GRANTS FUNDING TO COMMENCE IN 2015

The 2015 Grant Applications Round resulted in the commitment of $1,123,000 to fund 18 separate grants to universities and medical research institutions. The successful projects are listed below:

FLINDERS UNIVERSITY

CHIEF INVESTIGATOR: Professor Jamie Craig

FUNDING AMOUNT: $74,800

PROJECT TITLE: Improving genetic diagnosis and reproductive options for families with congenital, and developmental glaucoma

SIGNIFICANCE: Glaucoma in infants is a rare but devastating condition. Without treatment, elevated eye pressure leads to the expanding eyes with total blindness. Most cases need multiple surgical procedures and general anesthetics. The cause of infantile and childhood glaucoma is almost entirely genetic, but in most cases the causative gene is unknown. Parents usually seek an accurate understanding of the risk to subsequent children, and options for prevention. This project aims to define a greater proportion of the genetic risk for pediatric glaucoma, and to make improved testing available for families.

MENZIES SCHOOL OF HEALTH RESEARCH

CHIEF INVESTIGATOR: Dr Erin Price

FUNDING AMOUNT: $74,900

PROJECT TITLE: What are the important targets for prevention of Haemophilus influenzae lung infection?

SIGNIFICANCE: Preventable paediatric disease caused by infection with the nontypeable Haemophilus influenzae (NTHi) bacterium is a major yet under-recognised health burden. NTHi infection can lead to bronchiectasis, a severe and irreversible lung condition that disproportionately affects Aboriginal children in the Northern Territory, with 1 in every 68 suffering from this disease. It has lifelong consequences including premature death in the 3rd-4th decade of life. A vaccine that is effective across all NTHi strains is urgently needed to reduce the burden of this preventable disease in Aboriginal children.

CHIEF INVESTIGATOR: Dr Tonia Woodberry

FUNDING AMOUNT: $75,000

PROJECT TITLE: Understanding dendritic cell dysfunction in children with malaria

SIGNIFICANCE: Malaria, a disease caused by Plasmodium parasites affects ~450 million people each year with 0.6 million deaths, most in children less than 5 years old. Vaccine development is a key goal for malaria elimination. Vaccine responsiveness relies on functional dendritic cells (DC). However, we have identified that adults with malaria have dysfunctional DC, meaning vaccines may not work. We here will examine DC in children with malaria to determine if they are functional. The data will tell us whether parasite clearance is required before administration of childhood vaccines.

SOUTH AUSTRALIAN HEALTH & MEDICAL RESEARCH INSTITUTE

CHIEF INVESTIGATOR: Dr Susan Heatley

FUNDING AMOUNT: $75,000

PROJECT TITLE: Developing a robust screening tool to identify Children with high risk "Ph-like" Acute Lymphoblastic Leukaemia (ALL) that will lead to improved outcomes through the use of targeted therapies.

SIGNIFICANCE: High risk relapsed B-ALL remains the leading cause of non-traumatic death in children and young adults, with ~20% of patients dying from this disease. Novel chromosomal changes resulting in the formation of new proteins have recently been identified in a significant number of cases. Importantly, drugs that target these proteins are in use for other diseases and are safe. Rapid, accurate screening tests to identify these genetic lesions will greatly enhance the clinical application of anti-leukaemic drugs which are highly likely to improve the low cure rates in children with high risk ALL.

THE UNIVERSITY OF ADELAIDE

CHIEF INVESTIGATOR: Miss Zuleeza Ahmad

FUNDING AMOUNT: $35,000 (Early Career)

PROJECT TITLE: Investigation of a novel protein tyrosine phosphatase in Streptococcus pneumoniae

SIGNIFICANCE: Streptococcus pneumoniae causes 25% of all preventable deaths in children under the age of five. This equates to more than 1.2 million deaths annually. A putative protein tyrosine phosphatase (designated PTPa) has recently been identified as a virulence factor in the pneumococcus, as is the case in many other bacterial pathogens. This project will focus on uncovering the reasons for this effect, in an effort to investigate the role of PTPa in pneumococcal pathogenesis. As issues of vaccine ineffectiveness and antibiotic resistance prevail, PTPa may present a novel drug target.

CHIEF INVESTIGATOR: Associate Professor Vicki Clifton

FUNDING AMOUNT: $66,300

PROJECT TITLE: Intergenerational impact of maternal asthma on cardiovascular risk in offspring

SIGNIFICANCE: Asthma (12% adults) and cardiovascular disease (19% adults) are two non-communicable chronic diseases that are major health, social and economic burdens in our society. The major questions related to chronic disease are how to prevent them and in the absence of prevention, how to manage them clinically. We will identify how maternal asthma, asthma exacerbations and corticosteroid treatment during pregnancy affects cardiovascular risk in offspring. This study will provide us with important information on whether asthma control during pregnancy improves childhood cardiovascular health.

