



UNSW



Centre for Vascular Research

Annual Report 2010

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Director's Report

The Centre for Vascular Research in 2010 continued its mission of better understanding fundamental mechanisms in the cell and molecular biology of the vascular system and striving to develop new treatments to combat vascular disorders.

CVR, with its 5 national nodes (UNSW including laboratories at St George and Prince of Wales Hospitals, University of Sydney, Australian National University, Monash University, La Trobe University) again made many significant impacts on the international stage. In 2010 CVR researchers published their work in prestigious journals such as the New England Journal of Medicine, Nature Medicine, Circulation Research, Arteriosclerosis Thrombosis and Vascular Biology and the Journal of Biological Chemistry.

CVR procured significant grant support in 2010 to commence in 2011, and its researchers have been recognised with honours, awards and fellowships. Some notable highlights include Dr Till Böcking being awarded an ARC Future Fellowship, Drs Denuja Karunakaran and Jianmei Li being awarded Research Fellowships from the National Heart Foundation of Australia, Dr Elias Glaros being awarded a NHMRC Peter Doherty Fellowship, and Dr Alexander Benda being awarded a UNSW Vice Chancellor's Fellowship. Dr Artashes Guevorkian spent 4 months in CVR as a visiting scientist supported by the Armenian Academy of Sciences. Dr Vanessa Venturi was awarded a Young Tall Poppy Award in September. In 2010, CVR procured new NHMRC Projects, ARC Discovery and Linkage Grants. I would like to particularly acknowledge the NSW Office for Science and Medical Research for critical infrastructure funding through the Medical Research Support Program in 2010/11 and the UNSW Faculty of Medicine for ongoing support.

Consistent with its mission, and in a classic example of bench-to-bedside research, novel "home-grown" drugs developed over many years in CVR were evaluated in "first-in-human" clinical trials in cancer patients in Sydney. This work was recognised by the Premier's Award for Outstanding Translational Cancer Research in May and attracted a new Translational Program Grant from the Cancer Institute NSW.

This year also marked one full year of CVR occupancy in the new (and very green) Lowy Cancer Research Centre which was officially opened in May by the Prime Minister and NSW Premier.

I am grateful to Dr Kelvin Hopper and the CVR Management Board, and CVR Group Leaders who, together with CVR research staff, students and its dedicated management team helped further the mission of the Centre.

Levon Khachigian - CVR Director

Centre for Vascular Research Management Structure

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|-----------------|---|
| Director | Professor Levon Khachigian |
| Deputy Director | Professor Wendy Jessup |
| Group Leaders | Dr. Michael Buckley (SEZIAHS/Prince of Wales Hospital) Professor Beng Chong (UNSW/St. George Hospital) Professor Miles Davenport (UNSW) A/Professor Katharina Gaus (UNSW) A/Professor Michael Hickey (Monash University) Dr. Mark Hulett (La Trobe) Professor Wendy Jessup (UNSW) Professor Levon Khachigian (UNSW) Professor Leonard Kritharides (UNSW/Concord Hospital) Dr. Robert Lindeman (SEZIAHS/Prince of Wales Hospital) Professor Christopher Parish (ANU) Professor Roland Stocker (University of Sydney) Dr. Shane Thomas (UNSW) Dr. Vanessa Venturi (UNSW) |
| Unit Leaders | Dr. Till Böcking (UNSW) Dr. Craig Freeman (ANU) Dr. Mary Kavurma (UNSW) Dr. Sudha Rao (ANU) |
| Centre Manager | Ms M Hatton |

Research in the Centre

Biochemistry in Vascular Medicine Group (USyd)

Group Leader: Prof Roland Stocker

Our research aims

The research program in our laboratory relates to oxidative processes in vascular medicine. We focus on the roles of two enzymes, namely heme oxygenase-1 and indoleamine 2,3-dioxygenase in the pathology of atherosclerosis and related vascular diseases.

Our current research projects aim to:

- * Increase current knowledge of heme oxygenase-1 biology, how the enzyme regulates cell growth, iron homeostasis, and cellular antioxidant activity, and how this relates to vascular disease.
- * Investigate the contribution of indoleamine 2,3-dioxygenase to the regulation of vascular tone, with an emphasis on inflammation and vascular disease.
- * Develop novel technology to assess cellular oxidative stress, and apply these methods to vascular and other degenerative diseases

Achievements in 2010

We discovered that induction of indoleamine 2,3-dioxygenase contributes to the regulation of blood pressure in patients with sepsis, and that part of the protective activities of heme oxygenase-1 depends on the regulation of gene transcription including that of antioxidant genes and transcription factors. Also, we commenced applying our novel analytical tools to quantify superoxide in cells and are extending these methods to in vivo models.

Future Plans

We plan to fully characterise how heme oxygenase-1 regulates gene transcription. We will focus on the interplay of heme oxygenase-1 with transcription factors, and will examine whether expression of this enzyme is required in all vascular cells for in vivo protection. Finally, we will focus our research efforts on examining the role of indoleamine 2,3-dioxygenase in the regulation of blood flow under physiological and pathological conditions, and will characterize novel tryptophan metabolites derived from the action of indoleamine 2,3-dioxygenase and involved in the regulation of vascular tone.

Cancer and Molecular Immunology Group (La Trobe University)

Group Leader: Dr Mark Hulett

Our research aims

The migration and invasion of cells in the body is an important process in tumour progression and inflammation. Our research aims to better understand the molecular basis of tumour cell migration/invasion in the context of angiogenesis (new blood vessel growth) and metastasis, as well as leukocyte (white blood cells) migration in inflammatory disease. A current target of the laboratory is heparanase, an enzyme that degrades heparan sulphate (HS) - an important structural component of the extracellular matrix and vascular basement membrane. HS acts as a barrier to the migration of tumour cells and leukocytes as well as a depot for growth factors important for cell proliferation. The degradation of HS by heparanase promotes cell migration/invasion and liberates growth factors that stimulate angiogenesis, tumour growth and leukocyte activation. Research projects are aimed at defining the precise function of heparanase in tumour progression and inflammation to develop drug inhibitors of the enzyme for use as anti-cancer and anti-inflammatory agents.

Achievements in 2010

Highlights include the use of heparanase deficient mice to demonstrate that the enzyme plays an important role in leukocyte migration and contributes to progression of inflammatory disease. We have also identified a novel ligand for heparanase, the serum protein histidine-rich glycoprotein (HRG), and demonstrated that it modifies both the activity of the enzyme and interaction with cell surfaces. In addition, we have identified a number of ETS family transcription factors that regulate the expression of heparanase in tumour progression and inflammatory disease.

Plans for the future

Our plans for the future focus on: (i) Use of the heparanase deficient mice to further assess the role of heparanase in inflammation and tumour progression, (ii) to better define the molecular basis of heparanase gene dysregulation in the above disease settings, and (iii) to define the structural basis of heparanase activity for the design of inhibitors of the enzyme.

Cancer and Vascular Biology Group (ANU)

Group Leader: Prof Chris Parish

Our research aims

Our group aims to develop new treatments for cancer and autoimmune diseases such as Type 1 diabetes and systemic lupus erythematosus (SLE). Our research focuses on the molecular basis of cell adhesion, cell migration and cell invasions. We are particularly interested in how these cellular processes contribute to the immune system, tumour metastasis and angiogenesis (the growth of new blood vessels).

Our specialised expertise and experience lies in the design, synthesis and evaluation of novel oligosaccharides, e.g., sugar-based drug candidates, with Dr Craig Freeman making a major contribution in this area. Supported over many years by generous industry R&D grants, our research focuses on three areas: Firstly, we aim to understand how these drugs prevent the spread of cancer and inhibit its growth by starving tumours of a blood supply. Secondly, in collaboration with Dr Charmaine Simeonovic, we examine the effect of these drugs on certain autoimmune diseases, with our novel drugs compensating for deficiencies that cause autoimmune diseases such as Type 1 diabetes. We have also been studying the plasma protein, histidine-rich glycoprotein (HRG), which inhibits cell adhesion and plays an important role in regulating inflammation and angiogenesis. Thirdly, we are developing ways of harnessing the immune system against cancer. Our group carries out basic research on the immune system and cancer growth, which can potentially result in a better understanding of these systems.

Achievements in 2010

- (1) Utilising a technique for targeting tumour antigens to dendritic cells, a vaccine against human melanoma has now been manufactured by Lipotek, our commercial partner, and a Phase I clinical trials in melanoma patients undertaken in 2010.
- (2) We have also discovered that HRG may play an important role in controlling autoimmune diseases, such as SLE, by aiding the elimination of dead and dying cells.
- (3) Gained further support for our discovery that heparan sulfate is essential for the normal functioning of the insulin-producing beta cells in the Islets of Langerhans in the pancreas. During Type I diabetes we believe heparanase is delivered by autoreactive T lymphocytes to the islets and the enzyme destroys the heparan sulfate required for beta cell survival. In fact, we are gaining evidence that heparan sulfate replacement therapy represents a viable option for treating this disease.
- (4) Studies by Dr Sudha Rao have shown that heparanase, the enzyme that normally degrades extracellular heparan sulfate and aids cell invasion, can enter the nucleus of cells and regulate gene transcription.

Plans for the future

- Complete a Phase I clinical trial of our melanoma vaccine in melanoma patients.
- Further delineate the role of HRG in autoimmune disease.
- Characterise the molecular basis of heparan sulfate protection of insulin producing beta cells from reactive oxygen species damage.

Cellular Membrane Biology Laboratory (UNSW)

Group Leader: A/Prof Katharina Gaus

Our research aims

Our research aims to identify the principles that govern the organisation of lipids and proteins within the plasma membrane and thus define the mechanism of signal transduction processes. The overriding quest is to determine how specialised membrane domains organise signalling pathways. Because different signalling pathways share the same signalling machinery, it is the organisation of signalling cascades in time and space that establish hierarchies and, ultimately, control signalling outcomes that determine cell function in health and disease. The way forward for breakthrough science in membrane biology is to use high- and super-resolution fluorescence microscopy to measure membrane signalling events in live cells, while controlling signal triggering on a molecular level. We aim to link membrane organisation to cell signalling by implementing single-molecule imaging techniques and using novel cell-activating surfaces. This multidisciplinary approach encompasses cell biology, biophotonics and surface chemistry.

In 2010, we welcomed Dr Till Böcking from Harvard University to our group. Till is establishing the Molecular Machines Unit whose research focuses on elucidating the molecular mechanisms of cellular assembly and disassembly processes using a combination of biochemical and biophysical approaches. In particular he is developing fluorescence imaging techniques to observe reaction pathways at the single molecule level. Using single molecule approaches we can resolve details of molecular interactions that have not been accessible with traditional techniques.

Achievements in 2010 & plans for the future

To better understand the molecular mechanisms of the assembly of T-cell receptor (TCR) activation clusters, we established Photo-Activation Localisation Microscopy (PALM). This super-resolution microscopy approach images individual molecules with nanometre precision. This technology therefore breaks the century old diffraction limit and resolve structures that are below ~250 nm. This breakthrough in imaging technology was the reason why Nature Methods named super-resolution fluorescence microscopy Method of the Year 2008. From PALM images, we can determine the degree of protein clustering and hence measure signalling efficiencies.

