GRANTS FUNDING TO COMMENCE IN 2017

The 2017 Grant Applications Round resulted in the commitment of $1,342,299 to fund 20 separate grants to universities, medical research institutions and hospitals, as per the following table:

FLINDERS UNIVERSITY

Chief Investigator: **Dr Jacqui Beall**
Funding Amount: **$73,375**
Project Title: **Psychosocial risks during pregnancy: The impact of screening and early referral on child outcomes**

The first 1,000 days of a child's life, from pregnancy to their 2nd birthday, are crucial for development. It forms the foundation for lifelong health and functioning yet is also the time when children are most vulnerable. At Flinders Medical Centre we identify pregnant women who are facing difficulties which may pose risks to their baby, and aim to link them to services which can help even before their baby is born. But does this make a difference? In the first stage of a large cohort study we will look at how psychosocial risks identified during pregnancy impact on babies' health and safety.

Chief Investigator: **Dr Jillian Carr**
Funding Amount: **$74,027**
Project Title: **Definition of the ability of zika virus (ZIKV) to infect the placenta, brain and eye that will impact on our understanding of debilitating microcephaly and macular scarring in ZIKV exposed newborns**

The world was shocked by the threat of Ebola. Now we face the more insidious ZIKV. ZIKV is transmitted by a mosquito that spreads dengue, which with 390 million infections pa (Bhatt et al., 2013. Nature), paints a grim picture for future ZIKV. Epidemiology links ZIKV infection of pregnant women to microcephaly and macular scars in newborns with intellectual and visual impairment. A WHO alert suggests travel restrictions in pregnancy and presents ZIKV as an emerging threat to the health of newborns with permanent sequela for the next generation. ZIKV is thus a clear priority for child health.

Chief Investigator: **Dr Billy Tao**
Funding Amount: **$73,155**
Project Title: **Establishment of a new treatment for peanut allergy**

Peanut allergy affects 3% of Australian children. It affects family lifestyle, is dangerous for those allergic, and constant vigilance is required. No treatment is available. We will, through a network of allergists, treat peanut allergy using an improved treatment protocol that uses sequential ingestion of 2 types of boiled peanuts followed by roasted peanuts to safely desensitise peanut-allergic children. This world-first home-based treatment will be supervised by allergists and will allow peanut allergic children to be safe from dangerous allergic reactions.

Chief Investigator: **Dr Roger Yazbek**
Funding Amount: **$74,931**
Project Title: **Development and Validation of a New Breath Test for Intestinal Function**

Existing technologies for detection and monitoring of intestinal damage and repair in children are costly and invasive, leading to stress and unnecessary risks. New tests are needed that are non-invasive, rapid, and more suitable for a paediatric setting. We have developed a new, non-radioactive, stable-isotope breath test that can detect a marker of intestinal health and function and have demonstrated the specificity of this test in cells grown in the lab. We will now prove the efficacy of this test in a rat model of intestinal damage to provide proof-of-concept data for future human studies

MENZIES SCHOOL OF HEALTH RESEARCH

Chief Investigator: **Dr Michelle Boyle**
Funding Amount: **$72,000**
Project Title: **T-follicular helper cells in children with malaria**

Malaria caused by Plasmodium results ~ 500,000 deaths annually, the majority children under five years of age. Antibodies are important in immunity against malaria. Specific cells called T-follicular helper cells (TfH) are essential for antibody development. Malaria in children may disrupt TfH cells, but whether this occurs in all forms of malaria and in both children and adults, and the outcomes for antibody development is unknown. We will investigate TfH cells in two forms of malaria and study the impact of TfH on antibody responses. Results will inform the development of vaccines.

SA PATHOLOGY

Chief Investigator: **Professor Antonio Ferrante**
Funding Amount: **$74,833**
Project Title: **Complement Receptor Immunoglobulin and therapy for type 1 diabetes**

Type 1 diabetes (T1D) is a life-long disease that usually occurs in childhood. We have been researching a recently described receptor, Complement Receptor Immunoglobulin (CRIg) which is selectively expressed on white blood cells involved in induction of autoimmunity and damage to the pancreas (produces insulin). A recent report suggests that CRIg may be a key player in protection against development of diabetes, in an experimental model. We have made the cells rich in CRIg and propose to inject them to protection against T1D, providing a more effective, less toxic and less costly therapy.

