# St Vincent's Clinic Foundation
## 2003 Research Grant Recipients

This year the Clinic Foundation awarded a total of 12 grants amounting to $333,000.00 including two Travelling Fellowships and a Medical Student Grant. The research grants are listed as follows:

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

*Prof Bruce Brew - Chief Investigator*

**"The involvement of quinolinic acid and other tryptophan catabolites in the pathogenesis of Alzheimer's Disease"**

We propose to demonstrate that tryptophan metabolism within the brain plays an important role in the neurodegenerative mechanisms involved in Alzheimer's Disease. Our main hypothesis (based on preliminary results) is that a toxin named quinolinic acid produced by immune brain cells on the periphery of the senile plaques induces neuronal dysfunction and death. If this is correct, it would mean the identification of a new neurotoxic pathway leading to neuronal loss in Alzheimer's Disease.

*Research undertaken at St Vincent's Hospital Centre for Immunology*

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### Ladies' Committee Sr Mary Bernice Research Grant 2 - $30,000

*Prof Ken Ho - Chief Investigator*

**"Anabolic hormones in the therapy of glucocorticoid-induced protein wasting"**

Steroids (for example cortisone, prednisone) are commonly used to treat a range of medical conditions such as arthritis, asthma, kidney disease and transplant rejection. Long term use of steroids leads to substantial loss of body protein which causes frailty and debilitation. Our aim is to investigate whether growth hormone or androgens (male hormones) can be used to treat protein wasting induced by long term steroid use.

A key approach is the use of the leucine turnover technique which allows rates of overall protein synthesis and breakdown, key determinants of body protein status, to be measured accurately and non-invasively. This technique is not available elsewhere in this country and was established with previous support from the Clinic Foundation. This has allowed us to show that growth hormone increases protein mass by stimulating synthesis and reducing its breakdown for oxidation (burned to produce energy). We will determine how steroids alter the balance of protein metabolism to cause wasting and whether this can be prevented by growth hormone or androgens or both combined. This is a proof of concept study which will provide important information required for longer term treatment trials.

*Research undertaken at Garvan Institute of Medical Research*

## Ladies' Committee Sr Mary Bernice Research Grant 3 - $30,000

*Dr Joanne Joseph - Chief Investigator*

**"An evaluation of in-vivo platelet and monocyte activation in patients receiving standard compared to drug-elutine (Sirolimus) stents for stable coronary artery disease"**

Until recently, only standard metallic stents were available to treat patients with coronary artery diseases. New drug-eluting stents have been developed to eliminate the long-term problem of restenosis and will soon be in routine clinical use. However, their high cost will preclude their use in all patients. Our previous work has shown that blood cell activation may contribute to ischaemic complications associated with standard stents. This project aims to compare levels of blood cell activation between normal and drug-eluting stents.

*Research undertaken at St Vincent's Hospital Campus*

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## Kathleen & Ann Collins Cancer Research Grant - $50,000

*Dr D Segara - Chief Investigator*

**"Investigation of the WNT signalling pathway in the development and progression of pancreatic cancer"**

Cancer of the pancreas is the 5th largest cause of cancer death in our society. Despite advances in the treatment of other cancers, the death rate of patients developing pancreatic cancer is still over 95%. Over the past 3 years our group has made significant progress in the understanding of genetic events that occur during the development of pancreatic cancer. The major thrust of our group has been to assess the role of abnormal genes described in other cancers within pancreatic cancer.

Technological progress emanating from the Human Genome Project now gives us the capability to assess the state of activity of over 30,000 genes simultaneously on "RNA chips". We have used this technique to identify a new gene and pathway of importance in the progression of pancreatic cancer. Recently published data has linked aspirin as a preventative agent in the progression of pancreatic cancer. The main thrust of our work over the next year will be to assess the role of this pathway, and the role of aspirin in modulating this pathway using the large resource of pancreatic cancer specimens and pre-cancerous lesions that we have available in our laboratory.

*Research undertaken at Garvan Institute of Medical Research Cancer Research Program*

## Di Boyd Cancer Research Grant - $20,000

*Dr Helen Tao and Prof David Ma - Chief Investigators*

**"Gene expression profiling may reflect the clinical outcome in selected haematological malignant diseases"**

Bone marrow (BM) in chronic myelogenous leukemia (CML) and multiple myeloma (MM) patients has an accumulation of tumour cells. Current treatments focusing on these cells are unsatisfactory. It has been observed that the stromal cells in BM of these patients are also abnormal.

