

For 2018, 23 Research grants were awarded totalling \$877,000

### **St Vincent's Clinic Foundation 25 Year Research Grant - \$100,000**

*"Determining the extent to which NAD deficiency is the cause of miscarriage and congenital malformation"*

**Principal Investigator - Prof Sally Dunwoodie**

Finding more evidence that vitamins can prevent miscarriage and birth defects

We have made a ground-breaking discovery, that low levels of NAD (a substance that is required for normal cellular function) causes birth defects. We identified gene mutations in families with multiple miscarriage and babies that had multiple types of defects. Experimentally we showed in a model system that birth defects could be prevented through a diet supplemented with nicacin/vitamin B3. There is now great hope that many types of birth defects could be prevented by taking vitamin B3.

*Victor Chang Cardiac Research Unit*

---

### **SVPHS Ladies' Committee Sr Mary Bernice Research Grant - \$100,000**

*"Personalised medicine in prediabetes - towards preventing diabetes in individuals at risk"*

**Principal Investigator - Prof Jerry Greenfield**

Simple markers to guide successful treatment of individuals at risk of diabetes

Prediabetes is a condition in which blood sugar level is higher than normal and is a serious risk factor for diabetes and heart disease. Clinicians find that many individuals with prediabetes treated with diabetes medications do not improve their blood sugar levels. The aim of the study is to provide simple markers to improve success of prediabetes treatment regimen through straightforward blood and stool tests. This study may pave the way to effective diabetes prevention.

*Garvan Institute of Medical Research*

---

### **Adult Stem Cell Research Grant - \$100,000**

*"Exploring the role and kinetics of T memory stem cells in haematopoietic stem cell transplantation for autoimmunity"*

**Principal Investigator - A/Prof John Moore**

Exploring the Role of T Memory Stem Cells in Blood Stem Cell Transplantation for Autoimmune Diseases

Blood stem cell transplantation offers patients suffering from severe autoimmune diseases a chance to prevent the devastating progression of disease. We would like to better understand how patients improve with this therapy which entails high doses of chemotherapy. Unlocking the keys to the changes in the immune system is our major goal. If we can understand which cell types need to be removed to stop the immune attack, then we may be able to use less toxic, more targeted therapies.

*St Vincent's Health Network Sydney*

---

### **Tancred Research Grant - \$50,000**

*"Analysis of T follicular helper cell responses to influenza vaccine, by single cell RNA sequencing transcriptomics"*

**Principal Investigator - Prof Anthony Kelleher**

Analysis of the T cells involved in the protective immune response following routine influenza vaccination

Globally, many millions of people undergo vaccination, but the cellular details of the immune response within the local lymph node have never been studied. The current proposal will use ultrasound guided fine needle biopsies of axillary lymph nodes to study the development of germinal centres, after fluvax inoculation, that are responsible for the production of the effective antibodies that protect against infection. This information will aid rational development of improved vaccines.

*St Vincent's Health Network Sydney*

---

### **K&A Collins Cancer Research Grant - \$50,000**

*"Are cardiac complications following doxorubicin chemotherapy more common in carriers of titin mutation? Insights from a zebrafish model"*

**Principal Investigator - Prof Diane Fatkin**

Do genes influence the risk of cardiac side effects after cancer chemotherapy?

Doxorubicin (DOX) is a highly effective anti-cancer drug but serious cardiac side effects occur in some treated patients that reduce long-term survival. Mutations in the titin gene are an important cause of dilated cardiomyopathy and also occur in 1 in 200 people in the general population. In this study, we are using an established zebrafish model to investigate whether individuals who have a genetic predisposition to heart disease have an increased risk of developing DOX-induced heart dysfunction.

*Victor Chang Cardiac Research Unit*

---

### **Thelma Greig Cancer Research Grant - \$50,000**

*"DNA repair defects as a predictor of response to novel treatments in advanced castrate-refractory prostate cancer"*

**Principal Investigator - A/Prof Anthony Joshua**

DNA repair mutations as a predictor of response to new treatment strategies in advanced prostate cancer

Advanced prostate cancer remains a fatal disease. Up to a third of these cancers harbour mutations that may be exploited through various treatment strategies. We would like to explore the ability of these mutations to predict responses to new treatment strategies by sequencing the DNA of patients enrolled on clinical trials and comparing the responses of those with to those without mutations. This information may allow us to tailor treatments to each individual in the future.

