

For 2019, 20 Research grants were awarded totalling \$835,000

SVPHS Ladies' Committee Sr Mary Bernice Research Grant - \$120,000

"Vascular effects of the sodium-glucose cotransporter 2 inhibitor empagliflozin in people with type 2 diabetes and chronic kidney disease"

Principal Investigator - Prof Richard Day

Understanding the vascular effects of empagliflozin in patients with type 2 diabetes and chronic kidney disease

Sodium-glucose cotransporter 2 (SGLT2) inhibitors are medications which reduce blood sugar in patients with type 2 diabetes. These drugs have been shown to reduce cardiovascular deaths in high-risk patients.

There is limited information about the effects of SGLT2 inhibitors in severe kidney disease. People with kidney disease have poor cardiovascular health. The proposed study aims to examine if empagliflozin, an SGLT2 inhibitor, improves cardiovascular health (particularly the stiffness of arteries) in people with type 2 diabetes and severe kidney disease.

St Vincent's Health Network Sydney

Adult Stem Cell Research Grant - \$100,000

"Investigating cohesin and ERG as cooperating oncogenes that drive haematopoietic stem cell transformation to acute leukaemia"

Principal Investigator - Dr Tim Molloy

Investigating the cooperation of two potential cancer genes and their role transforming blood stem cells into acute leukaemia

Acute myeloid leukaemia (AML) has the highest mortality rate of any blood cancer in Australian adults, with an average 5-year survival rate of just 25%. In the current study we some of the key genetic changes that we

believe lead to AML. We also aim to test a promising new drug 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 this serious cancer in future.

St Vincent's Centre for Applied Medical Research

Tancred Research Grant - \$50,000

"Evaluation of cardioprotective effects of agents with newly identified Sodium Hydrogen Exchange inhibitor activity in H9c2 cells & an isolated working heart model of donor heart retrieval & cold storage."

Principal Investigator - Prof Peter Macdonald

Improving the function of "marginal" donor hearts with newly identified agents in clinical use that minimise toxic intracellular calcium accumulation.

Donor heart shortage has forced consideration of hearts from “marginal” donors such as those that have been exposed to an extended cold storage period between organ procurement and re-implantation. This project will test newly identified agents that minimise toxic calcium accumulation and activate protective signalling pathways for their ability to improve marginal heart recovery after donor heart retrieval and storage. Positive results will suggest further approaches that may significantly increase clinical usage of “marginal” hearts and other transplantable organs.

Victor Chang Cardiac Research Unit

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

“Blocking IL1R1 signalling to inhibit breast cancer metastasis”

Principal Investigator - Dr Christine Chaffer

Blocking the IL1R1 receptor to inhibit breast cancer metastasis

There are currently no treatments for patients with advanced-stage metastatic breast cancer. We have discovered that activation of a receptor (IL1R1) on the aggressive cancer cells that drive triple-negative breast cancer metastasis makes those cells chemo-resistant. We will now test whether blocking that receptor sensitises the aggressive cancer cells to chemotherapy. We propose that our novel therapy will push the aggressive cancer cells into a chemo-sensitive state, and that together with standard-of-care chemotherapy, will prevent breast cancer from spreading.

Garvan Institute of Medical Research

Thelma Greig Cancer Research Grant - \$50,000

“Single-cell analyses to tailor stratification in patients with intermediate-risk prostate cancer”

Principal Investigator - Dr Aurelie Cazet

Application of single-cell technology to guide personalised medicine for patients with prostate cancer

Patients presenting with intermediate-risk prostate cancer represent a crucial challenge in view of the high rates of clinical relapse. Here, we aim to use a revolutionising “single cell” approach to tackle this problem. This technology enables scientists and medical oncologists to analyse every single individual cell in a patient biopsy, including rare drivers of malignancy. It will help us to define new molecular biomarkers that will offer the potential for better risk assessment in this complex and multi-faceted disease.

