

For 2016, 21 Research grants were awarded totalling \$828,000

SVPHS Ladies' Committee Sr Mary Bernice Research Grant - \$150,000

"Identification of the immune mechanisms associated with response in Haematopoietic stem cell transplantation for Multiple Sclerosis: Eradication of autoimmune T cells and reconstitution of tolerance"

Principal Investigator - A/Prof John Moore

Eradicating Self-Destructive Immune Cells in Multiple Sclerosis and Regenerating a New Immune System by Blood Stem Cell Transplantation

Blood stem cell transplantation (SCT) offers patients suffering from severe Multiple Sclerosis a chance to prevent the devastating progression of disease, particularly where no other therapeutic options are available. Our research goal is to investigate the immune system changes occurring after SCT to better understand disease correction and to discover new therapies to eradicate self-destructive cells and promote regeneration of a new immune system. Ultimately, we aim to identify drug-based treatments to reduce risk to patients and increase treatment availability.

St Vincent's Hospital Sydney

Adult Stem Cell Research Grant - \$100,000

"Combination therapies targeting endogenous cardiac stem cells after ischaemic injury"

Principal Investigator - Prof Richard Harvey

Enhancing heart repair after myocardial infarction by targeting cardiac-resident stem cells

Heart attack and heart failure are in epidemic proportions. Tissue stem cells are immature cells capable of producing multiple specialised cell types. Such cells have been discovered within the heart and represent potential targets of new therapies that stimulate heart regeneration. We have developed a simple therapy that awakens cardiac stem cells from their dormant state. Our aim is now to develop an improved combinatorial therapy that both awakens stem cells and provides specific molecular instruction for heart repair.

Victor Chang Cardiac Research Institute

Tancred Research Grant - \$50,000

"Insulin resistance and fracture risk in the Dubbo Osteoporosis Epidemiology Study"

Principal Investigator - A/Prof Jerry Greenfield

A study to determine whether risk of fracture in obese humans is related to insulin resistance.

With the rise in the obesity epidemic, an important debate has developed as to whether excess body fat has a detrimental or protective effect on bone health. Type 2 diabetes patients have increased fracture risk,

despite having normal or increased bone mineral density (BMD). Similarly, recent studies have reported increased fracture risk in non-diabetic obese individuals, despite normal BMD.

Insulin resistance is a state of decreased responsiveness of the body tissues to the hormonal effects of insulin. Bone is an insulin-sensitive tissue and recent studies have suggested that effective insulin action in bone cells determines whole body insulin sensitivity.

We propose that insulin resistance increases fracture risk in humans. This project will investigate the effect of insulin resistance and body fat mass on fracture risk in the longitudinal Dubbo Osteoporosis Epidemiology Study, a longitudinal study with over 10 years of follow up. The findings will be clinically invaluable in guiding preventative bone therapy to individuals at high fracture risk.

Garvan Institute of Medical Research

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

"DNA methylation biomarkers: towards a diagnostic blood test for Barrett's oesophagus and oesophageal adenocarcinoma"

Principal Investigator - Prof Reginald V N Lord

Discovery and validation of biological changes occurring in oesophageal adenocarcinoma and its precursor disease, Barrett's oesophagus, to identify biomarkers that can be used to develop a blood test for early cancer detection.

This project aims to identify a panel of biomarkers for the early identification of oesophageal adenocarcinoma in the form of a simple blood test. The research initially focuses around confirmation of biological changes observed in oesophageal tissue at each stage of disease progression, and uses this information to perform targeted investigation in patient blood samples.