The roles of BM stromal cells in disease progress and their relationship with tumour cells are complicated, involving numerous genes and pathways that remain undefined. Microarray technology enables simultaneous analyses of molecular changes (up to 19,000 genes) per patient sample. We believe the information obtained from this technology can be used to judge clinical outcome and predict patient survival.

*Research undertaken at Garvan Institute of Medical Research*

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## Annual Grant I - $20,000

*Dr Alan Meagher - Chief Investigator*

**"Analysis of the class 2 HLA binding specification of the P53 vaccine (Pentrix TM) peptides"**

Vaccines must bind to class II HLA molecules on the surface of immune cells. These vary in type from individual to individual and have different binding capabilities. The project will use laboratory techniques to identify which HLA molecules bind the peptides. The laboratory findings will be correlated with the results from the clinical trial being conducted in the Clinical Trials Centre. This will help choose who is most likely to benefit from this promising new strategy to prevent colon cancer recurrence.

*Research undertaken St Vincent's Hospital Haematology Research Laboratory*

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## Annual Grant II - $20,000

*Dr Diane Fatkin - Chief Investigator*

**"Evaluation of "early disease" in familial dilated cardiomyopathy"**

Recently, it has been discovered that inherited gene defects are an important cause of familial dilated cardiomyopathy (DCM). Clinical screening of asymptomatic relatives of patients with familial DCM has identified a new population of individuals with echocardiographic changes that may represent early disease. In this study, we are (1) looking at new echocardiographic techniques to diagnose early heart muscle dysfunction and (2) determining whether carvedilol might improve or reverse these changes. Early diagnosis and intervention may ultimately prevent progression to symptomatic heart failure.

*Research undertaken at St Vincent's Hospital Victor Chang Cardiac Research Institute*

## Annual Grant II - $20,000

*Dr Nirmal Patel - Chief Investigator*

**"Inner ear neural stem cell transfer and neurotrophin-3 (NT3) production in the mouse model"**

The researchers would like to see if the nerve stem cells (NSC) survive in the mouse inner ear, produce growth factors (NT3) and effect hearing.

Forty mice will be deafened with antibiotics. Growth factor (NT3) or stem cells will be directly inserted into the mice ears under general anaesthetic.
Four groups (10 mice each):

- Control group
- Insert NT3
- Insert NSC
- Insert NSC producing NTC
- The researchers will compare groups for NT3 output, NSC survival and hearing results.

*Research undertaken at Garvan Institute of Medical Research*

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## Annual Grant III - $20,000

*Prof Terence Campbell - Chief Investigator*

**"Structure of the HERG K+ channel drug binding site"**

Disturbances of the normal rhythm of the heart are one of the major causes of death in Australia. In some instances this is due to an unintended side effect of prescription drugs. In the majority of cases this highly undesirable side effect is due to inhibition of human ether-a-go-go related gene (HERG) potassium channels. The aim of this study is to determine the structure of the drug binding site on HERG potassium channels.

*Research undertaken at Campbell University of NSW Research Laboratories*

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## Travelling Fellowship 1 - $10,000

*Dr David Brown*

Embarking on a 2-year post doctoral research program in the United States in the field of neuroimmunology, examining the function of macrophage inhibitory cytokine-1 (MIC-1) in the central nervous system.

## Travelling Fellowship 2 - $10,000

*Dr Andrew Biankin*

Undertaking further training at the Johns-Hopkins Hospital, Baltimore, Maryland, USA under the supervision of Prof Steven Leach in Division of Surgical Oncology. The training predominantly involves the investigation of early molecular events in the development of pancreatic cancer which follows on from work being done at the Garvan Institute of Medical Research / St Vincent's Hospital.

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## St Vincent's Hospital Medical Student Research Grant - $3,000

*Ms Lily Wang*

**"Does quinolinic acid cause astrocyte apoptosis?"**

Quinolinic acid (QUIN) is a toxin that is increased in inflammatory brain diseases especially meningitis / encephalitis. This project aims to investigate whether QUIN can cause the death of a particular brain cell, the astrocyte. This cell is important in providing nourishment for nerve cells and in removing toxins from nerve cells. If it is killed by QUIN, then this would in turn kill nerve cells.

*Research undertaken at St Vincent's Hospital Centre for Immunology*