

The 2014 Grant Applications Round resulted in the commitment of \$1,214,000 to fund 19 separate grants to universities, medical research institutions and hospitals. The successful projects are listed below in alphabetical order by Institution.

Recipient: **Flinders University**
 Chief Investigator: **Dr Billy Tao**
 Funding Amount: **\$73,000**
 Project Title: **A new oral immunotherapy treatment for nut allergy: translational research and pilot study**

Approximately 2% of Australian children are allergic to nuts, and there is currently no effective safe treatment. This study will provide the foundation for a new therapy with minimal or no adverse reactions that will allow children to be safe from accidental ingestion of nuts. The project combines laboratory-based proteomic and immunologic investigations with a clinical pilot study that will confirm the safety and efficacy of this new treatment method.

Recipient: **SA Pathology**
 Chief Investigator: **Dr Sharon Byers**
 Funding Amount: **\$74,500**
 Project Title: **Mesenchymal stem cell therapy for MPS I**

Children with mucopolysaccharidoses (MPS) suffer from a range of somatic and CNS symptoms that manifest early in life. In particular, progressive mental deterioration and skeletal abnormalities are not affected by current treatment modalities. We have shown that mesenchymal stem cells (MSCs) derived from compact bone differentiate into both neural and skeletal cells and distribute to somatic tissues and the brain. In this study we will determine if MSCs can alleviate both CNS and somatic symptoms in the MPS I mouse.

Recipient: **SA Pathology**
 Chief Investigator: **Dr Maria Fuller**
 Funding Amount: **\$75,000**
 Project Title: **Can linoleic acid improve cognitive function in a mouse model of an inherited metabolic disease of children**

Mucopolysaccharidosis type I is the most common in a family of inherited disorders that generally affect young children and have a devastating impact on the child and family. The burden of brain disease in these children, manifesting as severe neurocognitive decline, represents a most significant unmet therapeutic need. This project will test whether oral supplementation of linoleic acid, an essential fatty acid that passes into the brain, can alleviate aspects of brain disease by correcting lipid abnormalities. This may have application for many disorders with abnormal brain lipids.

Recipient: **University of Adelaide**
 Chief Investigator: **Dr Mark Corbett**
 Funding Amount: **\$74,000**
 Project Title: **Whole genome sequencing as a diagnostic and research tool to study neurodevelopmental disorders**

Intellectual disability, epilepsy, autism and cerebral palsy are childhood onset neurodevelopmental disorders that together affect ~5% of the world's population. We will use the latest DNA sequencing technologies to gain better understanding of their genetic determinants (which are presently poorly understood) and the interaction between these and environment, and to obtain insights into normal brain function. Identifying a genetic cause provides parents of affected children with an explanation for their child's disorder and opens the way for treatment based on a specific genetic diagnosis.

Recipient: **University of Adelaide**
Chief Investigator: **Professor Jenny Couper**
Funding Amount: **\$73,500**
Project Title: **Does the gut microbiome drive the development of type 1 diabetes?**

Every day in Australia two children will be diagnosed with type 1 diabetes (T1D). The incidence has doubled over the last 20 years. The gut microbiome, the name given to trillions of bacteria that live in our guts, appears to be key to the development of T1D. The changes in the gut microbiome that drive the immune system to destroy the insulin producing cells are not known. We will study the microbiome, gut leakiness, and immune function in those with, or at high risk of, T1D compared with controls. This will lead to therapies to restore the gut microbiome to health to prevent diabetes.

Recipient: **University of Adelaide**
Chief Investigator: **Dr Lachlan Jolly**
Funding Amount: **\$60,000– Withdrawn – Received WCH Foundation grant**
Project Title: **Severity of Intellectual Disability Caused by UPF3B Mutations in Children is Modified by UPF3A.**

Recipient: **University of Adelaide**
Chief Investigator: **Professor John Declan Kennedy**
Funding Amount: **\$74,000**
Project Title: **Does snoring in children affect vascular health for the future? An analysis of vascular structure and function in children that snore.**

Habitual snoring is considered a benign sleep process which affects 0.25 million Australian children. In adults, sleep apnea, is associated with increased cardiovascular morbidity and inflammation. Our pilot data suggests that even habitual snoring in childhood causes significant early changes in cardiovascular parameters. An important question therefore is whether snoring during childhood predisposes adults to poor cardiovascular health. This will be the first study to investigate the blood vessel structure, function and associated biomarkers in children that snore.