St Vincent's Centre for Applied Medical Research

Thelma Greig Cancer Grant - \$50,000

"Mechanism of action of the TGF- β superfamily cytokine MIC-1/GDF15 in treatment of obesity and cancer anorexia/cachexia"

Principal Investigator - Prof Samuel Breit

A new treatment for obesity and cancer anorexia/cachexia

Research from Prof Breit's lab at St Vincent's Hospital, identified MIC-1/GDF15 as an important cause of the anorexia/cachexia syndrome, which is the ultimate cause of death of about 1/3 of patients with advanced cancer and currently has no treatment. Further MIC-1/GDF15 protein, causes obese animals to lose weight. To turn these discoveries from Prof Breit's Lab, as quickly as possible into new treatments, St Vincent's Hospital have licensed them to two multinational pharmaceutical companies. Early phase trials of MIC-1/GDF15 based treatments for cancer anorexia/cachexia and severe obesity are expected to commence in 2016. In this grant we will explore how effective MIC-1/GDF15 is in causing and maintaining long term weight loss in experimental animals and how it achieves these effects. To undertake these studies

we need to measure food intake in experimental animals, which to do accurately in real time requires sophisticated equipment.

The grant application is to fund in whole or in part the purchase of such equipment.

St Vincent's Centre for Applied Medical Research

Froulop Research Grant - \$30,000

"Role of truncating titin mutations in dilated cardiomyopathy"

Principal Investigator - Prof Diane Fatkin

Role of the muscle protein titin in dilated cardiomyopathy, a common form of genetic heart failure.

One of the biggest breakthroughs in Cardiovascular Genetics in the last decade was the recent discovery that truncating mutations in titin, the largest protein in man, are the most common risk factor for dilated cardiomyopathy. This has not yet influenced clinical management because their infrequent presence in healthy individuals has raised doubt about their pathogenicity. We propose to use zebrafish models of titin truncation to determine whether titin truncations alone are sufficient to cause disease or require additional genetic/environmental factors.

Victor Chang Cardiac Research Institute

Annual Grant 1 - \$30,000

"Development of a new diagnostic assay to identify active and productive infection within HIV-1 latently infected reservoir cells"

Principal Investigator - Dr Kazuo Suzuki

Development of novel laboratory assays for the identification of active and productive HIV-1 infection in patient cells from HIV-1 infected individuals on effective antiretroviral therapy.

Currently antiretroviral therapy dramatically reduces HIV burden but does not lead to a cure. New laboratory tests are urgently needed to provide information about the residual disease activity during treatment, and particularly, we need better tests to predict possible virus rebound before treatment interruption or in case of treatment failure. This project aims to develop such laboratory assays. In addition, a new therapeutic technology will be tested for in principle efficacy as an alternative therapeutic approach for HIV infection.

St Vincent's Hospital Sydney

Annual Grant 2 - \$30,000

"Using patient-derived induced pluripotent stem cells to identify the genetic drivers of trisomy 21-associated acute leukaemia for the development of novel therapies"

Principal Investigator - Prof David Ma

Using patient-derived stem cells to find the causes of Down syndrome-associated leukaemia.

Infants with Down syndrome (DS) have a 500-fold higher risk of acute megakaryoblastic leukaemia (AMKL) than non-DS children. One in ten DS infants develops a blood disease called transient abnormal myelopoiesis (TAM), and 20% of these progress to the potentially fatal acute leukaemia AMKL. We aim to use cutting-edge stem cell technology to discover the genetic changes that lead to TAM and AMKL. This knowledge will be vital for the development of new diagnostic tests and treatments for these diseases.

St Vincent's Centre for Applied Medical Research

Annual Grant 3 - \$30,000

"The role of epigenetics in high blood pressure"

Principal Investigator - A/Prof Catherine Suter

Discovering the underlying cause of high blood pressure

High blood pressure is one of the biggest health burdens the world faces, affecting 30% of the population. Although we know that high blood pressure can lead to heart and kidney disease, and accounts for 13% of deaths worldwide every year, we don't know what causes it and this makes it difficult to prevent or treat. We propose that high blood pressure is caused by changes in the way genes are regulated, and that these changes can be inherited.

Victor Chang Cardiac Research Institute

Annual Grant 4 - \$30,000

"Fibrosis regression in HCV-related cirrhosis"

Principal Investigator - A/Prof Mark Danta

Improvement in liver injury following successful HCV therapy and its impact on clinical care.