We aim to determine how lipids affect signalling efficiencies and the balance of fluid/ordered membranes in T cells. To achieve this, we established time correlated single photon counting (TCSPC) that simultaneously detects protein diffusion and membrane order. This allows us to directly measure lipid-protein association and hence quantify how lipids affect the interactions of signalling proteins. Such interactions are a candidate mechanism of the underlying immune dysfunction in metabolic diseases such as obesity and diabetes. Ultimately, our goal is to image T cell migration and activation in vivo to understand how lipid disorders affect T cell function.

An ongoing project in our group examines the role of adhesive cues in cell migration. By using surfaces designed by our collaborators, Prof Justin Gooding and his team, we investigate how ligand density (uniform distribution), clustering (non-uniform distribution), and the temporal and laterally mobile presentation of ligands imposes a membrane organisation onto the plasma membrane and how this organisation influences signalling activities and efficiencies. We aim to investigate how sterol manipulations such as enrichment with oxysterol 7-ketocholesterol affects cell migration over 2D surfaces and through 3D scaffolds.

In collaboration with Dr Arindam Majumdar, Uppsala University, we succeeded in imaging membrane order in whole, living zebrafish embryos. The work was published in the Biophysical Journal in 2010 and was highlighted in Nature on 15 July 2010. This breakthrough opens the door to new and exciting research: How does membrane order aid the development of tissue? Do polarity proteins affect membrane order and development? What is the link between membrane organisation and cell migration in vivo? Armed with an arsenal of new imaging technologies, we hope to answer some of these questions in the near future.

Complex Systems in Biology (UNSW)

Group Leader: Prof Miles Davenport

Our research aims

There are currently a large number of successful vaccines for acute infections like influenza, measles, and smallpox. However, it has proved much more difficult to develop vaccines for chronic (persistent) infections like HIV or the hepatitis C virus. The CSB group studies the interactions between the host immune system and the infectious organism in a variety of animal and human infections. We apply statistical, mathematical and computational tools to understand the dynamics of infection, and how this determines whether a patient becomes ill or controls infection.

Achievements in 2010 & plans for the future

In 2010 we continued our work investigating how the immune system responds to HIV infection. It is usually assumed that a branch of the immune system known as “killer” T cells work to engage and kill HIV infected cells. However, our analysis of the dynamics of virus under immune control provide no evidence for direct killing of virus producing cells, and instead suggest alternative mechanisms of immune control are utilised. In 2011 we are extending our analysis of HIV infection dynamics to explore the persistence and turnover of latently infected cells in HIV, which persist despite therapy and prevent the eradication of the virus. In addition, we are studying the molecular evolution of HIV in vitro, and how it mutates to form new strains. Similarly, by studying the natural variation of HIV sequenced from infected patients, we are exploring how host immune mechanisms leave their ‘footprint’ on the virus. This work is done in collaboration with a number of experimental groups in Melbourne and the United States.

Another focus of our studies is on understanding how the dynamics of infection determine the nature of the immune response. This work investigated how different arms of the immune response such as Natural Killer (NK) cells respond to infection. In addition, our studies of malaria infection in humans and mice are exploring both the dynamics of parasite growth in the blood, as well as the mechanisms of host control. In 2011 we are extending these studies of malaria infection to provide new insights into how the parasite causes disease.

Computational Biology Group (UNSW)

Group Leader: Dr Vanessa Venturi

Our research aims

A major interest of the Computational Biology Group is the role of the T cell receptor (TCR) repertoire in immune responses to infectious diseases. The quest for successful vaccines for chronic infections, such as HIV, has led to a greater focus on T cell-based vaccine strategies. Studies in recent years have reported that the features of the repertoire of T cell receptors responding to a pathogen are an important determinant of immune control. The Computational Biology Group uses bioinformatics, biostatistical and computational approaches to study the role of the TCR repertoire in immune responses to infection and the factors that shape the TCR repertoire.

Achievements in 2010 and plans for the future

In 2010 we continued to investigate our previously proposed hypothesis that the production frequency of T cell receptors in the thymus plays an important role in shaping the peripheral T cell repertoire and in the inter-individual sharing of T cell receptors. This hypothesis had been proposed on the basis of previous observations of pathogen-specific T cell repertoires. In collaboration with scientists at the Vaccine Research Centre, National Institutes of Health, USA and Cardiff University School of Medicine, UK, both conventional and next generation sequencing techniques were used to investigate the naïve and total memory T cell repertoires. These investigations confirmed that TCR production frequency is indeed an important determinant of the shape of the peripheral repertoire. Moreover, we reported a substantial degree of sharing of T cell receptors between naïve and memory T cell populations and between individuals. In collaboration with scientists at the University of Arizona, we investigated the influence of the context of infection on a pathogen-specific TCR repertoire and ongoing collaborative projects with this group are focusing on how the TCR repertoire alters with age and during chronic infection.

Macrophage Biology Group (UNSW)

Group Leaders: Prof Wendy Jessup and Prof Leonard Kritharides

Our research aims

A major interest of the group is the role of leucocytes in cardiovascular disease. Much of our recent research addresses the role of macrophages in vascular cholesterol accumulation. In the early stages of atherosclerosis, excess cholesterol is deposited predominantly within lipid-engorged macrophages ('foam cells') that accumulate in the artery wall. Foam cells appear early and persist throughout the process of atherosclerosis. Besides being the main engine of lipid accumulation, they are also implicated in other aspects of plaque biology, such as the remodelling of the extracellular matrix in the plaque cap that leads to its weakening and increased susceptibility to rupture and thrombosis. Prevention or reversal of foam cell formation is therefore an important target for anti-atherosclerosis therapy. One of our goals is to understand the molecular events that lead to foam cell formation in the human artery.

Apolipoprotein E (apoE) is an important secretory product of macrophages that is protective against atherosclerosis. We have previously reported that macrophage apoE secretion is stimulated by HDL and apoAI (the main protein component of HDL), and one of our major research aims is to determine how apoE secretion is controlled and the intracellular signalling pathways responsible for this process.

We are also continuing our broader study of the relationships between cholesterol metabolism and inflammation, and investigating the relationships between dendritic cell biology and cholesterol accumulation and clearance. Dendritic cells play an important role in immune defence and inflammation, processes that are also central to the development of atherosclerosis.

Recent research achievements and future plans

We are investigating factors which control the expression and activity of ABCA1 and ABCG1, the main proteins involved in cell cholesterol export. In a study just published, we identified significant differences in the posttranslational stability of two distinct isoforms of ABCG1 that are expressed in human cells. We have now also found that the stabilities (and thus functional activities) of both ABCA1 and ABCG1 are increased when cell cholesterol levels rise. This is consistent with the need for sustained activity of these transporters under conditions of cholesterol excess. The mechanisms underlying these observations are now under investigation.

We are continuing a collaboration INSERM to study the mechanisms underlying the recently observed control of plasma cholesterol by dendritic cells. We are applying our expertise in sterol metabolism to several mouse models developed in Paris, in which dendritic cell

levels can be manipulated. This nicely complements our ongoing studies of the impact of cell cholesterol levels on dendritic cell function.

In 2010 we have also commenced studies to characterise a novel gene, identified in our laboratory, whose expression is strongly increased in macrophages loaded with cholesterol. Preliminary results suggest that the product of this gene is involved in cellular lipid metabolism.

We have extended our understanding of the intracellular transport processes and signaling pathways mediating apoE secretion and have identified a key role for Protein Kinase C in this process. Importantly, unlike other signaling molecules that we have identified previously, we found that apoE secretion can be increased by stimulation of the PKC pathway, a finding that will contribute to the development of therapeutics against atherosclerosis. We have also established that appropriate transport of apoE through the classical secretory pathway depends on RAB2A, a member of the vesicle tethering and docking family of Rab proteins. RAB2A appears critical in ensuring proper processing of apoE and studies are now underway to verify these studies in macrophages. We have also completed a study investigating the effect of cholesterol accumulation in macrophages on the secretion of apoE. Our studies showed that cholesterol loading leads to a decrease in apoE secretion. This was mediated post-transcriptionally via inhibition of apoE transport from the ER to the Golgi. This work helps to explain why, although apoE transcription is increased in many in vitro studies, a decrease in apoE secretion is found in vivo in whole animal studies. As a continuation of published work in 2009, we have started investigating the mechanisms behind the atherogenic effect of the immunosuppressant cyclosporin A in mice. A pilot study showed a clear increase in plasma lipid levels consistent with observations in humans treated with cyclosporin A. We are currently analysing tissues and using mouse models to further investigate the mechanism(s) behind this increase in plasma lipids.

In 2010 we were very pleased to note the grant successes of two members of our group; Dr Maaïke Kockx, who was awarded an NHF Project Grant to take some of her in vitro findings into an in vivo model and Dr Denuja Karunakaran who obtained an NHF Postdoctoral Fellowship.

Mechanisms of Leukocyte Recruitment Group (Monash University)

Group Leader: A/Prof Michael Hickey

Our research aims

The interest of our laboratory lies in understanding the mechanisms whereby leukocytes exit the bloodstream and enter sites of inflammation. Leukocyte recruitment underlies the pathology of inflammatory diseases such as asthma, arthritis, and multiple sclerosis, as well as diseases of the vasculature such as atherosclerosis, and as such is a major potential therapeutic target for these conditions. To understand the molecular basis of this process, our laboratory uses various forms of advanced in vivo imaging, including multiphoton microscopy, to image tissues during the development of the inflammatory response. The capacity of this technology, by which individual leukocytes can be examined in vivo in real time as they undergo the process of leaving the vasculature and entering sites of inflammation, allows a unique understanding of this fundamental element of the inflammatory response. Recent research has focussed on examination of inflammatory responses of the renal glomerulus and the skin. Our work has also examined the roles of proinflammatory cytokines such as macrophage migration inhibitory factor (MIF) in regulation of this process.

Achievements in 2010

Highlights included the first demonstration that the pro-inflammatory protein, MIF, regulates the response of the vascular endothelial cell to inflammatory stimuli. We found that endothelial cell expression of MIF increases the ability of these cells to express adhesion molecules and chemokines and thereby induce leukocyte adhesion. In addition we provided the first demonstration that MIF also acts in leukocytes, enhancing migratory ability of both neutrophils and macrophages, thereby increasing their ability to enter inflamed tissues. In other work, we used in vivo microscopy to study the inflammatory response in the kidney, and demonstrated the molecular basis whereby platelets contribute to recruitment of leukocytes to the inflamed renal glomerulus.

Plans for the future

In recent developments, we have updated the microscopy equipment in the laboratory such that we are now able to identify exceedingly rare leukocyte subsets, such as regulatory T cells, in vivo as they undergo adhesion and recruitment in blood vessels during the inflammatory response. In ongoing work we are using multiphoton and spinning disk confocal microscopy to examine T cell recruitment in inflamed skin, comparing the molecular basis of recruitment of pro-inflammatory effector cells and anti-inflammatory regulatory cells. The ultimate aim of these experiments is to identify the molecular mechanisms of recruitment which are specific to each of these subsets, and use this knowledge to inform design of therapeutic strategies in inflammatory disease which inhibit

recruitment of damaging effector T cells, while maintaining anti-inflammatory regulatory T cells. This knowledge will be potentially broadly applicable across numerous inflammatory diseases.

