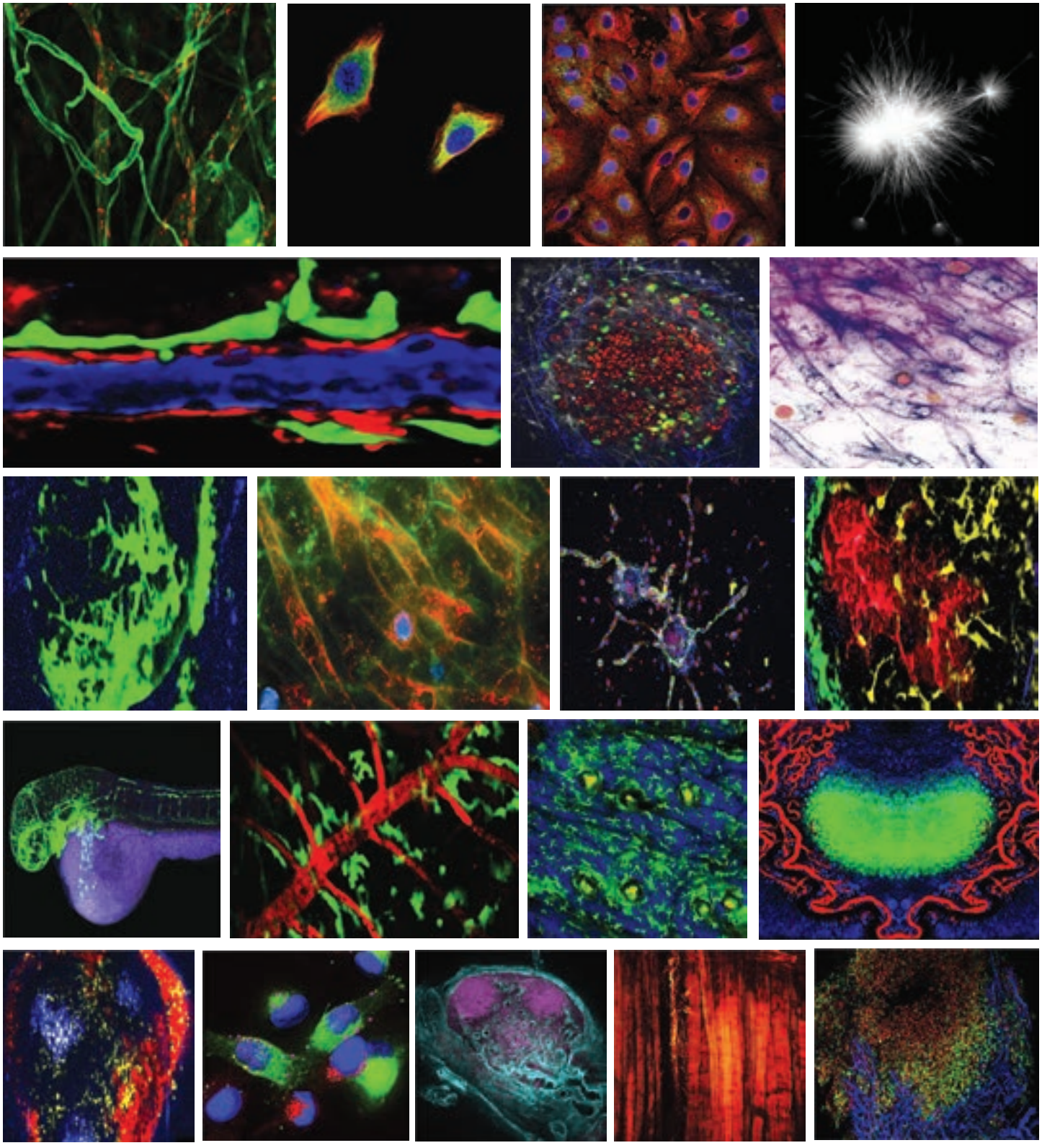
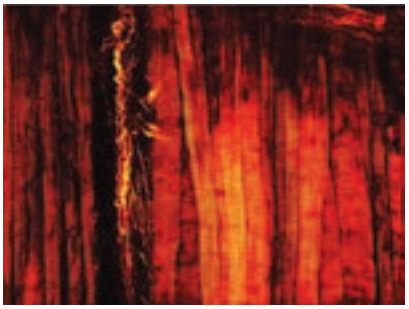
Centenary Institute research for life