With the new hepatitis c therapies most patients will clear the infection. This will result in improvement in liver damage in a majority of individuals but it is not known how this will impact long-term clinical outcomes. This study aims to identify non-invasive markers of liver improvement with the aim of identifying individuals who do not need long-term follow-up because they are not at risk of liver-related complications.

St Vincent's Hospital Sydney

Annual Grant 5 - \$30,000

"Expression and function of BCL 11b in multiple sclerosis patients"

Principal Investigator - Prof Bruce Brew

Investigation into the role of the BCL11b protein in multiple sclerosis

The role of viral infection in the pathogenesis of multiple sclerosis (MS) has been strongly debated. BCL11b is a protein known to be a transcriptional modifier expressed in both the brain and immune system. BCL11b has been shown to inhibit human immunodeficiency virus (HIV) gene transcription. We hypothesize that BCL11b may also be a marker of latent retroviral infection in MS and could play a role in the pathogenesis of the disease.

St Vincent's Hospital Sydney

Annual Grant 6 - \$30,000

"A new cardioprotective factor in the left ventricular hypertrophy?"

Principal Investigator - Dr Nicola Smith

A new player in an enlarged heart?

Heart disease kills one in three Australians and is a substantial health and economic burden. We have found a new gene that could protect the heart from the deleterious growth seen in response to high blood pressure, heart attack and blocked arteries. This project will examine the effects of deleting or increasing the amount of this gene specifically in heart muscle. These studies will reveal whether this gene is a possible therapeutic target for the treatment of heart disease.

Victor Chang Cardiac Research Institute

Annual Grant 7 - \$30,000

"Implementation of drug-drug interaction alerts: An investigation of burden on prescribers"

Principal Investigator - Dr Melissa Baysari

Implementation of drug-drug interaction alerts: An investigation of burden on prescribers

Research has shown that doctors are often presented with a large number of computerised alerts when prescribing, many of which warn of low severity, low probability events. The result is 'alert fatigue', doctors ignoring all alerts, even those that present useful information.

This project will explore the impact of introducing drug-drug interaction (DDI) alerts on the alert burden experienced by prescribers. With DDI alert implementation, is alert fatigue inevitable?

St Vincent's Hospital Sydney

Annual Grant 8 - \$30,000

"Ex Vivo Perfusion to optimise donor organ quality in multi-organ retrieval"

Principal Investigator - A/Prof Kumud Dhital

Improving quality of DCD organs through ex-vivo perfusion

Heart, lung, liver and kidneys from circulatory death donors carry a poorer outcome when compared to the

use of organs from brain dead donors. However, the shortage of suitable organs has led to increasing utilisation of marginal organs including those donated after determination of death following circulatory arrest. This study aims to assess methods to better preserve, recover and examine these organs prior to transplantation through the use of ex-vivo organ perfusion. This is performed through installing the organs on circuits which medicate to treat the organs to help recovery, and also assess the functional quality of these organs prior to transplantation.

Victor Chang Cardiac Research Institute

Multidisciplinary Grant 1 - \$25,000

"Maintaining normoTHERMia during SEDation: The THERMISED pilot study"

Principal Investigator - Dr Jed Duff

Hypothermia is a known adverse effect of general and regional anaesthesia. It is associated with increased risk of complications including surgical site infections and bleeding. For this reason, it is recommended that strategies are implemented to prevent hypothermia. The most effective strategy is forced-air warming. Of note, with advances in medical technology continuing to expand the indications for minimally invasive surgical techniques, sedation is likely to be increasingly used for many procedures that once could only be performed with general anaesthesia. Interventions to prevent hypothermia from occurring, such as forced air warming, are not currently used for sedated patients. Yet, we recently observed in one of our previous studies that about one quarter of patients undergoing procedures with sedation were hypothermic after their procedure. It stands to reason that sedated patients who become hypothermic are at a similar risk of developing complications, like infections and bleeding, to those patients who undergo a general or regional anaesthetic. As such, investigation of the clinical benefits of preventing hypothermia in sedated patients is required. This research aims to determine whether forced air warming reduces hypothermia in sedated patients. The results could potentially benefit the large number of patients undergoing interventional procedures with sedation.