Molecular Genetics Group (SEALS)

Group Leaders: Dr Michael Buckley and A/Prof Robert Lindeman

Recent research achievements and future plans

The focus of the research activities of the Molecular Genetics Group is disease gene identification. The group identified its third disease gene by showing that the SLC29A3 gene was mutated in the rare autosomal recessive disorder of pigmented hypertrichosis with insulin dependent diabetes mellitus. This research led to a plenary presentation at the European Society of Human Genetics Meeting where the six papers of greatest interest from among the 1700 proffered abstracts were showcased. In addition, the group continues to make progress in evaluating the function of Sp110, in which we have previously documented mutations to cause a syndrome of veno-occlusive disease with immunodeficiency. In collaboration with Dr Stuart Tangye of the Garvan Institute, the role of Sp110 in T and B cell development and interaction are under examination.

Catalina Palma has now been awarded a PhD for work examining the influence of synthetic scaffolds coated with a variety of adhesion molecules on the growth and differentiation of USSC (unrestricted somatic stem cells) derived from cord blood.

Robert Knight, under the joint supervision of Drs Alla Dolnikov and Robert Lindeman, has completed his laboratory work investigating the activity of the wnt pathway inhibitor Bio on the engraftment of human haemopoietic progenitors in mice and in particular on angiogenesis, and is currently preparing his thesis. Our group has expanded its portfolio of clinical trials, including a first-in-human trial of an Akt inhibitor in advanced haematological malignancies and a Phase I study investigating the use of Ofatumumab at high dose in patients with refractory chronic lymphocytic leukaemia. We have also now validated T2* measurement of hepatic iron against the gold standard Ferriscan, and this will have significant impact on monitoring of iron overload in patients with thalassaemia major.

Linkage analysis has been used to define the critical interval in an X-linked disorder SCAX (spinocerebellar ataxia) in an affected kindred. Further analysis of genes within the defect is underway, with the objective of identifying the causative genetic abnormality.

Molecular Machines Unit (UNSW)

Unit Leader: Dr Till Böcking

Our research aims

Chaperones are ATP-driven molecular machines that interact with proteins at every stage of their life cycle to maintain cellular homeostasis, from protein folding to transport, remodeling and finally degradation. It is therefore not surprising that chaperones play a critical role in a variety of pathological conditions including cancers, neurodegenerative disorders and cardiovascular disease. To develop therapeutic strategies targeting the chaperone system, we need to better understand the molecular basis for how chaperones carry out their diverse tasks.

The central aim of our research is to elucidate the molecular mechanism of how chaperones from the heat shock protein 70 family catalyze assembly and disassembly processes in the cell using biochemical and cell biological approaches in combination with cutting-edge fluorescence imaging. In particular we develop techniques that allow us to visualize the dynamic interaction between chaperones and their substrates at the single molecule level and in real time.

Achievements in 2010 and plans for the future

In 2010 the research efforts were divided between Harvard Medical School and the Centre for Vascular Research. The main outcome from the work initiated at HMS was the discovery of the molecular mechanism for the chaperone-mediated disassembly of the protein coat surrounding endocytic clathrin-coated vesicles. We developed a new fluorescence imaging approach that has enabled the first detailed visualisation of this uncoating reaction, revealing the unexpected accumulation of multiple chaperone molecules on the clathrin coat as a requisite for coat destabilisation via a fluctuation-capture mechanism. Future plans include the use of the single-molecule approach to study the role of chaperones in the assembly and disassembly of other macromolecular complexes. The set-up for these experiments incorporates fluorescence microscopy with microfluidics and surface chemistry and these technologies were established at the CVR. In collaboration with Katharina Gaus' group we are currently extending the use of microfluidics and surface chemistry to study cell migration in response to adhesive and soluble cues and to establish biomimetic membrane systems.

Molecular Signalling Unit (UNSW)

Unit Leader: Dr Mary Kavurma

Our research aims

Proliferation and apoptosis of cells is an intimately coupled process. We are interested in how molecules regulating aberrant proliferation and apoptosis of cells can lead to diabetes and cardiovascular diseases including atherosclerosis, calcification and ischemia-induced neovascularisation.

Tumour necrosis factor-related apoptosis-inducing ligand (TRAIL) is a protein that causes death of cells. Our recent studies however, have identified a new alternate and important function for this protein in the vasculature. We find that TRAIL also promotes survival of vascular smooth muscle cells

Aims:

- To increase our understanding of how TRAIL is regulated in the vasculature
- To increase our understanding of how TRAIL and its receptors control non-apoptotic functions in the vasculature
- To identify mechanism for the development of diabetes that are TRAIL-dependent

Achievements in 2010

We have shown that TRAIL promotes vascular smooth muscle cell proliferation and neointima formation following arterial injury *in vivo*. We also discovered that injury-inducible TRAIL transcription and expression involves FGF-2, and the co-operation actions of Sp1 and nuclear factor κ B.

Redox Cell Signalling Group (UNSW)

Group Leader: Dr Shane Thomas

Our research aims

The Redox Cell Signalling Group has two primary areas of research interest, of relevance both to cardiovascular disease and to the control of the immune system during cancer:

1. Cardiovascular disease: In cardiovascular disease, endothelial cells, which form the barrier between the flowing blood and the artery wall, become 'dysfunctional'. Endothelial dysfunction can increase the risk of heart attack and stroke for a cardiovascular disease patient. Growing evidence indicates that a protein that the immune system normally uses to destroy infectious microbes can cause such endothelial dysfunction. This protein, called myeloperoxidase (MPO), accumulates in the diseased arteries of cardiovascular disease patients, just below the endothelial cell layer where it promotes oxidative stress. We are studying how MPO-catalyzed oxidative reactions cause endothelial dysfunction and working towards the discovery of novel drugs capable of preventing the deleterious actions of MPO in diseased arteries, leading to improved endothelial function.

2. Immune control and Cancer: A protein called indoleamine 2,3-dioxygenase (IDO) is important in controlling the immune system under normal and disease conditions, including cancer, inflammation, infectious disease and autoimmunity. This protein acts to suppress the immune system and during cancer is employed by certain tumor cells to protect them against the patient's immune system. Our studies focus on understanding how the expression and activity of this protein is controlled in immune and cancer cells and in the discovery of potent, small molecule inhibitors of IDO that have the potential as anti-cancer agents.

Recent research achievements and future plans

In 2010 we made important findings towards understanding the oxidative reactions and cell signaling pathways through which MPO causes endothelial dysfunction. We have found that MPO acts by binding to specific proteins within the vascular endothelium where it produces damaging reactive oxidant species. These species alter the activities of specific proteins in endothelial cells and sub-endothelial space that increase the permeability of the endothelial layer that can lead to excessive tissue oedema during inflammatory disorders including vascular diseases. At the same time, we have found that MPO can activate cell signaling pathways that in the short term promote the production of molecules that endothelial cells rely on to maintain a healthy blood vessel. We believe this signaling represents a compensatory response aimed at maintaining endothelial cell function in the face of oxidative stress. In parallel, MPO also activates cell signaling events important in the expression of pro-inflammatory molecules. We are continuing to unravel the complex oxidative reactions and cell signaling mechanisms by which MPO impacts on endothelial function. In 2010, Dr Martin Rees, a senior post-doctoral scientist, has found that a novel class of MPO

inhibitory drugs effectively protect against MPO-mediated endothelial dysfunction. Together with Prof Chris Parish and Dr Craig Freeman (CVR, ANU) we also continue to study a class of novel drugs capable of selectively binding to MPO and removing this damaging enzyme from the vascular endothelium. Our current studies focus on testing the utility of these different MPO interventions to improve endothelial dysfunction in relevant animal models of cardiovascular disease. In collaborative studies with Dr Mark Hulett (CVR, La Trobe) investigating the role of heparanase in atherosclerosis we have promising data supporting that this inflammatory enzyme promotes the disease. We are currently investigating the mechanisms underlying the pro-atherogenic potential of the enzyme.

With respect to our research on IDO, we discovered a class of drugs that represent one of the most potent inhibitors of enzyme activity known to date. We have elucidated the molecular mechanism by which these drugs inhibit IDO and currently performing structure function studies to discover the chemical moieties of these drugs responsible for such potent enzyme inhibition. In 2011 we plan to initiate studies testing the ability of these drugs to inhibit IDO *in vivo* during cancer.

Our studies also continue to understand how IDO expression and activity is controlled at the level of cellular heme availability and by reactive oxygen and nitrogen species. Our mechanistic studies confirm that modulation of cellular heme availability by the enzyme heme oxygenase-1 controls IDO in human immune cells. Moreover, different reactive oxygen and nitrogen species also control IDO via distinct post-translational modifications. These studies are providing important new insights into how this key immune control enzyme is controlled in inflammatory or tumour tissue microenvironments where heme oxygenase-1 and the production of reactive oxygen and nitrogen species are elevated.

In collaboration with Prof. Nicholas King (University of Sydney) we are also making important findings on the role of IDO during viral infection. To date our studies indicate that IDO expression is increased in the response to infections with various virus strains and that IDO plays a dual role to control both the rate of viral growth and immune responses towards the virus. Our recent data support that this role of IDO is also relevant to other viral infections including herpes simplex virus infection.

Platelet and Megakaryocyte Group (UNSW)

Group Leader: Prof Beng H. Chong

Our research aims

Our research focuses on three areas: platelet production, immune thrombocytopenic disorders and venous thromboembolism (VTE).

Platelet production: The aim is to study the molecular regulation of platelet production and to obtain further insights into the regulatory mechanisms which will lead to better treatment of platelet quantitative disorders.

Immune platelet disorders: The aim is to study the pathogenesis of these disorders as understanding the disease mechanisms is the key to improved diagnosis and better treatment.

VTE: The aims are (1) to determine the incidence of deep vein thrombosis in the community and (2) to improve prevention and treatment of VTE.

Achievements in 2010

1. Platelet production

Thrombopoietin (TPO) is the primary growth factor involved in megakaryocyte maturation and hence platelet production. We have previously identified bone marrow stromal cells as one of the sources of TPO. TPO is produced at a constant rate in the kidney and liver to maintain homeostasis, but is regulated in bone marrow stroma cells largely by a negative feedback loop via the presence of platelet-derived factors such as PF4. This feedback mechanism is essential to maintain appropriate levels of TPO and to keep circulating platelets within the normal range.

Our aim is to define the TPO feedback mechanism in the bone marrow. Our preliminary studies have identified the transcription factor that binds to the TPO promoter and causes TPO gene suppression, the receptor on the stroma cells to which PF4 binds and the cell signaling pathway that becomes activated following TPO/receptor binding.

2. Immune platelet disorders: Mechanisms of immune thrombocytopenia

2.1. We have cloned a single chain Fv (scFv) antibody fragment that recognizes the Fc gammaRIIa on human platelets. Both murine and humanised scFv constructs have been created and successfully expressed and purified in bacteria. We have tested the purified scFvs and found that they were able to stop HIT antibody-induced platelet aggregation. We will now explore if they will also inhibit other

HIT-antibody induced activation processes in vitro and will also investigate the efficacy of these scFv in prevention of thrombocytopenia and thrombosis in vivo in a murine HIT model.

2.2. We successfully established a NOD/SCID mouse model with circulating human platelets for the study of drug-induced immune thrombocytopenia (DITP). We have already used this model to study the efficacy of IVIG for the treatment of DITP and ITP. We will now explore the efficacy of other known drugs as well as novel therapeutic agents.