Annual Report 2011



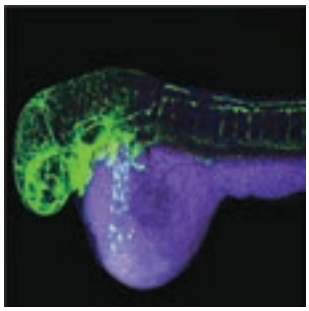
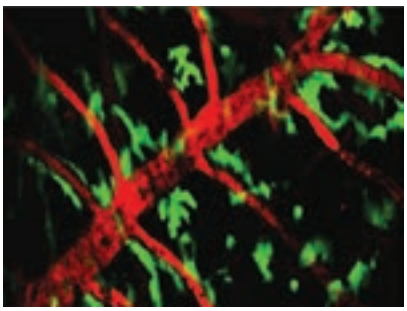
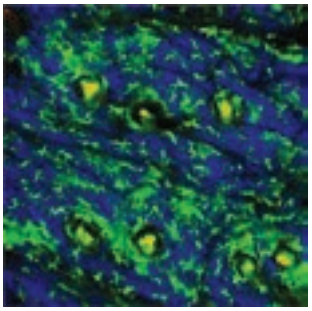
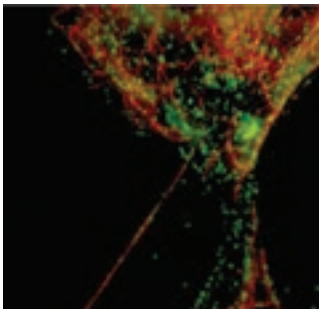
The Centenary Institute Annual Report 2011



The Centenary Institute is a world class medical research facility focusing on cancer, cardiovascular and infectious diseases. It is located between Royal Prince Alfred Hospital and the University of Sydney, and forms a critical point of contact and intellectual engagement between the Hospital and the University.

Our History

The Centenary Institute opened in 1989, under the stewardship of its founding Director Professor Anthony Basten, to commemorate the centenaries of the University of Sydney Medical School and the Royal Prince Alfred Hospital. Formal working relationships with the University and Hospital have provided unique opportunities for students to become involved both in research and the translation of basic discoveries into clinical practice, an area in which the Institute has become a leader.

Chairman's Report

The Honourable Michael Egan

The Honourable Michael Egan

"There are two achievements of the Centenary Institute of which I am particularly proud. The first is that Centenary is now well established as one of the leading medical research institutes in Australia and a vital part of the Royal Prince Alfred Hospital-University of Sydney campus—an important and functional link between hospital and university, in fact."

For example, the NSW Advanced Cytometry Facility, established jointly by the University of Sydney and the Centenary Institute and headed by Dr Adrian Smith, leads the world in cell measurement capability. It now has the world's first ten-laser cell analyser and ten-laser cell sorter. The former can measure cell properties that no other flow cytometer can; the latter can sort cells more finely than any other machine.

And Royal Prince Alfred and Centenary are both integral to Professor Chris Semsarian's three-year study of sudden cardiac death in the young, which has been financed by the National Health and Medical Research Council (NHMRC). This program is typically practical, focusing on understanding the causes of this devastating condition, and initiating and evaluating preventive measures and screening for susceptibility.

Second, the Institute is now reaching out nationally and internationally—nationally with the inauguration of the annual Centenary Lawrence Creative Prize and internationally through our work on tuberculosis in Asia.