Garvan Institute of Medical Research

Froulop Research Grant - \$30,000

“Pulsatility in continuous flow left ventricular assist devices - effect on microvascular beds”

Principal Investigator - Prof Christopher Hayward

Lack of pulsatility and its effect on end-organs following continuous flow left ventricular assist device support

As LVADs are run at constant pump speed, there is little variability in blood pressure pulsatility and flow around the body. It is suggested that increased pulsatility is associated with better outcomes.

This study will characterise blood flow in major organs and blood vessels and characterise changes in physiology and/or new blood vessel formation that results as a consequence of diminished pulsatility. This will enable us to understand physiological alterations associated with LVADs to enable us to mitigate adverse events.

St Vincent's Health Network Sydney

Annual Research Grant 1 - \$40,000

"Reactivating p53 to combat CDK4/6 inhibitor resistant ER positive breast cancer"

Principal Investigator - A/Prof Elgene Lim

A new class of drug, CDK4/6 inhibitors, is poised to become standard of care for treating patients with hormone-receptor-positive breast cancer. Unfortunately, resistance to CDK4/6 inhibitors is already emerging.

We hypothesise that activating a factor called p53 will be effective for treating resistant disease. We have developed breast cancer models that are resistant to CDK4/6 inhibitors. Using these models, we will test drugs that reactivate p53 and develop preclinical data leading to new strategies for treating resistant disease.

Garvan Institute of Medical Research

Annual Research Grant 2 - \$40,000

"Mechanisms of phenotypic diversity in cardiac sodium channelopathies"

Principal Investigator - Dr Nicholas Kerr

Young patients who die suddenly often have mutations in genes that control the electrical activity of the heart. Surviving family members who also carry the genetic mutation are at higher risk of dying suddenly. However, it is difficult to predict which patients with mutations are at highest risk and how they should be treated. By studying these mutations in human heart cells we aim to better understand how mutations, genetic background and environmental factors interact to cause the electrical problem.

Victor Chang Cardiac Research Unit

Annual Research Grant 3 - \$40,000

"Targeting the ASIC1a channel as a novel pathway of donor allograft cardioprotection with Hi1a, a disulphide-rich funnel web spider venom peptide"

Principal Investigator - A/Prof Kumud Dhital

This exciting research project aims to investigate the cardioprotective effects of Hi1a, a funnel web spider venom peptide. We propose that addition of Hi1a will afford significant and superior cardioprotection to currently used supplements and will allow us to extend the tolerable ischaemic time for donor hearts. This

will lead to both an increase in heart transplants performed as well as improve the early function of hearts post transplantation.

Victor Chang Cardiac Research Unit

Annual Research Grant 4 - \$40,000

"Metabolic Monitoring and the Microbiome in Gastrointestinal Disease Study (3M-G study)"

Principal Investigator - A/Prof Mark Danta

Diet is an important influence on the bacteria in the gut, termed the microbiome. Diseases of the gut such as inflammatory bowel and liver disease are influenced by unhealthy microbiomes. Continuously monitoring the body's pattern of blood glucose levels after eating has the potential to provide important data on the complex of interaction between the microbiome and the body in disease. By identifying a healthy glucose patterns to specific foods, personalised diet interventions could be developed to treat these diseases.

St Vincent's Health Network Sydney

Annual Research Grant 5 - \$40,000

"Accurately diagnosing fusion genes in paediatric and adolescent and young (AYA) sarcomas"

Principal Investigator - Dr James Blackburn

Cancers of connective tissue are rare in young patients, with survival rate remaining one of the lowest of all cancer types in this age group. Many cases are caused by fusion genes, but current diagnostics are incapable of detecting them effectively, limiting informed patient care. We have developed a new technology capable of identifying all fusion genes, which we will use to establish the true extent to which they contribute to cancers of the connective tissue in young patients.

Garvan Institute of Medical Research

Annual Research Grant 6 - \$40,000

"Investigating the genetic causes of platelet disorders in the Sydney Platelet Group"

Principal Investigator - Dr Joanne Joseph

A number of diseases that cause bleeding are from genetic changes affecting platelets. These are often misdiagnosed, leading patients to have inappropriate and ineffective drugs and surgeries. New testing allows us to identify patients with increased bleeding risk, and those at risk of developing life-threatening cancers like leukaemia. This allows treatment plans to be developed and patient education about their condition and transmission risk. We have established a Sydney Platelet Group to investigate genetic and other techniques to help diagnosis.