Our group has established an in vitro megakaryocyte (Mk) differentiation system using murine and human haematopoietic stem cells. We have now shown that drug-induced antibodies found in DITP patients are able to inhibit the growth of platelet precursors, megakaryocytes (Mks), inhibit proplatelet formation, induce MK apoptosis and consequently reduce platelet production. We intend to define the mechanism of antibody-induced MK apoptosis.

3. VTE incidence, Prevention and Treatment

VTE is the 3rd most common vascular disease after coronary heart disease and stroke. It has an incidence of 0.74 to 0.83 per 1,000 in Australia and the cost in terms of deaths, morbidity and healthcare cost is high. Up to 10% of hospital deaths are associated with VTE and VTE is estimated to cost Australia \$1.72 billion annually (0.15% of GDP).

Despite research findings showing clearly that VTE can be effective and easily prevented, there is still a gross underuse of VTE prophylaxis even in high risk patients in Australia and globally. To improve VTE prophylaxis use, it is essential to understand the reasons for the under-prescription. In depth interviews with medical staff identified that one of the main barriers to the implementation of evidence based practice with respect to VTE prevention was the fragmentation of care that is delivered when multiple members of multiple teams are delivering care to each patient and none of those teams or members of teams has particular responsibility for VTE risk assessment and prophylaxis implementation. We developed strategies for changing and improving that practice. Using admission process mapping and ward staff focus groups ideas from stakeholders for improving VTE prophylaxis rates in hospitalised patients were generated. One idea was implemented and tested. Using nurses to do VTE risk assessments and generate reminders for doctors to prescribe, risk assessments improved from 0% to 80% of notes audited and appropriate prophylaxis implementation improved from 67% to 83% of patients. We also tested NSW Health initiatives for improving VTE risk assessment and prescribing. A medication chart highlighting VTE prescribing had no impact on either patient risk assessment or prescribing.

We piloted a study to confirm that guidelines (i.e. the evidence based practice to which we are trying to change) do in fact improve patient outcomes – novel in practice change strategies. Recruiting 369 medically ill patients we were able to demonstrate that using a randomised controlled trial we could intervene to increase guideline compliant practice from around 66% of patients to 81% and preliminary outcome data found 1 (0.6%) symptomatic VTE occurred in the 3 months following hospital admission in the intervention group of patients and 5 (2.9%) in the usual care group of patients.

Chronic medical illnesses such as respiratory and heart failure are more and more likely to be treated in the community rather than in a hospital setting. These patients are at high risk of VTE in hospital but there is no data about the incidence of VTE in this population in the community. We conducted a study of 1869 community based medically ill people and found an incidence of VTE of 5.71 per 1000 patient years (compared to literature reports of 1.35 per 1000 patient years in the general community). Previous VTE and active cancer were the biggest predictors of VTE outcomes in this patient population.

We have participated in international multi-centre VTE prevention and treatment trials of novel agents such as new oral anti-FXa and anti-FIIa compounds. In prevention studies, the efficacy of these drugs are the same or better than the current drugs. Results of VTE treatment trials are still pending.

Transcription and Gene Targeting Group (UNSW)

Group Leader: Prof Levon Khachigian

Our research aims

Cardiovascular disease and cancer remain the most prevalent causes of morbidity and mortality. The pathogenesis of these and a myriad of related diseases are underpinned by molecular and cellular changes in our blood vessels. Our research is uncovering key networks of transcriptional control and inducible gene-regulatory circuits that lead to vascular disease. We are also developing new experimental drugs that have the potential to treat a diverse range of health problems from cancer and inflammation through to eye and heart disease.

Our research program has two major objectives:

1. To better understand how harmful genes are controlled in vascular cells. This part of the program investigates signalling and transcriptional mechanisms of pro-inflammatory cytokine-dependent gene expression, post-translational mechanisms that modify protein behaviour, proteinase control, the isolation and characterisation of new genes induced or repressed by vascular cell injury, and the molecular control of vascular cell migration and proliferation. We have considerable expertise in animal models of neointima formation, angiogenesis, tumour growth, myocardial ischemia, and inflammation.
2. To develop new vascular therapeutic agents. We are harnessing the outcomes of our fundamental research by pioneering the development of novel “anti-agent” and “gene-therapeutic” strategies targeting key regulatory genes in a myriad of vascular disorders. This involves strategic collaborations with a range of clinical specialists, academics and drug development consultants.

Research achievements in 2010

Among numerous achievements in 2010, the Khachigian team provided new insights into the transcriptional control in vascular cells. The transcription factor early growth response (EGR)-1 has been implicated as a key vascular phenotypic switch through its control of inducible transcription. EGR-1 autoregulation, and histone modification in the EGR-1 promoter, represent key mechanisms in EGR-1 control, but have not been explored. We found that that EGR-1 regulates its own transcription and that this involves histone H3 phosphorylation and acetylation. EGR-1 transactivates its promoter in smooth muscle cells (SMC) exposed to interleukin (IL) 1beta through a novel cis-acting element (-211/-203). PD98059, which inhibits mitogen-activated protein kinase/extracellular regulated kinase (MEK/ERK) attenuates IL-1beta-inducible phosphorylation of extracellular signal-regulated kinase 1/2 and mitogen and stress-activated protein kinases 1/2; and reduces levels of phosphorylated and acetylated histone H3. Histone deacetylase

inhibition enhances EGR-1 transcription in response to cytokine. Conversely, suppression of histone modification with mitogen and stress-activated protein kinase 1/2 short interfering RNA, or the histone H3 acetyltransferase inhibitor Garcinol, inhibits IL-1beta-inducible EGR-1 transcription. EGR-1 interacts with the acetyltransferase p300. Acetylated H3 and phosphorylated H3 are enriched at the promoter of EGR-1; and EGR-1 is enriched at the promoters of tissue factor and plasminogen activator inhibitor 1 in response to IL-1beta, and attenuated by PD98059, Garcinol, and mitogen and stress-activated protein kinase 1/2 short interfering RNA. Thus, IL-1beta induction of EGR-1 transcription involves histone H3 phosphorylation, acetylation, and autoregulation by EGR-1. This work was published in *Arteriosclerosis, Thrombosis and Vascular Biology* in 2010.

Coronary artery bypass graft failure represents an unsolved problem in interventional cardiology and heart surgery. Late occlusion of autologous saphenous vein bypass grafts is a consequence of neointima formation underpinned by SMC migration and proliferation. Poor long term patency and the lack of pharmacologic agents that prevent graft failure necessitate effective alternative therapies. Our objective here was to evaluate the effect of targeted inhibition of the bZIP transcription factor c-Jun on intimal hyperplasia in human saphenous veins and vein graft stenosis after autologous end-to-side transplantation. DNazymes targeting c-Jun attenuated intimal hyperplasia in human saphenous vein explants. Adenovirus-forced c-Jun expression stimulated SMC proliferation, proliferating cell nuclear antigen, and MMP-2 expression. c-Jun DNazymes abrogated Adeno-c-Jun-inducible SMC growth and wound repair and reduced intimal thickening in jugular veins of New Zealand white rabbits 4 weeks after autologous end-to-side transplantation to carotid arteries. Conversely, in a DNzyme-free setting, Adeno-c-Jun potentiated neointima formation in the veins compared with Adeno-LacZ. Inducible c-Jun expression is ERK1/2- and JNK-dependent but p38-independent. Injury- and shear-inducible c-Jun controls Egr-1. These data demonstrate that strategies targeting c-Jun may be useful for the prevention of vein graft stenosis. Control of one important shear-responsive transcription factor by another indicates the existence of transcriptional amplification mechanisms that magnify the vascular response to cell injury or stress through inducible transcriptional networks. This work was published in the *Journal of Biological Chemistry* in 2010. First-in-man trials of Dz13 commenced in skin cancer patients in 2010.

Centre Supported Students

| Student name | Location | Thesis topic | Supervisor(s) |
|---------------|-----------|---|---|
| A Abu Siniyeh | UNSW | Imaging membrane order in zebrafish | A/Prof K Gaus Prof T Becker |
| S An | UNSW | Characterisation of YrdC protein | Prof L Khachigian Dr L Lourenco-Dias |
| F Anwar | UNSW | Computational analysis of immune dynamics in response to infection | Prof M Davenport Dr Diako Ebrahimi |
| L Abeynaike | Monash | Mechanisms of T-cell recruitment in dermal inflammation | A/Prof M Hickey Dr J Deane |
| NS Azahri | UNSW | Transcriptional regulation of tumour necrosis factor (TNF)-related apoptosis inducing ligand (TRAIL) in vascular smooth muscle cells, | Prof L Khachigian Dr M Kavurma |
| M Balamurali | UNSW | Dynamics of immune escape in HIV | Prof M Davenport Dr J Petravic |
| S Bell | ANU | Molecular and cellular aspects of antigen receptor sharing | Prof C Parish Dr B Quah |
| V Benson | Concord | DNAzyme effects in diabetes | Dr H Lowe Prof L Khachigian |
| M Caramins | POW | Genetic determinants of the platelet count in the mouse | Dr M Buckley A/Prof R Lindeman |
| D Carter | St George | Transcriptional regulation of cardiac development | Prof B Chong Dr J Perdomo |
| S Cartland | UNSW | Macrophage and dendritic cell migration in atherosclerosis progression and regression | Prof W Jessup A/Prof K Gaus |
| C Chan | UNSW | Targeting c-Jun in age related macular degeneration | Prof L Khachigian Prof C Chesterman |
| KH Chan | Usyd | The role of heme oxygenase-1 in neovascularisation | D M Ng Prof R Stocker |
| J Chan | UNSW | Injury-induced gene expression in vascular smooth muscle cells | Prof L Khachigian Dr M Kavurma |

| Student name | Location | Thesis topic | Supervisor(s) |
|---------------------|---------------------|---|---|
| B Changsiri | Usyd | The role of indoleamine 2,3 dioxygenase in the regulation of vascular tone in humans | Prof D Celermajer Prof R Stocker |
| S Cliffe | POW | Genetic characterization of rare disorders by linkage analysis: Venous-occlusive disease with immunodeficiency, and hypertrichosis with insulin dependent diabetes mellitus | Dr M Buckley A/Prof R Lindeman |
| R Cornely | UNSW | The role of annexin A6 in T lymphocyte activation | A/Prof K Gaus Dr T Grewal |
| L Coupland | ANU | The role of platelets in tumour metastasis | Prof C Parish Dr L Hindmarsh |
| DS Davis | ANU | Role of histidine-rich glycoprotein in health and disease | Prof C Parish Dr B Quah |
| V Deswaerte | UNSW/ UPMC Paris | Dendritic cell control of plasma cholesterol | Prof W Jessup Dr P Lesnik |
| S Devi | Monash | Mechanisms of glomerular leukocyte recruitment | A/Prof M Hickey |
| X Du | UNSW | Atherosclerosis control of cholesterol export from macrophages | Prof W Jessup Prof L Kritharides |
| HY Greenaway | UNSW | The role of the T cell receptor repertoire in immune responses to infection | Dr V Venturi Prof M Davenport |
| K Goodall | La Trobe | Characterisation of the non-enzymatic role of heparanase | Dr M. Hulett |
| Y He | ANU | Functional role of nuclear heparanase | Dr S Rao Prof C Parish Dr C Freeman |
| C Horan | ANU | Regulation of heparanase gene expression in cancer and inflammation | Dr M Hulett |
| V Hsieh | UNSW | Molecular mechanisms of cholesterol export from macrophages in atherosclerosis | Prof W Jessup Prof L Kritharides |
| R Knight | POW | Angiogenic potential of cord blood progenitor cells | Dr A Dolnikov A/Prof R Lindeman |
| F Kordbacheh | ANU | Identification of natural products that enhance Angiogenesis | Prof C Parish Dr M Djordjevic |