St Vincent's Private Hospital Sydney

Multidisciplinary Grant 2 - \$25,000

"The impact of nutrition and swallowing on patients gastrostomy / PEG decision-making in Motor Neurone Disease (MND)"

Principal Investigator - Ms Julie Labra

Motor Neurone Disease (MND) is a rapidly progressive fatal neurological disorder which causes physical deterioration, and for some people cognitive impairments. Supportive interventions, such as a gastrostomy (PEG), may extend survival, increase comfort and preserve quality of life. However, there are no MND-specific evidence-based clinical guidelines regarding the best approach for recommending PEG to MND patients, nor are there clear guidelines suggesting the best time for inserting a PEG. Many MND patients take months to consent to PEG insertion following recommendation from the multidisciplinary care team. Delayed insertion of PEG for MND patients increases their risk of mortality and length of hospital stay, which negatively impacts on their quality of life (QOL).

Gastrostomy (PEG) decision-making for MND patients is influenced by a variety of factors including their

physical condition and personal beliefs. Currently it is suggested that swallowing and nutrition are key indicators for recommending PEG to patients with MND. However, it is not known if MND patients' perception of their ability to swallow and nutritional status, such as weight loss, influences their PEG decision making.

To understand the complex process of PEG decision-making in MND this pilot project will recruit 20 patients from two multidisciplinary MND clinics. Patients will be recruited at the time of PEG recommendation by the multidisciplinary care team. Semi-structured interviews will be conducted, as well as quantitative measures of physical function, swallowing, and nutrition. The results of this study will allow us to better understand MND patients' PEG decision-making. We will specifically explore MND patients' perception of their swallow function and nutritional status; how their perceptions compare with clinical assessment and; whether their perception of swallowing and nutrition impact upon PEG decision-making.

This project will provide the foundation towards developing a shared decision-making tool for PEG insertion in MND. This will improve decision-making capacity for patients and clinicians. Through shared decision-making it is anticipated MND patients will have reduced decisional conflict. It is also anticipated that patients with MND will have reduced latencies when making PEG decisions, which will improve their QOL life and reduce healthcare costs.

St Joseph's Hospital

Multidisciplinary Grant 3 - \$25,000

"A transfer training program to reduce falls in cognitively impaired older adults with higher level gait disorders: A pilot study"

Principal Investigator - Ms Weihong Zhang

This research project will investigate the feasibility and acceptability of combined Errorless Learning (EL) and Spaced Retrieval (SR) techniques in a 3 week transfer training program to prevent falls in adults aged 65 and over with mild to moderate cognitive impairment and higher level gait disorders. Participants are recruited from those admitted to St Vincent's Hospital (SVH) under the Geriatric team. The baseline assessments and initial intensive intervention (week 1) are conducted by a senior occupational therapist and a senior physiotherapist who work on the acute geriatric ward under the supervision of geriatricians. Week 2 and week 3 intervention is either conducted on the ward or in the participants home if they are discharged. The occupational therapist will visit participants at home for intervention. Follow up assessments at 3 months post intervention are conducted by the occupational therapist at the participants home. This project will form the pilot study for a larger multi-centre clinical trial, which will assess the long-term effect of this novel falls prevention program targeting older adults with cognitive impairment and higher level gait disorders.

St Vincent's Hospital Sydney

Multidisciplinary Grant 4 - \$25,000

"A study evaluating the feasibility and acceptability of the Modified Kimberley Indigenous Cognitive Assessment (mKICA) to Aboriginal people attending an acute tertiary hospital"

Principal Investigator - Miss Danielle Gately

The aim of this study is to investigate the feasibility and acceptability of the Modified Kimberley Indigenous Cognitive Assessment (mKICA) to Aboriginal people attending a tertiary hospital, and to Occupational Therapists (OTs) and Aboriginal Health Workers who administer the assessment. A protocol/guideline for the administration of the mKICA in the clinical and will be developed using the results of this study.