St Vincent's Centre for Applied Medical Research

Annual Research Grant 7 - \$40,000

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

Principal Investigator - Prof Samuel Breit

MIC is a protein overexpressed by a high proportion of cancer patients and 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 understanding how MIC stimulates anti-tumor immunity- a new arm of cancer therapy. There is strong potential for clinical application of MIC to improve anti-cancer treatment by stimulating antitumor immunity.

St Vincent's Centre for Applied Medical Research

Annual Research Grant 8 - \$40,000

"PRIMARY TRIAL – Can combined multiparametric MRI and PSMA PET imaging replace prostate biopsy in the primary diagnosis of prostate cancer?"

Principal Investigator - Prof Phillip Stricker & A/Prof Louise Emmett

This project aims to change the way prostate cancer is diagnosed. We are investigating if adding 68Ga PSMA-PET to mpMRI can reduce and potentially replace the need for biopsy in the diagnosis of prostate cancer. Biopsy of the prostate is invasive, painful and can lead to lifethreatening infections. Also, prostate biopsy is inaccurate and can miss up to 40% of aggressive cancers. Even when guided by MRI, about half of the biopsies performed may not find significant cancer, and may not be required. PSMA PET may help men avoid unnecessary biopsies. This ambitious prospective multisite study aims to revolutionise the diagnostic pathway of prostate cancer.

St Vincent's Health Network Sydney

Multidisciplinary Research Grant 1 - \$25,000

"Steps to Recovery Program - Promotion of physical activity in hospitalised patients, a pilot feasibility study"

Principal Investigator - Ms Sarah Sweeney

The project seeks to explore a new method of increasing the levels of physical activity for hospitalised patients. This pilot study will investigate the feasibility of a group exercise class, for ambulant patients admitted to St Vincent's Hospital. Initially, the study will recruit a single population of patients from one acute care ward, namely, haematology/oncology patients on the 9 South ward. Patients who are independently mobile will attend 1 hour group exercise classes daily during admission. Physical activity levels will be monitored, and the feasibility of this service will be assessed.

St Vincent's Health Network Sydney

Multidisciplinary Research Grant 2 - \$25,000

“Randomised phase II clinical trial investigating benefit of immuno-nutrition in patients with squamous cell carcinoma of the head and neck (SCCHN) receiving curative intent radiotherapy or chemotherapy (INTAKE)”

Principal Investigator - Ms Amanda Duffy & Dr Hao-Wen Sim

The majority of patients with squamous cell carcinoma of the head and neck (SCCHN) present with locally advanced disease. Despite curative intent treatment, approximately 40% of patients eventually relapse (Kim, Radiat Oncol J 2017). One of the factors that has been shown to correlate with unfavourable clinical outcome after curative-intent therapy in SCCHN is an immunosuppressive tumor microenvironment (Balermipas, BJC 2014). Indeed, cancer immunosurveillance is increasingly understood as an important aspect of tumor eradication. Increasing understanding of mutational signatures in head and neck cancers reveal a neo-antigen landscape that is intrinsically immunogenic (Rizvi, Science 2015). Enteral immuno-nutrition has been shown to enhance host immunity and improve clinical and oncological outcomes in patients undergoing surgical resection of gastrointestinal cancers (Cheng, BMC Gastro 2018). Nutritional intervention is an integral component of head and neck cancer management; SCCHN patients receiving curative intent radiotherapy or chemoradiotherapy, in the radical or post-operative setting, almost universally require nutritional support. Incorporating immune-nutrition into current nutrition support practices, therefore, has the potential to improve in this SCCHN patient population. The INTAKE study will be a single institution, randomised phase II clinical trial to investigate the benefit of immune-nutrition in SCCHN patients receiving curative-intent radiotherapy for chemoradiotherapy.