| Student name | Location | Thesis topic | Supervisor(s) |
|---------------------|-----------------|--|---|
| A Kross | UNSW | Structure-function relationship of olfactory receptor neurons | A/Prof K Gaus Dr J Reisert |
| M Kurniawan | UNSW | Understanding the T cell receptor repertoire | Dr V Venturi Prof M Davenport |
| D Li | UNSW | Novel approaches to inhibit restenosis | Prof L Khachigian |
| J Li | ANU | Epigenetic control of T cell memory | Prof C Parish Dr S Rao |
| S Liu | St George | Regulation of human thrombopoietin | Prof B Chong Dr S Liang |
| A Nath | UNSW | Targeting transcription factors in pancreatic cancer | Prof L Khachigian Prof B Chong Dr K Malabanan |
| JY New | St George | Single chain variable region (scFv) antibody to inhibit activation and aggregation in heparin-induced thrombocytopenia/thrombosis (HITT) | Prof B Chong Dr J Perdomo |
| SH Ngalim | UNSW | How cells make decisions: engineering surfaces for cell migration | A/Prof Gaus |
| J Ni | UNSW | Targeting immediate-early genes in bypass graft stenosis | Prof L Khachigian Prof C Chesterman |
| K Patel | La Trobe | Structure and function of histidine-rich glycoprotein | Dr M Hulett Dr I Poon |
| M Pinkevych | UNSW | Dynamics of infection using mathematical models | Dr. Janka Petravic Prof M Davenport |
| A Pollock | UNSW | How lipids modulate early T cell and immune responses | A/Prof K Gaus Dr N Tedla |
| E Sanchez-Guerrero | UNSW | Signalling and transcription in vascular smooth muscle cells | Prof L Khachigian Prof C Chesterman |
| F Santiago | UNSW | Isolation and characterisation of novel genes in response to vascular injury | Prof L Khachigian Prof C Chesterman |
| S Susanti | ANU | Identification of novel pro-angiogenic compounds | Prof C Parish Dr M Djordjevic |

| Student name | Location | Thesis topic | Supervisor(s) |
|---------------------|-----------------|---|--|
| T Thai | UNSW | The role of myeloperoxidase in endothelial dysfunction | Dr S Thomas Prof C Geczy |
| A Truong | UNSW | Anti c-Jun agents for the treatment of diabetic retinopathy | Prof L Khachigian Prof T Wong |
| D Williamson | UNSW | The role of membrane condensation in T cell signalling | A/Prof K Gaus |
| G Yee | UNSW | Targeting transcription factors in prostate and cervical cancer | Prof L Khachigian Dr Paul De Souza |
| A Yeung | Usyd | Anti-viral actions of Indoleamine 2,3-dioxygenase | Prof N King Dr S Thomas |
| A Zafar | ANU | Epigenetic control of the epithelial-to-mesenchymal transition | Prof C Parish Dr S Rao |
| N Zhang | UNSW | Transcription regulation of platelet-derived growth factor receptor-alpha | Prof L Khachigian Prof C Chesterman |

Postgraduate Completions 2010

| Student name | Location | Thesis topic | Supervisor(s) |
|--------------|----------|---|--|
| D Chan | UNSW | Viral Pathogenesis of Human and Simian Immunodeficiency Virus (HIV/SIV) | Prof M Davenport Dr Janka Petravic |
| H French | ANU | Heparanase expression and regulation in vascular disease | Dr M Hulett |
| M Leffler | ANU | Expression and function of novel members of the MS4A family | Dr M Hulett |
| G Le Saux | UNSW | Modified silicon surfaces for controlled cell interactions | Prof J Gooding A/Prof K Gaus |
| E McNaughton | ANU | B cells as antigen presenting cells | Prof C Parish Dr B Quah |
| C Palma | POW | Differentiation potential of cord blood progenitor cells | A/Prof R Lindeman |
| M Rodriguez | UNSW | The structure-function relationship of plasma membrane domains in endothelial cells | A/Prof K Gaus |
| S Roman | POW | Angiogenesis in wound healing | A/Prof R Lindeman Dr J Hunt |
| T Schlub | UNSW | Modelling in infection and immunity | Prof M Davenport Dr Vanessa Venturi |
| D Yee | ANU | Heparanase in Natural Killer cell migration | Dr H Warren Dr M Hulett |

Publications

Refereed Journal Articles

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External Research Funds

Program Grants

| | Years | (\$ pa) |
|--|---------|------------------|
| NHMRC Program Grant No. 455395 "Vascular Biology" Prof LM Khachigian (UNSW), Prof BH Chong (UNSW), Prof PJ Hogg (UNSW), Prof C Parish (ANU), Prof R Stocker (USYD), A/Prof MJ Hickey (Monash) | 2007-11 | 2,593,537 |
| Heart Research Institute NHMRC Program Grant No. 482800 "Atherosclerosis: Lipoproteins, cell biology and vascular physiology" Prof W Jessup (UNSW), Prof L Kritharides (UNSW) | 2008-12 | 862,521 |
| Cancer Institute NSW Translational Program Grant No.06/TPG/1/04 "Novel Gene-Targeted Therapies for Basal Cell Carcinoma" Prof L Khachigian (UNSW), Prof R Barnetson (USYD) Prof G Halliday (USYD), Prof C Chesterman (UNSW) | 2007-11 | 441,470 |
| Total 2010 Program Grant Funds | | 3,897,528 |

Project Grants

| | Years | (\$ pa) |
|---|---------|---------|
| NHMRC Project Grant No. 510225 "Membrane order at T cell activation sites" A/Prof K Gaus (UNSW) | 2008-10 | 176,656 |
| NHMRC Project Grant No. 568627 "The role of TRAIL and TRAIL receptors in atherosclerosis" Dr M Kavurma (UNSW) | 2009-11 | 193,099 |
| NHMRC Project Grant No. 568721 "Oxidative stress, heparan sulfates and endothelial dysfunction" Dr S Thomas (UNSW) | 2009-11 | 150,174 |
| NHMRC Project Grant No. 568774 "Post-translational control of indoleamine 2,3-dioxygenase" Dr S Thomas (UNSW) | 2009-11 | 170,477 |
| NHMRC Project Grant No. 568823 "CD4+T-cell in HIV-regulator or target of viral infection: a modelling approach" Prof M Davenport (UNSW) | 2009-11 | 111,835 |
| NHMRC Project Grant No. 630587 "Biochemistry and functional significance of glycosylation of apolipoprotein E" Dr L Kritharides (UNSW) | 2010-12 | 164,262 |

| | Years | (\$ pa |
|--|--------------|------------------|
| NHMRC Project Grant No. 630545 "The implications of focal adhesion organisation on signal transduction" A/Prof K Gaus (UNSW) | 2010-12 | 185,260 |
| ARC Discovery Project No. DP0985891 "YrdC translational control: physical and functional interactions, identification and influence of amino acid phosphorylation" Prof L Khachigian (UNSW) | 2009-11 | 114,556 |
| ARC Discovery Project No. DP0987339 "The dynamics of viral latency in chronic infection" Prof M Davenport (UNSW), Prof S Kent (UMelbourne), A/Prof J Mak (Monash University) | 2009-11 | 177,042 |
| ARC Discovery Project No. DP1095468 "Molecular microscopy: protein and membrane dynamics in resting and activated T cells" A/Prof K Gaus (UNSW), Dr DM Owens (UNSW) | 2010-12 | 30,437 |
| ARC Discovery Project No. DP1095581 "Understanding the dynamics of T cell responses to chronic infection" Dr V Venturi (UNSW), Prof M Davenport (UNSW) | 2010-14 | 30,045 |
| Human Frontier Science Program Ref. No. RGY0079/2008-C "Olfactory receptor neurons - linking membrane organisation to neuronal functionality" A/Prof K Gaus (UNSW) | 2008-11 | 137,468 |
| Cancer Institute NSW "Premier's Award for Excellence in Translational Cancer Research" Prof L Khachigian (UNSW) | 2010 | 20,000 |
| Total 2010 Project Grant Funds | | 1,721,003 |

Fellowships

| | Years |
|---|--------------|
| NHMRC Australia Fellowship No. 568602 Prof L Khachigian (UNSW) | 2010-14 |
| NHMRC Research Fellowship No. 510108 Prof W Jessup (UNSW) | 2008-12 |
| NHMRC Research Fellowship No. 568716 A/Prof K Gaus (UNSW) | 2009-13 |
| NHMRC RD Wright Career Development Award No. 401113 Dr S Thomas (UNSW) | 2006-10 |
| NHMRC Australian-based Biomedical Fellowship No. 568961 Dr D Ebrahimi (UNSW) | 2009-12 |
| NHMRC Research Fellowship No. 630542 Prof M Davenport | 2010-14 |
| ARC Future Fellowship No. FT0992111 Dr V Venturi (UNSW) | 2009-13 |
| ARC APD No. DP1095468 Dr DM Owen (UNSW) | 2010-12 |
| NHF Australia Postdoctoral Fellowship ref. PF 09S 4695 Dr M Traini (UNSW) | 2010-11 |
| Human Frontier Science Program Organisation-grants and long term Fellowships LT00517/2007 Dr T Böcking (UNSW) | 2010-11 |
| Natural Sciences and Engineering Research Council of Canada/Postdoctoral Fellowship Dr D Dinnes (UNSW) | 2008-10 |

| | |
|--|---------|
| Vice Chancellor's Postdoctoral Fellowships (UNSW) Dr Jian-Mei Li (UNSW) | 2008-10 |
| Vice Chancellor's Postdoctoral Fellowships (UNSW) Dr M Kavurma (UNSW) | 2009-11 |
| Vice Chancellor's Postdoctoral Fellowships (UNSW) Dr D Cromer (UNSW) | 2010-12 |
| Total 2010 Fellowship Funds | |
| \$2,066,955 pa | |

Scholarships

| | Years |
|--|--------------|
| NHMRC Scholarship No. 466017 S Cartland (UNSW) | 2007-10 |
| NHMRC Scholarship No. 455420 M Rodriguez (UNSW) | 2007-10 |
| NHMRC Training Scholarship No. 510441 D Williamson (UNSW) | 2008-10 |
| UIPA Scholarship D Chan (UNSW) | 2007-10 |
| UIPA Scholarship R Cornely (UNSW) | 2010-11 |
| UIPA Scholarship A Abu Siniyeh (UNSW) | 2010-11 |
| IPRS Scholarship G Yee | 2010-11 |
| Australian Postgraduate Award T Schlub (UNSW) | 2007-10 |

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|--|---------|---------------------|
| Australian Postgraduate Award E Sanchez Guerrero (UNSW) | 2010 | |
| Australian Postgraduate Award A Nath (UNSW) | 2010-11 | |
| Australian Postgraduate Award X Du (UNSW) | 2009-11 | |
| Australian Postgraduate Award A Pollock (UNSW) | 2010-11 | |
| Australian Postgraduate Award F Anwar (UNSW) | 2009-11 | |
| Australian Postgraduate Award M Kurniawan (UNSW) | 2009-11 | |
| Australian Postgraduate Award HY Greenaway (UNSW) | 2009-12 | |
| Total 2010 Scholarship Funds | | \$272,075 pa |

