Media Release May 26, 2016

The Queensland Health and Medical Research Awards

FINALISTS ANNOUNCED

The Queensland Health and Medical Research Awards, an initiative of ASMR, honour the quality of scientific endeavour in Queensland. Announcing the finalists today, convenor Dr Jill Larsen applauded the overall quality of scientific research in the many excellent applications received.

Winners and runners-up for all categories will be announced at the

ASMR Medical Research Week® Gala Dinner
Friday June 3rd
Hillstone, St Lucia (The Grant View Room)

Postgraduate Student Award Finalists

Faith H 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.

Kai D 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 tumor 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.

Sarah L 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.

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.

Aleena M Wojcieszek, **Mater Research Institute, The University of Queensland**

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

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.

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.

Postdoctoral Researcher Award Finalists

Dr.

Dr. Mark Adams, Queensland University of Technology, Translational Research Institute

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.

Dr. Brooke Coombes, 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.

Dr Zeinab Khalil, Institute for 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 multidrug 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.

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.

Senior Researcher Award Finalists

Dr Michelle K 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.

Dr Michele WL 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.

Dr Makrina M 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.

Clinical Researcher Award Finalists

Professor Louise Cullen, Metro North Queensland Health, Queensland University of Technology

Improved management of Emergency Department patients with chest pain reduces time in hospital and saves health care costs

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.

Dr Jonathon P 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 'goldstandard' 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. In fact, 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.

Dr W Phillip Law, The University of Queensland, Translational Research Institute

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 18F-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 18F-florbetaben. Early diagnosis is important as there has been considerable progress in the treatment of amyloidosis which will hopefully improve survival from this disease.

Abstracts and biographical information are available from http://asmr.org.au/MRWMedia

For further information about the finalists and announcement of the winners/for interviews contact

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