St Vincent's Health Network Sydney

Multidisciplinary Research Grant 3 - \$25,000

“Exploring patient attitudes, barriers and enablers of exercise-based rehabilitation in patients with Pulmonary Arterial Hypertension (PAH)”

Principal Investigator - Ms Karen Brown

Pulmonary Arterial Hypertension (PAH) is a serious cause of breathlessness due to abnormal changes in the pulmonary circulation. This disease is severe and disabling causing limitations in physical activity, quality of life, right heart failure and ultimately death in many people. Despite recent advances in drug treatment, treatment options are limited and the prognosis of PAH remains poor. Rehabilitation incorporating exercise training is known to be beneficial for patients with PAH [1], and is now recommended part of their management [2].

Over the last two years, we have been conducting a novel Australian trial of outpatient exercise in patients with PAH, at both St Vincent's Hospital Sydney and a rural study site (Coffs Harbour Health Campus) [3].

During recruitment for this trial, we have observed (in our regional site in particular) a reluctance to exercise. It is a well recognised phenomenon that although cardiac rehabilitation, including exercise training is of benefit, uptake of exercise as a therapeutic intervention is often poor [4].

We want to explore this in more detail, in order to better educate and support patients with serious health conditions to engage in beneficial exercise treatments. The proposed qualitative study will investigate patients' attitudes, barriers and enablers to exercise with the aim of understanding the experience of patients with PAH.

This study will place patients living with PAH at the centre of their own health management, and use their insight to better inform the design of health services to meet their needs. The results of this study will have important implications for outpatient treatment of PAH, for both patients of St Vincent's Hospital Sydney and as a centre of excellence for PAH, as well as for the overall management of PAH internationally.

St Vincent's Health Network Sydney

Multidisciplinary Research Grant 4 - \$20,000

"Impact of lung ultrasound findings on clinical decisions and ability to predict patient outcome in intensive care"

Principal Investigator - Dr George Ntoumenopoulos

Background: Clinical assessment tools such as lung auscultation and chest radiograph information used by clinicians in intensive care have limited diagnostic accuracy. Hence, the clinical decisions made by intensive care team (physiotherapists, doctors and nurses) may lead to in-appropriate patient care. Lung ultrasound outperforms clinical assessment for the diagnosis of acute lung complications in intensive care. Lung ultrasound has been demonstrated to significantly improve clinical decisions and therapeutic management by physicians in intensive care. Hence, lung ultrasound has the potential to improve clinical decision-making by wider intensive care team including intensive care physiotherapists. This project aims to evaluate the impact of lung ultrasound on clinical decision-making by intensive care physiotherapists' and physicians in the mechanically ventilated patient in intensive care.

- Objectives: 1) To evaluate the impact of lung ultrasound on clinical decisions for chest physiotherapy and general care in mechanically ventilated patients in the intensive care.
2) To evaluate the diagnostic accuracy of lung ultrasound to predict duration of mechanical ventilation, risk of reintubation and mortality.

Study design: Multi-centre prospective observational study

Planned sample size: 200 patients

Selection criteria: Patients over 18 years of age hospitalised in the ICU, mechanically ventilated for greater than 48 hours and who have not been previously given chest physiotherapy in their current ICU admission.

St Vincent's Health Network Sydney

Travelling Fellowship 1 - \$10,000

"Clinical and Research Cardiac Electrophysiology Fellowship at the Libin Institute and University of Calgary, Alberta, Canada"

Principal Investigator - Dr William Lee

Clinical and Research Cardiac Electrophysiology Fellowship at the Libin Institute and University of Calgary, Alberta, Canada

St Vincent's Health Network Sydney

Travelling Fellowship 2 - \$10,000

"Clinical and Research Fellowship in Advanced Echocardiography (and Cardiovascular Magnetic Resonance Imaging), Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA"

Principal Investigator - Dr Mayooran Namasivayam

Clinical and Research Fellowship in Advanced Echocardiography (and Cardiovascular Magnetic Resonance Imaging), Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA

St Vincent's Clinic Foundation

Research Grants 2019



St Vincent's Health Network Sydney