Equipment Grants

| | Years | (\$ pa |
|---|-------|------------------|
| ARC LIEF Grant LE100100089 "Super-resolution fluorescence microscopy" A/Prof K Gaus (UNSW) | 2010 | 700,000 |
| UNSW "Super-resolution fluorescence microscopy" A/Prof K Gaus (UNSW) | 2010 | 400,157 |
| University of Sydney "Super-resolution fluorescence microscopy" A/Prof K Gaus (UNSW) | 2010 | 120,000 |
| Macquarie University "Super-resolution fluorescence microscopy" A/Prof K Gaus (UNSW) | 2010 | 40,000 |
| University of Technology Sydney "Super-resolution fluorescence microscopy" A/Prof K Gaus (UNSW) | 2010 | 20,000 |
| University of Western Sydney "Super-resolution fluorescence microscopy" A/Prof K Gaus (UNSW) | 2010 | 10,000 |
| Major Research Equipment & Infrastructure Scheme (UNSW) "Multichannel myograph system" Dr S Thomas (UNSW) | 2010 | 79,935 |
| Total 2010 Equipment Grants | | 1,370,092 |

Infrastructure Grants, Operating Funds and Institutional Support

| | Years | (\$ pa) |
|--|---------|---------|
| ARC Infrastructure Funding "T cell recognition and control of virus: the balance between T cell receptor diversity and degeneracy" Dr V Venturi (UNSW) | 2009-13 | 52,072 |
| University contribution to NHMRC Australia Fellowship (UNSW) Prof L Khachigian (UNSW) | 2010-14 | 300,000 |
| CVR Infrastructure allocation (UNSW) | 2010 | 196,897 |
| Fellow Enhancement (UNSW) Prof W Jessup | 2010 | 17,500 |
| Fellow Enhancement (UNSW) A/Prof K Gaus | 2010 | 17,500 |
| Fellow Enhancement (UNSW) Dr S Thomas (UNSW) | 2010 | 17,500 |
| Fellow Enhancement (UNSW) Prof M Davenport (UNSW) | 2010 | 35,000 |
| Fellow Enhancement (UNSW) Dr D Ebrahimi (UNSW) | 2010 | 10,000 |
| Fellow Enhancement (UNSW) Dr M Traini (UNSW) | 2010 | 10,000 |
| Fellow Enhancement (UNSW) Dr DM Owen (UNSW) | 2010 | 10,000 |
| Fellow Enhancement (UNSW) Dr T Böcking (UNSW) | 2010 | 10,000 |
| Fellow Enhancement (UNSW) Dr V Venturi (UNSW) | 2010 | 35,022 |

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|--|---------|----------------|
| Early Career Research (UNSW) Dr A Magenau (UNSW) | 2010 | 20,000 |
| FRG (UNSW) Dr M Rees (UNSW) | 2010 | 20,000 |
| FRG (UNSW) Dr V Venturi (UNSW) | 2010 | 20,303 |
| ILP/HDR (UNSW) | 2010 | 24,000 |
| Career Advancement Fund (UNSW) Dr C Quinn (UNSW) | 2010-11 | 10,000 |
| Total 2010 Infrastructure Grants, Operating Funds and Institutional Support | | 805,795 |

Industry Funding/Donations

| | Years | (\$ pa) |
|--|-------|---------------|
| Donation of The Maxwell Charles Schroder Family Trust for PCR machines | 2010 | 17,500 |
| Total 2010 Industry Funding & Donations | | 17,500 |

Grants Administered At Other Institutions

| | Years | (\$ pa) |
|---|---------|---------|
| NHMRC Project Grant No.570861 "Dilation of blood vessels in response to a natural amino acid" Prof R Stocker (Usyd), C Sobey | 2009-11 | 221,835 |
| NHMRC Project Grant No.471424 "Dissecting the function of heparanase in inflammatory disease using genetic tissue-specific ablation" CIA Hulett, CIB Matthaai | 2009-11 | 186,000 |
| NHMRC Project grant "Drug-induced immune thrombocytopenia: Understanding the disease mechanisms is the key to better treatment" B Chong, M Davenport (UNSW) | 2010-12 | 163,900 |
| NHMRC Project Grant shared grant no. 603714 "Macrophages drives the diversity of HIV" A/Prof J Mak (Monash University), Prof M Davenport (UNSW) | 2010-12 | 59,692 |
| JDRF-NHMRC Special Program Grant in Type I Diabetes C Parish (ANU), C Simeonovic, C Freeman, G Hoyne | 2008-12 | 600,000 |
| ARC Centre of Excellence Grant "Integrative Legume Research" Prof C Parish (ANU), Dr P Bhalla, Prof C Beveridge, Dr B Carroll, Prof B Rolfe, Prof M Djordjevic, Prof P Gresshoff, Dr G Weiller, Dr U Mathesius, Dr R Rose, Prof M Singh | 2003-10 | 100,000 |

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|---|---------|---------|
| ARC Discovery Grant No. 1096299 "New functions for bioactive flavonoids in plants and mammals" M. Djordjevic (ANU), L. Mander (ANU) and C. Parish (ANU) | 2010-12 | 130,000 |
| ARC Discovery Grant No. DP0988470 "Cellular responses to adversity: Oxidative stress and protection against oxidative damage" Prof R Stocker (Usyd) | 2009-11 | 103,101 |
| ARC Lief Grant (LE110100100) "Biophysical surface characterisation facility" CIs Adam I Mechler, James R Friend, Marilyn A Anderson, Mark D Hulett, Conor, F Hogan, Paul J Pigram, Leslie Y Yeo | 2010 | 250,000 |
| Single Chief Investigator AICR project grant (United Kingdom) (#08-0215) "Role of the heparan sulphate degrading enzyme heparanase in tumour progression" CI Hulett | 2009-11 | 120,000 |
| Asthma Foundation of Victoria 'Helen Macpherson Smith' Grant 'Investigation of the role of tetraspanin MS4A8B in asthma.' M Hulett | 2010 | 25,000 |
| Diabetes Australia Research Trust Grant No. Y10-SIMC "Molecular remodeling of isolated islets for optimal survival and function of islet transplants". C. Simeonovic (ANU), C. Freeman (ANU), H. Irving-Rodgers (UAdelaide), R. Rodgers (UAdelaide) and C. Parish (ANU) | 2010 | 58,290 |

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|--|---------|------------------|
| Juvenile Diabetes Research Foundation No. 25-2010-716 "Heparan sulfate levels mark the health status of human islet beta cells" C. Simeonovic (ANU) and C. Parish (ANU) | 2010-11 | 55,000 |
| Cardiovascular Lipid Research Grant, Pfizer Australia Dr Dechaboon Changsirivathanathamrong (USYD) | 2010 | 50,000 |
| University of Sydney Early Career Researcher Grant Dr G Maghzal (USYD) | 2010 | 58,800 |
| University of Sydney Early Career Researcher Grant Dr S Wimmer-Kleikamp (USYD) | 2010 | 60,000 |
| Major Equipment Grant ANU "Integrated imaging platform for biomolecular gels, blots and arrays" C Parish (ANU) | 2010 | 150,000 |
| ARC LIEF Grant No. LE100100125 "Oxidative Stress Bioanalytical Facility" Prof R Stocker (USYD), Prof NH Hunt (USYD), Prof RS Mason (USYD), Dr PK Witting (USYD), Prof BD Roufogalis (USYD), Prof MJ Davies (HRI), Prof IW Dawes (UNSW), Prof G Drummond (Monash), Prof CL Geczy (UNSW), Prof L Khachigian (UNSW), Prof PJ Hogg (UNSW), A/Prof M Lackmann (Monash), Prof T Tiganis (Monash), Dr SR Thomas (UNSW), Prof KD Croft (UWA), Prof NJ King (USYD), Prof DE James (Garvan) | 2010 | 330,000 |
| Total 2010 Grants Administered at Other Institutions | | 2,661,926 |

Fellowships Administered At Other Institutions

| | Years |
|--|----------------|
| NHMRC Senior Principal Research Fellowship No. 401106 Prof R Stocker (USYD) | 2006-10 |
| NHMRC CJ Martin Fellowship No. 384352 Dr Sabine Wimmer-Kleikamp | 2006-10 |
| Professorial Fellowship – The University of Sydney Prof R Stocker (USYD) | 2007-11 |
| Total 2010 Fellowships Administered at Other Institutions | 344,292 |

Scholarships Administered At Other Institutions

| | Years |
|---|---------------|
| St George Medical Research Foundation Post-graduate Scholarship Dr Philip Choi | 2010 |
| International Post-graduate Scholarship Jaa Yin New | 2010 |
| Total 2010 Scholarships Administered at Other Institutions | 52,500 |

Statement of Financial Performance

UNSW

For the year ended 31 December 2010

| | Notes | 2010 |
|---|-------|-------------------|
| | | \$ |
| Income | | |
| External Funds: | | |
| Grant Income | | 6,923,986 |
| Program Partners Income | | 1,722,215 |
| UNSW Contribution: | | |
| Special Infrastructure and Strategic Research Initiatives | | 490,632 |
| Academic Support and Operating Contributions | | 1,691,994 |
| | | <hr/> |
| Total Income | | 10,828,827 |
| Expenses | | |
| Payroll | | 5,355,711 |
| Equipment | | 870,138 |
| Materials and Maintenance | | 2,151,736 |
| Travel | | 169,518 |
| Program Partners Contribution | | 1,722,215 |
| | | <hr/> |
| Total Expenses | | 10,269,318 |
| Operating Result | | 559,508 |
| Surplus (Deficit) Brought Forward from Prior Year | | 3,065,814 |
| | | <hr/> |
| Accumulated Funds Surplus (Deficit) | | 3,625,323 |
| | | <hr/> <hr/> |
| Unpaid invoices | | 126,099.48 |

Prizes and Awards

Biochemistry in Vascular Medicine Group

- Prof Roland Stocker, Lifetime Achievement Award. Society for Free Radical Research (Australasia)
- Dr Jun Ni, Prize for outstanding oral presentation for an early career scientist at the Australian Vascular Biology Society Annual Scientific Meeting

Cellular Membrane Biology Group

- A/Prof Katharina Gaus, Young Investigator Award from the Australia and New Zealand Society for Cell and Developmental Biology

Computational Biology Group

- Dr Vanessa Venturi, Young Tall Poppy Award, Australian Institute of Policy and Science

Transcription and Gene Targeting Group

- Prof Levon Khachigian, The Royal Society of Victoria Research Medal
- Prof Levon Khachigian, Premier's Award for Excellence in Translational Cancer Research, Cancer Institute NSW
- Prof Levon Khachigian, NewSouth Innovations Inventor of the Year Award in Biomedicine
- Dr Kristine Malabanan, Young Investigator Award, 16th International Vascular Biology Meeting, Los Angeles
- Dr Kristine Malabanan, Young Investigator Award, Australian Health and Medical Research Congress, Melbourne
- Estella Sanchez-Guerrero, Young Investigator Award, 16th International Vascular Biology Meeting, Los Angeles