*Garvan Institute of Medical Research*

---

### **Froulop Research Grant - \$30,000**

*"Investigating the interplay between the sympathetic nervous system, anxiety and gender on blood pressure homeostasis"*

**Principal Investigator - Dr Nicola Smith**

A new link between blood pressure and stress in women

Women are usually protected from the majority of cardiovascular disease until they reach menopause, when the prevalence of disease rises to meet that of men. In cases of psychological stress, however, women are far more likely to develop high blood pressure. We have identified a gene that may be the nexus between stress and blood pressure control in women. The studies proposed will shed light on whether this process is a viable future therapeutic target.

*Victor Chang Cardiac Research Unit*

---

### **Annual Research Grant 1 - \$30,000**

*"Elucidating the pathophysiology of spontaneous coronary artery dissection"*

**Principal Investigator - Prof Robert M Graham**

Discovering the genes causing coronary arteries to tear and, thus, a heart attack or death

In younger women, a heart attack can, not uncommonly, be due to a tear in one or more coronary artery, which provides blood to the heart. The cause of this condition, called spontaneous coronary artery dissection (SCAD) is unknown. Here, we propose to explore the genetics of SCAD by sequencing patients' genes, by studying their skin cells and by making blood vessel cells to screen for drugs that might help to prevent or reduce the occurrence of SCAD.

*Victor Chang Cardiac Research Unit*

---

### **Annual Research Grant 2 - \$30,000**

*"The TGF-B superfamily cytokine Macrophage Inhibitory Cytokine-1 (MIC) protects from development of prostate cancer"*

**Principal Investigator - Prof Samuel Breit**

MIC protects from prostate cancer

MIC is a protein overexpressed by a high proportion of cancer patients. MIC is suggested to have a protective role in early cancer but its mode of action is not certain. Our unpublished data, using transgenic prostate cancer prone mice shows that MIC inhibits cancer development by stimulating anti-tumor immunity. This project is directed to understand how MIC stimulates anti-tumor immunity- a new arm of cancer therapy. There is potential for clinical application for improving anti-tumor immunity, based on the use of MIC.

*St Vincent's Health Network Sydney*

---

### **Annual Research Grant 3 - \$30,000**

*"The genomic basis of locoregional metastasis in head and neck squamous cell carcinoma"*

**Principal Investigator - Prof Neil D Watkins**

Head and neck biobank project

The aim of this project is to look at the DNA mutations in the primary tumour and lymph nodes of patients with head and neck cancer, and to collect samples for a biobank. Part of the tumour, affected lymph nodes and a blood sample will be taken to the Garvan Institute for analysis. The tissue will be used for DNA analysis and stored for future use for creating mouse models, analysing DNA in the blood and immune cell analysis.

*Garvan Institute of Medical Research*

---

### **Annual Research Grant 4 - \$30,000**

*"A novel biosensor to predict prostate cancer spread - implications for anti-invasive drug discovery"*

**Principal Investigator - Dr David Herrmann**

Predicting prostate cancer spread to improve therapeutic intervention

Cancer spread is the leading cause of death in cancer. Here, we aim to improve prostate cancer outcomes by blocking early events prior to cancer spread. We will use our world-first biosensor mouse technology to predict cancer spread in a well-characterised model of locally invasive prostate cancer. Characterising tumour cell behavior at a resolution that has not been achieved before, we will evaluate the potential of our biosensor to predict prostate cancer spread and establish effective anti-invasive treatment regimens.

*Garvan Institute of Medical Research*

---

### **Annual Research Grant 5 - \$30,000**

*"Using stem cell models to characterise cohesin mutations in acute megakaryoblastic leukaemia"*

**Principal Investigator - Dr Tim Molloy**

Using adult stem cells to characterise the genetic events that lead to acute leukaemia in Down Syndrome infants for the development of improved drugs

Children with Down syndrome have a staggering 500-fold increased risk of developing potentially fatal acute leukaemia within their first 5 years of life compared to non-DS infants. In the current study we aim to use disease-specific stem cells to discover the key genetic changes that lead to AMKL. We also aim to test a promising new drug that in our preliminary work has shown to selectively target the specific DNA defects we suspect are driving this leukaemia. Success in this research project could lead to significant improvements in the treatment of these infants in future.

*St Vincent's Health Network Sydney*

---

---

### **Annual Research Grant 6 - \$30,000**

*"Combined cardiac magnetic resonance imaging and arterial tonometry to non-invasive quantitate ventricular pressure-volume relationships and vasculo-ventricular interaction"*

**Principal Investigator - A/Prof David Muller**

Understanding the mechanics of the heart's function

This study aims to better understand the mechanics underlying the heart's function using sophisticated imaging analysis to improve upon existing methods of assessing how well the heart is contracting. This information is extremely valuable to healthcare teams looking after patients with a wide range of heart conditions including heart failure and heart valve diseases and will also allow better research tools in the future to continue to develop our understanding of heart function in health and disease.