CHIEF INVESTIGATOR: Professor Jenny Couper

FUNDING AMOUNT: $59,500

PROJECT TITLE: Can the glucagon-like peptide-1 agonist, exenatide, improve blood glucose control in young people with cystic fibrosis related diabetes?

SIGNIFICANCE: Cystic fibrosis is a severe genetic disorder affecting the lungs, liver and pancreas of children. Life expectancy has improved greatly; however, with this comes the development of cystic fibrosis related diabetes. Diabetes is associated with worsening nutrition and lung function, and increased mortality. We have shown that blood glucose control in teenagers with CF is improved by slowing gastric emptying and increasing incretin hormone secretion. Exenatide is an incretin-like medication and we wish to investigate whether this can improve blood glucose control as a more effective strategy.

CHIEF INVESTIGATOR: Professor Stan Gronthos

FUNDING AMOUNT: $75,000

PROJECT TITLE: Identification of TWIST-1 regulated microRNAs which control cranial bone development in children.

SIGNIFICANCE: Saethren-Chotzen Syndrome (SCS) is a disorder associated with craniosynostosis, leading to abnormal head shape, asymmetrical facial features and increased pressure on the growing brain in infants. One cause of SCS is a mutation in the TWIST-1 gene, involved in mesodermal development. MicroRNA (miRNA) have emerged as important regulators of bone development. The identification of Twist-1 regulated miRNAs and their gene targets during cranial development and SCS will help identify novel molecular pathways for exploiting in new therapeutic strategies.

CHIEF INVESTIGATOR: Dr Luke Grzeskowiak

FUNDING AMOUNT: $35,000 (Early Career)

PROJECT TITLE: CODDLED: A Double-Blind Randomised Controlled Trial Comparing Two Domperidone Doses on Duration and Exclusivity of Breastfeeding in Mothers of Term Infants Experiencing Lactation Difficulties

SIGNIFICANCE: The presence of lactation difficulties is one of the most commonly reported reasons for discontinuation of breastfeeding. Within South Australia alone, it is estimated that >1,000 mothers are given domperidone each year to improve breast milk supply. This is despite limited evidence to guide its optimal use. Improving existing evidence on domperidone is of major public health importance as expected improvements in breastfeeding outcomes will provide immense immediate and long-term benefits towards infant growth and development.

CHIEF INVESTIGATOR: Dr Nicolette Hodyl

FUNDING AMOUNT: $58,600

PROJECT TITLE: Regulating inflammation in the preterm neonate: the contribution of microRNAs

SIGNIFICANCE: Seventy percent of the neonatal deaths due to infection occur in preterm infants. This is due in part to a functionally immature innate immune system. Inflammation is central to combating infection, but its dysregulation leads to pathology. MicroRNAs (miRs) critically regulate inflammation in adults yet the contribution of miRs to the dysregulated preterm innate immunity is unknown. We will characterise the role of miRs in regulating preterm innate immunity, providing a target for future interventions.

CHIEF INVESTIGATOR: Dr Nicolette Hodyl

FUNDING AMOUNT: $49,200

PROJECT TITLE: Cord blood miRNA expression profiles and childhood cognitive outcomes following preterm birth

SIGNIFICANCE: Poor neurodevelopment is a major adverse outcome of prematurity, reflected by reduced cognitive performance in school-aged children, and poorer health and socioeconomic status later in life. Recent data associates placental microRNAs with neonatal neurodevelopmental indices yet links to child outcomes are unknown. Using our cord blood biobank with matched cognitive assessments at 5 years of age, we will determine cord blood microRNA profiles that predict poor cognitive development in children born preterm. This will lead to targeted, cost effective interventions to improve future outcomes.

CHIEF INVESTIGATOR: Dr James Hughes

FUNDING AMOUNT: $75,000

PROJECT TITLE: Phenotypic analysis and pharmacological rescue of a novel genetic mouse model for childhood focal epilepsy.

SIGNIFICANCE: Epilepsy is a common and debilitating disorder. In 2013 we showed that mutations in DEPDC5, a key inhibitor of mTORC1 signalling, are a major cause of Focal Epilepsy (FE) in children. We have recently generated a Depdc5 KO mouse model of FE and have preliminary data showing deregulation of mTORC1 signalling. The goal of this proposal is to fully characterise the neuronal phenotype of these mice using biochemical and behavioural analyses. We will also test the exciting possibility that mTORC1 inhibitors rescue the Depdc5 KO phenotype, which has obvious implications for FE treatment.