Molecular Signalling Group

- Dr Belinda Di Bartolo, The Australian Atherosclerosis Society Young Investigator Award
- Dr Belinda Di Bartolo, The APSAVD Young Investigator Award
- Dr Belinda Di Bartolo, The BioAssay Link Award
- Dr Belinda Di Bartolo, UNSW Faculty of Medicine Travel Scholarship
- Mr Jeff Chan, The Australian Society for Medical Research MRW® Best Student Oral Presentation
- Mr Jeff Chan, The Australian Vascular Biology Society Travel Award to attend the International Vascular Biology Meeting in Los Angeles
- Mr Jeff Chan, CVR “Paper of the Month”

Platelet and Megakaryocyte Group

- Prof Beng Chong, Distinguished Research Award by the Ministry of Science and Technology, People's Republic of China

Activities Outside the Centre

Invited Talks

Dr Till Böcking

International:

- Northwestern University, Chicago, USA

National:

- Invited Speaker, OzBio 2010, Lorne

Prof Beng Chong

International:

- 13th ASEAN Conference of Clinical Laboratory Scientists Conference, Kuala Lumpur
- American Society of Hematology, Orlando, USA
- Haematology Society of Australia (NSW Branch) meeting
- Integrated Korean Haematology Society Annual Meeting, Seoul, Korea
- Thailand ITP Symposium, Pullman King Power Hotel, Bangkok
- Invited speaker, Phramongkut Hospital, Bangkok, Thailand
- International ITP Registry Investigators' Meeting, Singapore

Prof Miles Davenport

International:

- International Workshop: Systems Approaches in Immunology: Advances and Challenges in Multi-scale Modelling, Santa Fe, NM, USA
- Nature Medicine Colloquium on Systems Biology in HIV Vaccine development. February 2010, Atlanta, Georgia, USA

National:

- Australian Society for Biochemistry and Molecular Biology - 16th Annual NSW Cell and Development Biology Meeting, Sydney
- The use of modeling to inform infectious disease policy in Australia Workshop, Mt Eliza, Victoria, Invited Speaker
- Australasian Society for Immunology Annual Meeting, Perth

A/Prof Katharina Gaus

International:

- Keystone Symposium on Molecular Basis for Membrane Organization

National:

- Annual meeting of the Australian Neuroscience Society & Australian Physiological Society, Sydney, 31st January – 4th February 2010
- Hunter Cellular Biology Meetings, Hunter Valley
- HFSP Intergovernment meeting, Canberra
- International Nanomedicine Conference, Sydney
- 21st Australian Conference on Microscopy and Microanalysis, Brisbane
- OzBio and Super-resolution Microscopy Workshop, Melbourne

A/Prof Michael Hickey

International:

- Invited Speaker, FASEB Summer Conference – Renal Hemodynamics: Mechanisms to Understand Disease, Saxton's River, Vermont USA, June 2010
- Invited Speaker & Visiting Professor, Singapore Immunology Network (SIgN), Singapore, September 2010

National:

- Invited speaker, Monash Health Translation Precinct, June 2010

Dr Mark Hulett

International:

- 14th Annual International Congress of Immunology, Kobe, Japan

National:

- 25th Australian Health and Medical Research Congress, Melbourne, Australia

Prof Wendy Jessup

International:

- 6TH ISA Sponsored Workshop on HDL, Whistler, Canada (Session Chair)
- Invited speaker, International Forum of Arteriosclerosis, Thrombosis and Vascular Biology, China

Dr Mary Kavurma

National:

- Expanding your research profile. The Australian Society for Medical Research, Career Development Day for Early Career Researchers
- Postdoc positions in medical science. UNSW Post PhD Careers Seminar Series
- Session Chair, AVBS Scientific Meeting

Prof Levon Khachigian

International:

- UK Biomedical Event, AustraliALIVE, Australian High Commission (Austrade), London, UK
- Chair, “Cardiovascular” session, 2nd International Conference on Drug Discovery and Therapy, Dubai, UAE
- Inaugural International Annual Conference of Models of Human Diseases, Canadian Institute of Health Research, Toronto, Canada
- 16th International Vascular Biology Meeting, Los Angeles, USA
- Centre for Cardiovascular Biology & Medicine, University College London, UK
- UCL Division of Surgery & Interventional Science, University College & Royal Free Hampstead NHS Trust Hospital, London, UK
- Addenbrooke’s Centre for Clinical Investigation, Addenbrooke’s Hospital, Cambridge University, UK

National:

- 19th Annual Scientific Meeting of the Australasian Health and Research Data Manager’s Association, Sydney
- 18th National Scientific Meeting of the Australian Society for Medical Research, Lorne, VIC
- The Royal Society of Victoria
- 5th Australian Health and Medical Research Congress (AHMRC), Melbourne (Australia and New Zealand Orthopaedic Research Society)
- 5th Australian Health and Medical Research Congress (AHMRC), Melbourne (Australian Vascular Biology Society)
- Graduation Occasional Address, Faculties of Medicine and Science, UNSW
- 3rd SuTEN Tissue Engineering Symposium, Sydney University
- National Scientific Conference of the Australian Vascular Biology Society, Lorne, VIC
- School of Molecular and Microbial Sciences, University of Sydney
- Monash Health Translation Precinct (joint Monash University, Monash Institute, Prince Henry’s Institute and Southern Health).
- Peter MacCallum Cancer Centre, Melbourne
- Co-Chair, “Novel Targets”, Lowy Symposium “Discovering Cancer Therapeutics”, Sydney
- Chair, Australian Vascular Biology Society Symposium, Australian Health and Medical Research Congress, Melbourne
- Panelist, 3rd SuTEN Tissue Engineering Symposium, Sydney University

Prof Leonard Kritharides

International:

- Invited speaker, OzBio (combined meeting of International Biochemical Society and COMBIO), New Zealand 'Cellular trafficking pathways in the secretion of apoE.'

National:

- Invited speaker, Pulmonary Hypertension Experts Meeting Australia "Tyrosine Kinase Inhibitors in the treatment of Pulmonary Hypertension.'
- Invited speaker, Concord CT Meeting, Concord Hospital, Australia, 'What have we learnt about Cardiac Disease from Cardiac CT?'
- Invited speaker, Australian Vascular Biology Society Annual Scientific Meeting, Australia, 'Shear stress related activation of platelets and leucocytes in coronary disease.'
- Invited speaker, Port Douglas Cardiology and Echo Meeting, Australia, 'Targets for LDL lowering- should we remove them?' and 'Side effects of lipid lowering agents.'

Prof Chris Parish

International:

- Invited plenary lecturer, Indonesian Association of Clinical Immunology, Bandung, Indonesia
- Invited symposium speaker, 6th Annual Meeting of Self Reliance on Vaccine Production, Bandung, Indonesia
- Invited workshop presenter and workshop chair, 14th International Conference of Immunology, Kobe, Japan

National:

- Invited symposium speaker, 3rd Australasian Vaccines and Immunotherapeutics Development Conference, Melbourne,
- Invited plenary speaker, IgV-Mitenyi Winter Seminar, Melbourne
- Invited Symposium speaker, Bootes Course on Translational Medicine: The Pathway from Discovery to Healthcare, Canberra

Prof Roland Stocker

International:

- Invited Lecture: Gordon Research Conference on Oxygen Radicals, Ventura, CA USA
- Plenary Lecture: 3rd Singapore Lipid Symposium, Singapore
- Invited Lecture: 15th Biennial Meeting of the Society for Free Radical Research International, Orlando FL, USA
- Session Chair/Discussion Leader: 'Biomarkers & methods for detection oxidative stress' Gordon Research Conference on Oxygen Radicals, Ventura CA, USA
- Session Chair and organiser: 'Coenzyme Q10' Oxygen Club of California 2010 Congress, Santa Barbara, CA USA
- Session Chair: 'Biosynthesis' 6th Conference of the International Coenzyme Q10 Association, Brussels, Belgium
- Guest Speaker: University of Washington, Seattle, WA
- Guest Speaker: Children's Hospital Oakland Research Institute, Oakland, CA

National:

- Invited Lecture: Annual Scientific Meeting of The Australian Vascular Biology Society, Lorne
- Invited Lecture: 19th Annual Meeting of the Society for Free Radical Research, Australasia

- Barbara Ell Seminar Series, Victor Chang Cardiac Research Institute, Sydney NSW, Australia

Dr Shane Thomas

International:

- Invited Speaker, 2010 Australasian Society for Free Radical Research (SFRR), Akaroa, New Zealand.

National:

- Invited Speaker, 2010 Australian Vascular Biology Society Meeting (AVBS), Lorne, Victoria

Dr Vanessa Venturi

National:

- Invited Speaker & Session Chair, 3rd Australasian Vaccines & Immunotherapeutics Development meeting, Melbourne

Editorial Appointments

Prof Beng Chong

- *Thrombosis Journal*, Editorial Board
- *Asia-Pacific Journal of Oncology and Haematology*, Editorial Board

Prof Miles Davenport

- *Journal of Immunology*, Associate Editor

Prof Michael Hickey

- *Microcirculation*, Associate Editor
- *Frontiers in Gastrointestinal Sciences*, Editorial Board

Prof Wendy Jessup

- *Atherosclerosis*, Editorial Board
- *Arteriosclerosis, Thrombosis and Vascular Biology*, Editorial Board
- *Biochimica et Biophysica Acta: Molecular Biology of Lipids*, Editorial Board
- *Essays in Biochemistry*, Editorial Board

Prof Levon Khachigian

- *American Journal of Pathology*, Editorial Board
- *Cardiovascular Pathology*, Editorial Board
- *Current Drug Targets: Cardiovascular and Haematological Disorders*, Editorial Board

- *Endothelium*, Associate Editor
- *International Journal of Molecular Medicine*, Editorial Board
- *Journal of Cardiothoracic-Renal Research*, Editorial Board
- *Open Cardiovascular Medicine Journal*, Editorial Board

Prof Leonard Kritharides

- *Atherosclerosis*, Editorial Board
- *Research Reports in Clinical Cardiology*, Editorial Board
- *Current Clinical Pharmacology*, Editorial Board

Prof Chris Parish

- *Immunology and Cell Biology*, Editor-in-Chief

Prof Roland Stocker

- *Redox Report*, Editorial Board
- *Archives in Biochemistry and Biophysics*, Editorial Board
- *Free Radicals in Biology and Medicine*, Editorial Board
- *Encyclopedia of Dietary Supplements*, Editorial Board
- *Antioxidant Redox Signalling*, Editorial Board

Dr Shane Thomas

- *Clinical Science*, Scientific Advisory Panel
- *International Journal for Tryptophan Research*, Editorial Board

External Policy and Research Review Committees

Dr Till Böcking

- Member of Royal Australian Chemical Institute, Certified Chemist (MRACICChem)
- Member of Australian Society for Biophysics (ASB)
- Member of Australian Society for Biochemistry and Molecular Biology (ASBMB)
- Member of the Gesellschaft für Biochemie und Molekularbiologie (GBM)

Prof Beng Chong

- NHMRC Project grant assessment panel member 2010
- Member of the Board of St George Medical Research Foundation and Deputy Chair, Scientific Advisory Committee, St George Medical Research Foundation
- Member, Medical & Dental Appointments Committee, St George Hospital, Sydney
- Member of Clinical Council, St George Hospital, Sydney

Prof Miles Davenport

- ARC OzReader (Discovery & Linkage).
- Health Research Council of New Zealand. Member, BioMedical Assessment Committee.
- Member, National Committee for Biomedical Sciences (NCBMS), Australian Academy of Sciences
- Member of the Immune Based Therapies Working Group at the Kirby Institute.