Recipient: **University of Adelaide**
Chief Investigator: **Dr Angela Kinnell**
Funding Amount: **\$34,000 (Early Career)**
Project Title: **Learning from success: Child development improvements in Northern Territory and South Australian Aboriginal communities**

Australian Early Development Index (AEDI) 2009 & 2012 data provide the best opportunity to see how large numbers of Aboriginal children are developing before school. Non-Aboriginal children outperform Aboriginal children on the AEDI. However, there are communities with large numbers of Aboriginal children doing well. Taking a strengths-based approach, we will identify & profile these Aboriginal communities with children doing well on the AEDI in NT & SA. The aim is to learn from success to better focus policy & improve early childhood health & development outcomes for all Aboriginal children.

Recipient: **University of Adelaide**
Chief Investigator: **Professor Michael Sawyer**
Funding Amount: **\$58,000**
Project Title: **Does nurse home-visiting improve the longer term health and wellbeing of mothers and children?**

The South Australian Family Home-Visiting program is a targeted 2-year intervention delivered by nurses to mothers of children aged 0 to 2 years. The program aims to improve the health and wellbeing of mothers and young children. As well as having immediate benefits, there is evidence from overseas studies that home-visiting programs may improve longer term maternal and child outcomes. The present application seeks funding for a longer-term follow-up to determine whether mothers and children who received the South Australian program have better outcomes when children are aged 5 years than a comparable group of mothers and children who did not receive the program.

Recipient: **University of Adelaide (Transferred from WCHRI)**
Chief Investigator: **Dr Raman Sharma**
Funding Amount: **\$58,000**
Project Title: **Mutations in the mRNA export factor THOC2 cause intellectual disability**

Intellectual disability encompasses numerous clinically complex, causally heterogeneous and largely untreatable disorders that affect >2% of the world's population. High throughput DNA sequencing of affected individuals from 500 families identified six different disease-causing mutations in the THOC2 gene. THOC2 facilitates transport of molecules within a cell and thus ensures proper cell function. Understanding how THOC2 mutations disrupt cellular processes crucial for the function of neurons will offer therapeutic and diagnostic help for patients and their families.

Recipient: **University of Adelaide**
Chief Investigator: **Associate Professor Cheryl Shoubridge**
Funding Amount: **\$74,500**
Project Title: **Time-lapse live cell imaging of neurons to investigate the impact of mutations in IQSEC2 on the plasticity of dendritic spines contributing to intellectual disability.**

Intellectual disability is frequent in the population with as many as 1 in every 50 people affected. The cost to Australia of intellectual disability is estimated at \$14 billion annually. Mutations in the gene IQSEC2 lead to substantial limitations in intellectual functioning and adaptive behaviour in children, including Autistic traits. Our study will specifically address the functional impact of these mutations using cell models relevant to the brain to better understand the cellular processes required for normal memory and learning.

Recipient: **University of Adelaide**
Chief Investigator: **Associate Professor Michael Stark**
Funding Amount: **\$52,000**
Project Title: **Transfusion related immunomodulation in the preterm newborn**

Over 90% of extremely preterm newborns require red blood cell (RBC) transfusions yet they are independently associated with more frequent and severe neonatal morbidities. RBCs are biologically active and result in inflammation and oxidative stress. This transfusion related immunomodulation (TRIM) might contribute to the association between PRBC transfusion and adverse outcomes. In other populations benefit is gained from washing RBCs before transfusion. This study aims to identify if transfusion with washed RBCs reduces TRIM in the recipient improving transfusion safety and clinical outcome.

Recipient: **University of Adelaide**
Chief Investigator: **Miss Alexandra Tikhomirova**
Funding Amount: **\$30,000** (Early Career)
Project Title: **The molecular basis for the multi-species bacterial biofilms that are formed during chronic and recurrent infections of the middle ear.**

Otitis media is an important childhood disease. Bacteria are a major contributor to the disease pathogenesis, which currently is not well understood. Increasingly, important are chronic and recurrent forms of this disease. These are caused by bacterial biofilms. This project will elucidate the molecular basis for how different bacteria form biofilms together.