SOUTH AUSTRALIAN HEALTH & MEDICAL RESEARCH INSTITUTE (SAHMRI)

Chief Investigator: **Dr Laura Eadie**
Funding Amount: **$75,000**
Project Title: **Using in vivo modelling to investigate therapeutic approaches to reverse/prevent disease resistance in children with high-risk Ph-like B-ALL and T-ALL treated with targeted therapies**

Relapsed acute lymphoblastic leukaemia (ALL) is the leading cause of childhood non-traumatic death (15% of T-ALL and 20% of B-ALL patients relapse). Chemotherapy results in adverse side effects and a lifelong risk of other malignancies. Risk stratification and targeted therapy based on the molecular genetics of an individual's disease is warranted. We will test the efficacy of novel drugs and combination therapies in mouse models of ALL. Findings will inform clinical practice; therapeutic strategies will be optimised to ensure the best chance of cure for children with high-risk forms of ALL.

Chief Investigator: **Associate Professor Philippa Middleton**
Funding Amount: **$75,000**
Project Title: **Increasing breastfeeding and Aboriginal children's health through culturally appropriate and responsive support**

Breastfeeding is one of the most important health behaviours for survival, growth, development and overall health of the child, yet only half of Aboriginal babies are being breastfed at 6 months, and only 7% are exclusively breastfed. Infant and child nutrition, especially breastfeeding, is consistently identified as one of the highest priorities for action by Aboriginal communities in SA.

THE UNIVERSITY OF ADELAIDE

Chief Investigator: **Dr Kerrilyn Diener**
Funding Amount: **$75,000**
Project Title: **Investigations into sepsis-induced high-mobility group box 1 (HMGB1) and effects on neurodevelopment in survivors of neonatal sepsis**

Preterm babies are particularly vulnerable to acquiring sepsis during their hospital stay, which not only increases the risk of mortality, but also the likelihood of brain-related disorders in survivors from 28% to 49%. There is an emerging concept that HMGB1, a danger molecule released within the body as a result of sepsis, can perpetuate this abnormal brain development. We will investigate this further, as our aim is to develop a targeted therapy that will increase survival rates and support normal brain development. This will significantly benefit the long-term health for preterm neonates.

Chief Investigator: **Dr Nicholas Eyre**
Funding Amount: **$71,386**
Project Title: **Identification and development of inhibitors of the Zika virus NS2B/3 protease**

The recent outbreak of Zika virus (ZIKV) in South America and its association with birth defects has been declared by the World Health Organization (WHO) as a"public health emergency of international concern". Accordingly, there is an urgent need for improved diagnostics, vaccines and antiviral therapies to combat the spread and impact of ZIKV. This project will identify inhibitors of the ZIKV NS2B/3 protease that may be developed as future antiviral therapies to treat ZIKV infection.

Chief Investigator: **Dr Kathryn Gatford**
Funding Amount: **$75,000**
Project Title: **A novel intervention strategy to prevent IUGR**

Intrauterine growth restriction (IUGR) increases risks of perinatal death >5-fold, and has lifelong adverse effects on health. There is currently no treatment to prevent or cure IUGR. We wish to test a novel approach to stimulate the mother's own production of hormones that promote placental function and fetal growth. We are requesting support to test active ghrelin treatment in mice with variable litter size and prenatal constraint. Importantly, diet can be used to induce activation of ghrelin, providing a pathway for developing a therapy to prevent IUGR which is acceptable to patients.

Chief Investigator: **Dr Angela Gialamas**
Funding Amount: **$69,574**
Project Title: **Parenting as an investment in child development: what matters and when?**

Parents "invest" in their children's health and development in many ways, but not all parents have the same resources to invest. Less parental investment is a key mechanism for inter-generational transmission of socioeconomic disadvantage. In Australia we have no comprehensive picture of how parents invest in their children at different ages. This project will identify the parenting investments that matter most for children's development, and when these investments matter most. This is central to informing interventions to improve outcomes for disadvantaged children.

Chief Investigator: **Dr Chantelle McIntyre**
Funding Amount: **$34,412**
Project Title: **Gene therapy for cystic fibrosis [ECR]**

From birth, individuals who inherit cystic fibrosis (CF) face a life-long, relentless, regime of medical treatments and physiotherapy in an effort to manage respiratory and digestive complications, and thereby prolong life. However, no cure for CF exists, and premature death is inevitable. Respiratory failure is the most common cause of death. The current study is focused towards developing gene therapy for CF airway disease. This treatment approach has the potential to provide long lasting therapeutic benefit to patients, significantly improving their quality of life, and extending life.