The sites where this study will be conducted are the acute wards at St Vincent's Hospital (SVH) and Sacred Heart Rehabilitation.

OTs have always played a key role in assessing the patients cognitive abilities. The Occupational Therapy (OT) Department at SVH has been concerned about a gap in tools available to screen cognition among Aboriginal people, and has identified only one validated cognitive screening tool for use with this population, the mKICA. The mKICA was originally developed for rural and remote populations, was modified for use among urban Aboriginal population and has been recently validated. This study found that this tool is an effective cognitive screening tool in urban Aboriginal populations, however, its performance in the clinical setting has not been investigated.

Since early 2015, following consultation with the Aboriginal Health Unit (AHU), the SVH OTs have administered the mKICA to a small number of Aboriginal patients. Whilst generally acceptable, the OTs believe further investigation is required and a protocol for its use in the clinical setting should be developed.

St Vincent's Hospital Sydney

Multidisciplinary Grant 5 - \$23,000

"A prospective study assessing the incidence of Deep Venous Thrombosis (DVT) in low-risk patients with 6 weeks non-weight bearing period following elective foot or ankle surgery"

Principal Investigator - Prof Kim Walker

The main objective of the study is to determine the incidence of symptomatic and silent DVT diagnosed in low-risk patients who have a prolonged non-weight bearing period (6 weeks) after elective Foot or Ankle surgery without thromboembolic prophylaxis. The research design is a prospective case series with a planned sample size of 113 patients. The main inclusion criteria of the study are patients more than 16 years old and undergoing elective foot and ankle surgery to be 6 weeks non-weight bearing. The exclusion criteria are known thrombophilia, active malignancy, heart failure, liver failure, renal failure, pregnancy, Achilles tendon repair, acute trauma, forefoot surgery, history of previous DVT or thromboembolic events, family history of DVT, and current use of Anti-coagulant/Anti-platelet agent therapy within 6 weeks prior to surgery. After the patient's elective foot or ankle surgery, the patient will be instructed to be non-weight bearing for 6 weeks. During the patient's initial follow-up at 2 weeks, a preliminary lower extremity Doppler ultrasound will be conducted to assess for DVT. During the second follow-up at 6 weeks, a repeat Doppler ultrasound will be made. Clinical findings suspicious of DVT will also be recorded on both follow-up visits. The incidence of DVT confirmed by ultrasound in both 2nd or 6th week post-op, as well as any venous thromboembolic complications will be noted.

St Vincent's Private Hospital Sydney

Multidisciplinary Grant 6 - \$25,000

"A pilot study evaluating functional, cognitive and nutritional changes during the first 3 months post-haematopoietic stem cell transplant"

Principal Investigator - Ms Cindy Tan

The aim of this pilot study is to evaluate the extent of cognition, functional and nutritional changes in haematopoietic stem cell transplant (HSCT) patients pre-transplant and up to 3 months post-transplant. At present, there is insufficient evidence-based information on the relationship between changes in nutritional status and body composition on the functional and cognitive capacity of patients receiving hamatopoietic stem cell transplant. This lack of information compromises provision of best practice by Allied Health Practitioners, who are unable to develop targeted interventions and practice guidelines according to know cognitive, nutritional or functional needs during the critical post-transplant period.

This information gap also means that there are no benchmarks against which to measure the effects of new interventions. This pilot study will provide us information to guide us on the design of future studies to improve the nutritional, cognitive and functional aspects of patient care.

The team aspires to develop best practice guidelines to improve the outcomes for patients receiving HSCT.

St Vincent's Hospital Sydney

Travelling Fellowship Grant - \$10,000

"Clinical Fellowship in Adult Congenital Heart Diseases/Pulmonary Hypertension at Oxford University at Oxford University Hospitals, UK"

Principal Investigator - Dr Gayathri Kumarasinghe

St Vincent's Hospital Sydney