A/Prof Michael Hickey

- MHMRC Grant Review Panel – Immunology
- National Heart Foundation – Reviewer
- National Sciences & Engineering Research Council of Canada – Assessor
- Health & Research Council of New Zealand - Assessor

A/Prof Katharina Gaus

- Member of the organising committee for the inaugural BMIF Imaging symposium.
- Member of the Australian Advisory Board of the Leica Scientific Forum
- Member of the NHMRC Grant Review Panel
- Arc OZReader
- Member of the Postgraduate Review Committee of the Faculty of Medicine UNSW.

Dr Mark Hulett

- Panel member, NHMRC Career Development Awards
- ASMR Policy Advisory Committee

Prof Wendy Jessup

- Member of Board of Governors, Heart Research Institute, Sydney.
- Heart Foundation of Australia, Fellowships Panel
- NHMRC Fellowships Interview Panel

Dr Mary Kavurma

- Australian Society for Medical Research
- Australian Vascular Biology Society
- Australian Atherosclerosis Society
- Associate Member - Australian Institute of Policy and Science
- Member, Australian Vascular Biology Society Committee
- Convenor – Australian Society for Medical Research NSW Committee
- CSIRO, Scientists in Schools Outreach Program (Oatley Primary School)
- Heart Foundation Biomed-Postgraduate Scholarships Committee
- Australian Institute of Policy and Science – Tall Poppy Program

Prof Levon Khachigian

- Member, NHMRC Australia Fellowship Review Panel (Round Five)
- Assessor, Senior Clinical Research Fellowship, Queensland Government Office of Health & Medical Research
- Assessor, Qatar National Research Fund
- Chair, Postgraduate Review Panel (D), School of Medical Sciences, UNSW
- Member, Board of the Lowy Cancer Research Centre, UNSW
- Member, Faculty Executive Group, Faculty of Medicine, UNSW
- Member, Eureka Prize for Scientific Research, The Australian Museum
- Member, Scientific Advisory Committee, North Shore Heart Research Foundation, Sydney

- Member, Ambassadorial Advisory Council, Business Events Sydney
- Panel Member, RGMS Improvements Workshop, National Association of NHMRC Research Fellows (NARF), Sydney
- Address to the Federal Government's Social Policy Committee, Parliament House, Canberra
- Member, Medical Research Hub Liaison Group, NSW Government
- Member, Management Board, Collaboration for Thrombosis and Bleeding Disorders Research, St George Hospital, Kogarah
- Member, NSW Cardiovascular Research Network

Prof Leonard Kritharides

- Member, Heart Foundation of Australia (NSW)

Prof Chris Parish

- Council Member, The International Union of Immunological Societies (IUIS)
- Founding Member, World AllergoOncology Task Force (Vienna- based)
- Committee Member, Medical Research Advisory, Australian Cancer Research Foundation
- Member, Melbourne International Congress of Immunology 2016 Bid Committee

Prof Roland Stocker

- Heart Foundation of Australia, Grant Review Panel Member
- Vice-President, Swiss Australian Academic Network
- Member, The Bosch Institute Executive Leadership Group.
- Member, The Linus Pauling Institute Prize for Health Research Selection Committee.
- International Fellow, Council on Arteriosclerosis, Thrombosis and Vascular Biology of the American Heart Association.

- Executive Committee Member, International Coenzyme Q10 Association.

Dr Shane Thomas

- Member, NHMRC Grant Review Panel (Cardiovascular/Renal/Diabetes)
- Member, National Heart Foundation Postgraduate Scholarships Assessment Panel

Scientific Conference Organisation

Dr Till Böcking

- Biomedical Imaging Symposium “From seeing to believing: Quantitative Microscopy” Sydney, 24th September 2010

Prof Miles Davenport

- Member, Melbourne International Congress of Immunology 2016 Bid Committee

A/Prof Michael Hickey

- Australian Health & Medical Research Congress, Melbourne, 2010 – Chair, Program Committee
- 18th Australian Vascular Biology Society Annual meeting, Lorne, September 2010, Member, Local Organising Committee

Dr Mark Hulett

- Organising Committee, 4th Australian Health and Medical Research Congress, Brisbane

Prof Levon Khachigian

- Member, Scientific Program Committee, The Lowy International Cancer Symposium “Discovering

Cancer Therapeutics”, ACRF Drug Discovery Centre & Lowy Cancer Research Centre, Sydney, 16-18 May, 2010

- Member, Scientific Advisory Board, 16th International Vascular Biology Meeting, UCLA, Los Angeles, June, 2010
- Member, Scientific Program Committee, 3rd Australia-China Biomedical Research Conference, Melbourne, 2011
- Member, Scientific Advisory Committee, Australian Vascular Biology Society, Bowral Southern Highlands, NSW, 2011

Prof Chris Parish

- Member, Melbourne International Congress of Immunology 2016 Bid Committee

Prof Roland Stocker

- Chairman, Organising Committee, 8th International Congress on Heme Oxygenases (Sydney 2013)

Society Office Bearers

Prof Levon Khachigian

- Director, North Shore Heart Research Foundation
- Company Director, Vascular Biology Limited
- Member, Education Committee of the Australian Vascular Biology Society

Prof Miles Davenport

- President, Australasian Society for Immunology

A/Prof Katharina Gaus

- Treasurer, Australian and New Zealand Society for Cell and Developmental Biology

A/Prof Michael Hickey

- International Member, Liaison Committee, The Microcirculatory Society (USA)
- President, Australian & New Zealand Microcirculation Society

Prof Beng Chong

- Co-chair, Platelet Immunology Subcommittee, International Society of Thrombosis and Haemostasis.
- Vice-President, Australian Bid Committee, International Society of Thrombosis and Haemostasis.

Seminar Program 2010

Lily Vardimon – ‘A novel mechanism for regulation of the proto-oncogene c-Jun in normal and malignant cells’

Paul Timpson – ‘Imaging cancer cell invasion in live animals in real time’

Chris Parish – ‘The role of heparanase and heparan sulfate in health and disease’

Alan Perelson – ‘Modeling HCV Infection and treatment: How viral dynamics gives insights into HCV biology and treatment’

Victar Hsieh – ‘Cholesterol-dependent post-translational control of ABCG1 and ABCA1 expression’

Nicola Chapman – ‘Venous thromboembolism prevention – what doctors think and why it isn’t implemented’

Mohammed Freewan – ‘The selenazal drug ebselen potently inhibits indoleamine 2,3-dioxygenase by targeting enzyme cysteine residues’

Kristine Malabanan – ‘Activation transcription factor-4: a novel regulator of wound repair mechanisms, through Tenascin C transcriptional control’

Jeffrey Chan – ‘TRAIL Promotes VSMC Proliferation and Neointima Formation In A FGF-2, Sp1 and NFκB-Dependent Manner’

Ning Zhang – ‘Transcriptional regulation of PDGF-receptor-alpha by TNF-alpha is c-Fos/IRF-1 dependent’

Diako Ebrahimi – ‘Footprint of the host immune system on the pathogen genome’

Hong Cai – ‘Dz13 targeting C-Jun inhibited skin cancer growth in both immunodeficient and immunocompetent syngeneic mice’

Margaret Morris – ‘Cardiovascular and metabolic effects of maternal obesity – opportunities for intervention’

Thuan Thai – ‘Endothelial-transcytosed myeloperoxidase activates endothelial nitric oxide synthase by inducing redox cell signalling pathways’

Mary Kavurma – ‘The role of TRAIL in CVD’

Jian-Mei Li – ‘Role of RZR-alpha in Smooth Muscle Cell Growth and Neointimal Hyperplasia’

Nicholas Proschogo – ‘Lipid Analysis of Phagosomal Membranes’

Martin Ng – ‘New directions in coronary revascularisation: from therapeutic angiogenesis to tissue engineering’

Sian Cartland – ‘The effect of cholesterol on cell phenotype and migration’

Feng Yan – ‘Impaired megakaryocyte and proplatelet production by antibodies from quinine induced thrombocytopaenia patients’

Daniel Chan – ‘Modelling host resistance in SIV infection’

Paulus Mrass – ‘A view to killer cell migration and interaction within live tumors by two photon microscopy’

Macarena Rodriguez – ‘The structure-function relationship of membrane domains in endothelial cells’

Tim Schlub – ‘Kinetics of the NK cell immune response’

Donna Dinnes – ‘Rab2A participates in the trafficking and secretion of apolipoprotein E’

Amanda Yeung – ‘West Nile virus induces indoleamine 2,3-dioxygenase in human monocyte-derived macrophages’

Robert Lindeman & Michael Buckley – ‘POWH Haematology / Genetics update’

Deborah Cromer – ‘How fast could HIV change gene frequencies in the human population?’

Sabine Wimmer-Kleikamp – ‘Imaging of cell surface receptor activation and redox signalling’

Cecilia Chan – ‘Dz13 suppresses retinal neovascularization in murine retinopathy of prematurity model via c-Jun’

David Williamson – ‘High resolution imaging of LAT at the immunological synapse’

Belinda di Bartolo – ‘The role of TRAIL in advanced atherosclerosis’

Jinbiao Chen – ‘Nuclear import of early growth response is mediated by importin-7 and the novel translocation signal serine-proline-serine’

Fernando Santiago – ‘Generation of Phospho-specific antibody to Egr-1’

Dylan Owen – ‘Quantitative measurements of membrane protein diffusion in live cells’

Mi-Jung Kim – ‘Understanding the mechanism of ATP-binding cassette A1 (ABCA1)-mediated cholesterol efflux’

Till Böcking – ‘Watching a molecular chaperone in action: Mechanism of clathrin coat disassembly’

Lei Dang – ‘Role of mitochondria in vascular endothelial growth factor signalling in endothelial cells’

Simon Liang – ‘Proliferation, differentiation and migration of SCA1+/CD31+ cardiac side population cells, an endothelial progenitor in vitro and in vivo’

Xianming Du – ‘Profiling of high density lipoprotein’

Lionel Lourenco-Dias – ‘Novel transcriptional Factor AP-1 inhibitors’

Nor Saadah binti Md Azahri – ‘PDGF-BB-induced TRAIL expression in VSMC involves Sp1 and acetylation of histone 3’

Galina Schevzov – ‘Regulation of cell proliferation by a specific population of actin filaments’

Mary Myerscough – ‘Atherosclerosis and mathematics – an unlikely combination?’

Mykola Pinkevych – ‘Understanding natural immunity to malaria’

Matthew Traini – ‘Characterisation of a novel cholesterol responsive gene’

Jose Perdomo – ‘Quinine-induced thrombocytopenia: drug-dependent antibodies inhibit megakaryocyte and proplatelet production’

Siti Ngalim – ‘Surface chemistry and its relation with cell migration’

CVR Management and Advisory Committees

Management Board

Dr Kelvin Hopper (Chair)
Prof Terry Campbell (UNSW)
Prof Ian Dawes (UNSW)
A/Prof Roger Wilson (SESIAHS)
Ms Cath Whitehurst (SESIAHS)
Prof Ben Freedman (University of Sydney)
Prof Colin Chesterman (Ex Officio)
One vacancy

The Management Board met in 2010 on 25th March, 11th August and 3rd December.

Scientific Advisory Committee

Prof Robert Graham FAA (Victor Chang Cardiac Research Institute)
Prof Mathew Vadas (Centenary Institute)
Prof Robert Baxter FAA (Kolling Institute)

The CVR was reviewed on 7th October 2010.