*St Vincent's Health Network Sydney*

---

### **Annual Research Grant 7 - \$30,000**

*"Why are hERG K<sup>+</sup> channels so promiscuous with respect to drug binding?"*

**Principal Investigator - Prof Jamie Vandenberg**

Why do so many drugs have the unwanted side effect of disturbing the rhythm of the heart beat?

The human ether-a-go-go-related gene (hERG) K<sup>+</sup> channels are of great clinical and pharmaceutical importance as they interact with a wide range of medications thereby increasing the risk of cardiac arrhythmias. We aim to develop tools to help predict which drugs will be problematic and how these drugs may be modified to remove this unwanted side effect. These algorithms could provide a blueprint for future pharmaceutical design of all classes of drugs to limit off target effects and increase the throughput of drug development.

*Victor Chang Cardiac Research Unit*

---

### **Annual Research Grant 8 - \$30,000**

*"Hepatic Encephalopathy DECMRI (HED-M) Study"*

**Principal Investigator - A/Prof Mark Danta**

Imaging the liver brain

When the liver begins to fail the brain function changes, which is termed hepatic encephalopathy. This major cause of death and debility in liver disease is related to a toxin called ammonia crossing the blood brain barrier. With new MRI imaging techniques we are able to analyse the barrier between the blood and the brain which we will examine before and after treatment to better understand the condition in the hope of improved treatment of this important problem.

*St Vincent's Health Network Sydney*

---

### **Multidisciplinary Research Grant 1 - \$25,000**

*"A pilot single ceNtre study of the impActs and imPlications of the quality of sleep for adult ICU patients (NAP-ICU)"*

**Principal Investigator - Mr Jeff Breeding**

Sleep patterns in ICU are different to physiological sleep patterns. The lack of sleep for ICU patients may possibly be associated with increased mortality, delirium in ICU, decreased immune function and increased length of ICU stay. It appears likely that good quality sleep for ICU patients is more important than for the general population and that identifying areas for improvement and possible interventions and related techniques is vital. Measuring sleep quality in the ICU setting is challenging and finding the least invasive but reliable monitoring tool is essential to test interventions aimed to improve sleep. Previous studies in our unit found that noise and light exposure to our patients can be above recommended levels secondary to the around the clock monitoring and treatment in critically ill patients.

The aim of this pilot prospective observational longitudinal cohort study of 25 consecutive patients in ICU exploring sleep of ICU patients is to determine the most suitable design, objectives, measurement techniques and interventions for future interventional studies and to explore the influence of noise and light exposure to sleep quality.

*St Vincent's Health Network Sydney*

---

### **Multidisciplinary Research Grant 2 - \$25,000**

*"Club Connect: A healthy brain ageing cognitive training program for older adults"*

**Principal Investigator - Ms Claudia Woolf**

While the hallmark symptoms of major depression are widely recognised to include persistent low mood and anhedonia, many patients also describe changes to their cognitive function. These cognitive deficits may be more pronounced in older adults and often persist despite depressive symptom resolution.

Given this, depression is now well recognised as a prodromal feature and independent risk factor for cognitive decline and dementia. Strategies to promote the prevention and adequate treatment of depression may have a major public health impact as they may potentially prevent or delay dementia in older adults. Traditionally however, treatments for depression have not focussed on cognition.

Multifaceted cognitive training (CT) holds promise as a novel intervention to address the deleterious effects of depression on cognition and day-to-day functioning via the postulated effects of CT on neuroplasticity.

While efficacy for group CT in older adults has been demonstrated by this team in individuals with mild cognitive impairment [1-5], evidence in other 'at risk' groups, like those with depression, remains an avenue yet to be explored. In addition, there are very few studies that explore the feasibility of implementing CT in hospital or community settings, which ultimately should be the goal of CT research.

*St Vincent's Health Network Sydney*

---

### **Multidisciplinary Research Grant 3 - \$25,000**

*"Diaphragm ultrasound in lung transplant patients study (LUST)"*

**Principal Investigator - Ms Elise Crothers**

This is a collaborative project between Intensive Care and Lung Transplant physicians and physiotherapists to prospectively identify the incidence and severity of diaphragm dysfunction (DD) after lung transplant surgery using diagnostic ultrasound.