CHIEF INVESTIGATOR: Dr Lachlan Jolly

FUNDING AMOUNT: $75,000

PROJECT TITLE: Identifying pathological mechanisms underlying intellectual disability

SIGNIFICANCE: An estimated 2-3% of children suffer from intellectual disability and in Australia it costs in excess of $14.7 billion/annum. In up to 80% of the affected children, the cause remains unidentified. We have however identified genetic mutations in multiple genes that are common to a single 'quality control' pathway in cells that do cause intellectual disability. We now seek to understand when and where this pathway is required during brain development as a prerequisite to peruse design and testing of treatment strategies aimed at improving the affected children's quality of life.

UNIVERSITY OF SOUTH AUSTRALIA

CHIEF INVESTIGATOR: Professor Gregory Goodall

FUNDING AMOUNT: $75,000

PROJECT TITLE: miR-200 and its targets as inhibitors of neuroblastoma growth and metastasis

SIGNIFICANCE: Neuroblastoma almost exclusively strikes infants and children, is the third most common type of childhood cancer and the leading cause of cancer deaths of children under 5 accounting for 15% of all pediatric cancer deaths. Aggressive neuroblastoma has not seen a major change in the survival rate in the last ten years. Metastasis is the main cause of death for these children, so finding ways to combat metastasis is a priority. We are examining the potential for a microRNA and its targets to be exploited therapeutically to combat growth, invasion and metastasis in neuroblastoma.

CHIEF INVESTIGATOR: Associate Professor John Hayball

FUNDING AMOUNT: $74,700

PROJECT TITLE: Modulating Fc receptor signalling to treat and prevent peanut allergy

SIGNIFICANCE: Peanut allergy prevalence in Australian children has risen to 3% in recent years. Despite the risk of potentially fatal reactions, there is currently no method available in routine clinical practice for treating peanut allergies. We have established a robust murine peanut-induced anaphylaxis model that will be used to test an immunotherapic approach which aims to selectively inhibit the production of peanut allergen-specific antibodies and decreases the risk of anaphylaxis during the desensitization process. This type of immunotherapy could have broad application in treating allergic diseases.

CHIEF INVESTIGATOR: Dr Melanie Ramiasa

FUNDING AMOUNT: $35,000 (Early Career)

PROJECT TITLE: Point of care device for early diagnosis and prognosis of paediatric kidney diseases - a non-invasive alternative to renal biopsy

SIGNIFICANCE: The prevalence of chronic Kidney Disease (KD) in children is reported to be around 40 per million children of the world population. Australia is no exception with more than 1200 children developing end stage kidney failure or hefty kidney illnesses such as nephrotic syndrome each year. Children suffering kidney failure require life-long dialysis treatments or transplantation. Early detection can delay or even prevent kidney failure. Yet, current strategies to diagnose the early stage of KD rely on blood analysis and invasive biopsies, thus more accurate non-invasive tests for KD are needed.

CHIEF INVESTIGATOR: Dr Yu-Wen Su

FUNDING AMOUNT: $35,000 (Early Career)

PROJECT TITLE: Accelerating bone healing by locally delivering osteogenic and angiogenic factor neurotrophin-3 (NT-3)

SIGNIFICANCE: About 50% children experience a bone fracture. Whilst most fractures can heal, delayed/impaired healing remains a key challenge as it causes substantial morbidity, time off school, and healthcare burden. More work is needed to find ways to promote bone healing. Our pilot work shows dramatic induction of NT-3 & receptor TrkC in healing rat tibia, and it induces the major osteogenic factor BMP2 and angiogenic factor VEGF (both critical for bone repair). This work addresses if NT-3 local delivery accelerates bone healing, and could lead to a novel approach for overcoming impaired healing.

CHIEF INVESTIGATOR: Professor Shudong Wang

FUNDING AMOUNT: $75,000

PROJECT TITLE: Discovery of CDK6 inhibitors for treatment of childhood medulloblastoma

SIGNIFICANCE: Medulloblastoma (MB) is the most common malignant brain tumor of childhood, accounting for up to 30% of central nervous system tumors in children. Current therapies are associated with poor survival rate and significant long-term side effects. Cyclin-dependent kinase 6 (CDK6) is highly activated in MB patients and is associated with the adverse prognosis. Inhibiting CDK6 activity can stop MB tumour cells to proliferate leading to cancer cells death. This project aims to develop first-in-class CDK6 inhibitors which will have significant impact on developing new treatment for childhood MB cancer.