Recipient: **University of Adelaide**
Chief Investigator: **Dr Astrud Tuck**
Funding Amount: **\$33,000** (Early Career)
Project Title: **Is childhood allergy susceptibility increased by maternal asthma?**

Childhood allergic disease has increased dramatically in recent years and can be a significant burden on the lives of sufferers. Maternal asthma may alter programming of the immune system during fetal development, increasing susceptibility to childhood allergy. This project aims to discover whether the presence of asthma during pregnancy causes genetic changes to the placenta, which may affect fetal immune development and result in childhood allergy. Understanding the molecular mechanisms can lead to the development of therapies to help prevent maternal asthma increasing allergic risk.

Recipient: **University of South Australia**
Chief Investigator: **Professor Allison Cowin**
Funding Amount: **\$75,000**
Project Title: **Development of new dressings for burn injuries**

Burns are one of the most common injuries in young children. They cause lifelong scarring and frequently contract as the child gets older, requiring extensive surgical intervention to prevent deformity and loss of movement. We aim to develop new dressings for burn wounds that actively stimulate wound healing, improve angiogenesis and reduce scarring. To do this we will produce new burn wound dressings that are able to deliver novel biological agents directly to the wound and actively promote healing and reduce scarring and contracture post burn injury.

Recipient: **University of South Australia**
Chief Investigator: **Associate Professor Leanne Dibbens**
Funding Amount: **\$72,000**
Project Title: **The frequency of DEPDC5 mutations in sporadic cases of childhood focal epilepsy.**

This project aims to improve the diagnosis and treatment of children with focal epilepsy, a common form of epilepsy which is often difficult to treat and for which there are few known causes. We have recently discovered that mutations in the DEPDC5 gene are the most common cause of familial focal epilepsy and now aim to determine their contribution to sporadic cases of focal epilepsy in children. Providing a genetic diagnosis in children with epilepsy as early as possible can have a major impact on clinical management, prognosis and often alleviates the distress and costs of further testing.

Recipient: **University of South Australia**
Chief Investigator: **Dr Sarah Heron**
Funding Amount: **\$74,000**
Project Title: **Identification of DEPDC5 and PRRT2 deletions and duplications in causing childhood epilepsies.**

This project will improve the diagnosis of childhood epilepsies caused by mutations in the genes DEPDC5 and PRRT2 by enabling the detection of gene deletions and duplications. These mutations are not detectable using the genetic tests currently available for these genes. In childhood epilepsies, a genetic diagnosis can have a major impact on clinical management and prognosis. The identification of a particular mutation may indicate a particular drug of choice and a genetic diagnosis limits the need for further clinical investigations, minimising distress to patients and healthcare costs.

Recipient: **University of South Australia**
Chief Investigator: **Professor Nicolas Voelcker**
Funding Amount: **\$75,000**
Project Title: **Porous silicon based siRNA delivery to glioblastoma**

Glioblastomas are a class of aggressive primary brain tumours in childhood with devastating outcomes for families. Apart from surgery, current treatment approaches have modest effects on survival. We have demonstrated a novel gene based therapy approach using porous silicon wafers in vitro and now propose to study the efficacy of nanoparticles made from porous silicon to deliver therapeutic oligonucleotides. This approach will result in innovative new therapies to overcome the resistance of glioblastomas to standard cancer treatment.

Recipient: **Women's and Children's Health Network**
Chief Investigator: **Associate Professor Helen Marshall**
Funding Amount: **\$74,500**
Project Title: **Incorporating young people's views into priority setting for preventative health strategies to improve the health of adolescents**

Engaging adolescents in decisions concerning their health is vital to improve health for this at risk group. The prevalence of health risk behaviours rises markedly during adolescents as individuals become increasingly responsible for their own health. The views and values of adolescents in public health policy are seldom investigated and yet their opinions may impact on the success of adolescent health programs. The systematic incorporation of adolescents' views will lead to improvement in the health of adolescents by developing programs that are most relevant to the needs of adolescents.