It is important to identify diaphragm dysfunction in this patient group because it can have serious consequences on patient outcomes including recurrent infection, graft dysfunction, and in the long-term reduced quality of life and increased mortality. Previous research has indicated rates of diaphragm dysfunction as high as 40% after lung transplantation, however, the diagnostic methods previously used such as fluoroscopy and magnetic phrenic nerve stimulation are not readily applied at the bedside, so the exact incidence is unknown. Assessment by ultrasound is quick and easy to perform at the bedside, gives immediate results and avoids patient exposure to radiation. Our study will be a landmark study that aims to find the true incidence of diaphragm dysfunction after lung transplantation and identify the consequences of DD on patient outcomes.

In the early post-operative phase, patients with diaphragm dysfunction are likely to develop basal atelectasis and associated respiratory compromise. Early and accurate diagnosis of DD will facilitate timely supportive management and the application of more intensive and specific physiotherapy techniques to optimise lung function including strengthening the diaphragm and inspiratory muscles. This has the potential to reduce patient time on mechanical ventilation, length of time in intensive care and/or hospital, and prevent readmissions to intensive care and/or hospital, thereby reducing health care costs and improving quality of life after transplant.

Participant enrolment and data collection for this study commenced in February 2016. Funding kindly provided by Professor Allan Glanville has enabled us the research time to recruit 41 participants from the Lung Transplant waiting list and complete post-operative ultrasound studies on 19 participants who have since undergone transplant. To continue this project we require \$25,000 in additional funding to provide backfill personnel to complete our data collection, analysis and publication. If funding is obtained, we are certain our study can be completed within 12 months.

*St Vincent's Health Network Sydney*

---

### **Multidisciplinary Research Grant 4 - \$25,000**

*"Dietary intervention to improve the gut microbiome and body composition for better physical health in newly diagnosed type 1 diabetes mellitus"*

**Principal Investigator - Ms Bonnie Lai**

The gut microbiome is a complex organ that interacts with a large surface area of the body and positively or negatively affects immune function, metabolism and weight regulation. In type 1 diabetes mellitus (T1D), large differences in bacterial species and diversity have been described. Improving the gut microbiome improves metabolism and lowers glucose levels.

This study will examine the impact of the addition of whole foods providing acetate & fermentable dietary fibre on the gut microbiome and body composition in younger people with newly diagnosed T1D. This information will be used to develop nutritional and patient resources that will be immediately applicable to everyday management of T1D.

*Garvan Institute of Medical Research*

---



### **Multidisciplinary Research Grant 5 - \$12,000**

*"Utility of remote mapping of cochlear implants"*

**Principal Investigator - Dr Nigel Biggs**

Using new technology the capability exists now for patients from remote regions to have most if not all of their post-operative care and audiology rehabilitation following cochlear implantation performed remotely.

This would save an enormous amount of travel time and expense to country patients and secondarily provide increased ability of audiologists to provide timely care of cochlear implant patients. This study is to investigate the patient and healthcare professionals' perception of programming cochlear implants through telemedicine.

*St Vincent's Private Hospital Sydney*

---

### **Multidisciplinary Research Grant 6 - \$25,000**

*"Can Emergency nurses safely and effectively insert ultrasound guided fascia iliaca blocks compared to medical practitioners in patients with a fractured neck of femur: A retrospective descriptive cohort study"*

**Principal Investigator - Ms Julie Gawthorne**

This project aims to determine if trained emergency nurses can effectively and safely insert Fascia Iliaca Blocks (FIB's) under ultrasound guidance compared to medical practitioners in patients with a fractured neck of femur (NOF). Medical and nursing staff at SVH already have completed the same formalised FIB training program. Medical record audits of a retrospective convenience sample of patients presenting to ED with a fracture NOF who received a FIB between 2014 and 2017 will be undertaken. The primary outcome measure will be a reduction in verbal numerical pain score within one hour post FIB insertion. The secondary outcome is the number of adverse events documented. Differences between these outcomes by professional group (medical versus nursing) will be determined.

*St Vincent's Health Network Sydney*

---

### **Travelling Fellowship 1 - \$10,000**

*"Clinical and Research Fellowship in Cardiovascular Medicine & Cardiovascular Imaging at the Brigham and Women's Hospital, Boston, Massachusetts, USA"*

**Principal Investigator - Dr Louis Wang**

---

### **Travelling Fellowship 2 - \$10,000**

*"Fellowship in structural heart intervention at the New York Presbyterian Hospital/Columbia University Medical Centre, New York, USA"*

**Principal Investigator - Dr Roberto Spina**

---