 138 (\pm 0.08) μ L/lesion. Anatomical characterisation of these lesions revealed that 81% (p <0.0001) occurred in the right hemisphere, and 91% (p <0.0001) occurred in the posterior circulation. Standardised clinical assessments (secondary endpoints) identified 1 stroke (minor), 2 episodes of cognitive dysfunction and 1 episode of delirium.

Conclusions: Neurological injury is common post TAVI. Lesion distribution suggests particular vulnerability of the right hemisphere and posterior circulation. This research provides the first 'real world' assessment of neurological injury in the modern era of TAVI and in a moderate-risk cohort of patients. Furthermore, our findings provide robust data to more accurately inform patients and clinicians, improve patient selection, and create a platform for trialling novel neuroprotective strategies.

DR W. PHILLIP LAW

The Princess Alexandra Hospital

Translation Research Institute

The University of Queensland

Cardiac amyloid imaging with ^{18}F -florbetaben positron emission tomography



Amyloidosis is a diverse group of disorders that results from the abnormal deposition of proteins eventually leading to dysfunction of the affected organs. It is notoriously difficult to diagnose because the first signs and symptoms of the disease are nonspecific and usually attributed to other conditions, resulting in delayed diagnosis and late introduction of appropriate treatment. When the heart is affected, the prognosis is very poor – about 6 months survival in certain types of amyloidosis. Currently, there is no definitive test to diagnose cardiac amyloidosis other than an invasive biopsy of the heart muscle. A new imaging agent known as ^{18}F -florbetaben is derived from a compound which binds to amyloid proteins. This study is the first to demonstrate that cardiac amyloidosis can be diagnosed non-invasively using ^{18}F -florbetaben. Early diagnosis is important as there has been considerable progress in the treatment of amyloidosis which will hopefully improve survival from this disease.

Scientific Abstract:

OBJECTIVE: This is a pilot study to determine the feasibility of ^{18}F -florbetaben positron emission tomography (PET) in diagnosing cardiac amyloidosis.

METHODS: ^{18}F -florbetaben PET was performed in 14 subjects: 5 light chain (AL) amyloid, 5 transthyretin (ATTR) amyloid, and 4 control subjects with hypertensive heart disease causing left ventricular (LV) myocardial thickening. Qualitative and quantitative assessments of ^{18}F -florbetaben activity were performed using mean standardised uptake value (SUV) of the LV myocardium and blood pool, and calculation of target-to-background SUV ratio. Percentage myocardial ^{18}F -forbetaben retention was also calculated as the percentage mean myocardial SUV change between 0-5mins and 15-20mins after intravenous ^{18}F -forbetaben injection. Global LV longitudinal and right ventricular (RV) free wall longitudinal strain were calculated using two-dimensional speckle tracking echocardiography.

RESULTS: Target-to-background SUV ratio and percentage myocardial ^{18}F -forbetaben retention were significantly higher in amyloid patients compared to hypertensive control subjects. A cut-off value of 40% ^{18}F -forbetaben retention was able to differentiate between cardiac amyloid patients and hypertensive control subjects. Percentage myocardial ^{18}F -forbetaben retention was an independent determinant of both global LV longitudinal and RV free wall longitudinal strain via an inverse curve relationship.

CONCLUSIONS: ^{18}F -florbetaben PET imaging can accurately identify and differentiate between cardiac amyloidosis and hypertensive heart disease as the underlying cause of LV myocardial thickening. To the authors' knowledge, this has not previously been demonstrated and may become an important tool in the diagnosis of cardiac amyloidosis without the need for invasive biopsy procedures. The degree of myocardial ^{18}F -florbetaben retention was an independent determinant of myocardial dysfunction suggesting ^{18}F -florbetaben PET may also have a role in the monitoring of cardiac amyloid disease particularly with the emergence of new treatments for amyloidosis.

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8:00 – 8:45am	Official Welcome and ASMR Presentation:
8:45 – 9:00am	ASMR QLD Convenor Dr Jill Larsen
9:00 – 9:45am	Keynote Speaker 1: Prof Ranjany Thomas – UQDI
9:45 – 10:30am	Queensland Health & Medical Research Awards Part 1 (Sponsored by Queensland Health)
10:30 – 11:15am	Morning Tea – Poster Session 1 (Poster Sessions are sponsored by Translational Research Institute)
11:15 – 12:00pm	Queensland Health & Medical Research Awards Part 2 (Sponsored by Queensland Health)
12:00 – 12:45pm	Keynote Speaker 2: A/Prof Stephen Mahler – AIBN
12:45 – 01:30pm	Lunch Break
Afternoon Session	
01:30 – 02:30pm	Oral Presentations Session 1 (Sponsored by UQ Diamantina Institute)
03:15 – 04:00pm	Afternoon Tea – Poster Session 2 (Poster Sessions are sponsored by Translational Research Institute)
02:30 – 03:15pm	Keynote Speaker 3: Dr Keili Macdonald – QIMRB
04:00 – 05:00pm	Oral Presentations Session 2 (Sponsored by QIMR Berghofer Medical Research Institute)
05:00 – 05:15pm	Award Ceremony and Official Closing
05:30 – Late	Post Conference Reception: Normal Hotel

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05:30 – Late	Post Conference Reception: Normal

About the 2016 ASMR MRW® Queensland Postgraduate Student Conference

As part of Australian Society for Medical Research Medical Research Week®, ASMR Queensland holds a postgraduate student conference to showcase the high quality of research undertaken by students in universities and other institutions. The work presented at this conference is that of postgraduate students and the conference is well attended by a broad range of researchers and academics. The 2016 ASMR Queensland Postgraduate Student Conference will take place at the Translational Research Institute on Wednesday 1st June 2016. This year the six finalists for this award are: Faith Brennan, Ka Tang, Sarah Walton, Haolu Wang, Aleena Wojcieszek and Arabella Young.

The organising committee would like to take this opportunity to thank our keynote speakers, Professor Ranjeny Thomas for sharing their science and experience with the young researchers of Queensland.

We would also like to show our appreciation to all of our judges, sponsors, presenters, supervisors and registrants; without you, this conference would not be possible.



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