Chief Investigator: **Professor Vivienne Moore**
Funding Amount: **$73,942**
Project Title: **Children with a marked increase in internalizing behaviour as tweens: determinants and mental health at 16 years.**

Anxiety and mood disorders are among the most common mental health problems experienced by young people. Not only do they have acute impacts on learning and social relationships, they are often followed by long-term impacts on mental health and life opportunities. Prevention and early intervention are thus recognized as essential. As well as society-wide initiatives, targeted efforts are needed in order to make the best use of finite resources. Thus identifying at-risk families and at-risk children is important, as is knowledge of what could be modified to improve mental health trajectories.

Chief Investigator: **Associate Professor Mark Nottle**
Funding Amount: **$74,882**
Project Title: **Directed differentiation of embryonic stem cells to insulin producing cells as a cure for Type 1 diabetes**

The directed differentiation of human embryonic stem cells to insulin producing cells is seen as a cure for Type I diabetes. However human ESCs are not the same as those originally isolated in mice which has led to the suggestion that these may not be the best cell type for this therapy. We have developed a method which allows us to isolate ESCs similar to that originally isolated in mice. In characterising these cells we have shown that these can be directed to differentiate to insulin producing cells. The aim of the present study is to complete the characterization of these cells.

Chief Investigator: **Dr Rhiannon Pilkington**
Funding Amount: **$69,574**
Project Title: **Child maltreatment and school outcomes**

In 2012-13 there were 19,120 child protection notifications in South Australia (AIHW, 2014). By the age of 16, 1 in every 4 children will have had a child protection notification, and 1 in 20 will have had that notification substantiated (Hirte, 2008). Child maltreatment is common, and likely to have detrimental short and long-term consequences.

This will be the first study in SA to investigate the developmental, academic, and behavioural outcomes in school according to the type and timing of exposure to child maltreatment.

Chief Investigator: **Dr Elizabeth Ngoc Hoa Tran**
Funding Amount: **$65,000**
Project Title: **Investigating the relationship between the ABO blood group system and Shigella interaction with cells**

Shigella is the leading cause of bacillary dysentery, a human inflammatory disease of the intestines that causes severe diarrhoea in children under the age of 5. Sugar structures (LPS O antigens) on Shigella's surface have recently been shown to adhere directly to ABO blood group sugars on gut cells. This project will investigate the relationship between ABO blood groups and the adherence/invasion of different Shigella strains to cells, potentially determining if children of a certain blood type are more susceptible to infection, and providing informed approaches to vaccine developments.

UNIVERSITY OF SOUTH AUSTRALIA

Chief Investigator: **Dr Qian Tang**
Funding Amount: **$34,995**
Project Title: **Preventing childhood glucocorticoid therapy-induced bone growth defects by blocking the aggravated chemokine SDF-1 signalling [ECR]**

Glucocorticoids are commonly used in children and cause bone defects, for which mechanisms are unclear and preventative means are lacking. Our in vitro work now showed that dexamethasone (Dex) damages skeletal cells and induces chemokine SDF-1 most prominently, and that the induced SDF-1 increases recruitment of bone-degrading cells (osteoclasts). In Dex-treated rats, this project aims to establish if SDF-1 induction causes bone loss and if blocking SDF-1 protects bone. This work will provide novel mechanistic insights and can lead to a bone protective strategy for children on glucocorticoids.

WOMEN'S AND CHILDREN'S HEALTH NETWORK

Chief Investigator:	**Dr Martin Donnelley**
Funding Amount:	**$74,213**
Project Title:	**Improving the efficiency of cystic fibrosis airway gene therapy**

Treatments for cystic fibrosis (CF) have improved in recent years, enhancing survival and quality of life, but these interventions are not curative. Gene therapy is likely the only mutation-class-independent method of overcoming CF lung disease, however achieving therapeutic levels of gene transduction is a challenge. This study will assess whether altering our current gene vector pseudotype - the coating that controls the types of cells transduced - can result in higher levels of airway gene expression. This will allow us to assess which pseudotype to progress towards clinical trials.

Chief Investigator:	**Dr Thomas Goddard**
Funding Amount:	**$32,000**
Project Title:	**Breath Testing for Allergic Bronchopulmonary Aspergillosis in Cystic Fibrosis - Can Volatile Organic Compounds Predict Disease State and Treatment Response? [ECR]**

CF is the most common fatal genetic condition in our community. Children die from respiratory disease caused by recurrent & chronic lung infections. Currently, sputum or broncho-alveolar lavage samples are cultured for several days before lung infection is diagnosed and treated. Because children cannot produce sputum on demand they can require an anaesthetic with a small camera inserted into their lungs to obtain the sample. However, if infections are detectable in the breath, diagnosis and monitoring is far simpler, cheaper and faster, enabling prompt treatment and prevention of disease.

[Early Career Researcher - ECR]