The Lawrence Prize—named for Neil Lawrence, inaugural Chairman of The Centenary Institute Foundation—is awarded to a researcher with fewer than eight years as a postdoctoral fellow under his or her belt, for originality and hard work.

Announcement of the prize led to applications from more than 30 of the nation's most talented scientists. The stellar international judging panel included immunologist Professor Sir Marc Feldman of Oxford University and Professor Ian Frazer, a former winner of the Prime Minister's Prize for Science. It was won by a brilliant young Melbourne cancer researcher, Dr Marie-Liesse Asselin-Labat.

We are proud to have been a catalyst in this new national event and thank our generous major sponsors including FOXTEL, Mindshare and the STW group, and supporting sponsors The Australian, UBS, Deloitte and Crosby | Textor.

About two billion people worldwide are harbouring the tuberculosis bacterium, and each year more than one million die of the disease it causes—about three people every minute. Clearly, TB is still a serious problem.

In keeping with our tradition of forming a bridge between laboratory research and clinical treatment, the Institute's Dr Magda Ellis is now searching the genomes of rural China for genetic clues that may one day lead to new targets for TB treatments or vaccines. The work is financed with an NHMRC grant and carried out with assistance from Britain's Wellcome Trust and Chinese colleagues.

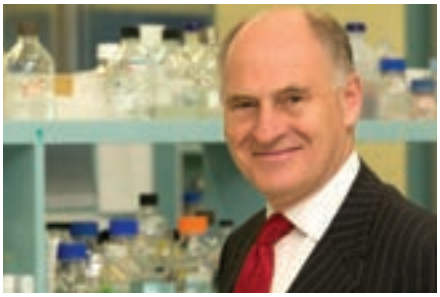
A TB project in Vietnam is even further down the track. Dr Greg Fox has moved to Ho Chi Minh City with his young family to study the genetic differences between TB patients and family members free of the disease. The work, undertaken in collaboration with researchers in Vietnam's National Tuberculosis Program, is going stunningly well and a delegation of senior scientists from Vietnam recently visited the Centenary Institute to present their research and discuss the next phase of their campaign against TB.

I have been excited and inspired by the emergence of the Young Centenary Foundation. Here is a group of young people who recognise that they are not totally bullet-proof, and wish to do something positive about it. They are putting their special skills and talents—energy, facility with computers, mobile phones and social media, even their ability to organise great parties—into raising money for the work of the Institute. I commend them for it.

I wish to thank all the members of the Board, as well as the Foundation Trustees, for their hard work. We all know that without your efforts there would be no Institute or resources for its operation. In particular, I want to commend the efforts of those on the Board sub-committees—Risk and Audit, Commercialisation, and Investment. This Annual Report is as much a celebration of their success, as that of the researchers. Both are integral to continued wellbeing of a great institution.

Executive Director's Report

Professor Mathew Vadas AO



Faculty, Executive Director, Professor Mathew Vadas AO

It is a very special time for medical research—particularly for an Institute such as Centenary, where we see the clinical benefits of basic research every day. The dreams we had of new treatments for disease some 20 years ago, one by one, are becoming realities.

We now have new cancer therapies, for instance, which target molecules in cancer cells that drive tumour growth, and new biological therapies to control inflammatory diseases, such as arthritis and psoriasis, built on the studies which recognised Tumour Necrosis Factor as a key player in their development.

This is significant not only for patients who are living longer and whose quality of life has improved, but also because it gives medical researchers the confidence to dream. There is no more powerful impetus to creativity than seeing the difference it can make to people's lives.

And there is no more powerful instrument of invention than imagination. It is time to ensure we treasure this finely honed talent. At Centenary we have initiated the Lawrence Creative Prize that recognises this talent not only within our Institute but nationally (see Chairman's report)!

At all levels of Australian government there is increasing recognition of the importance of medical research to the fabric of our society. Centenary was delighted to welcome the Hon Tania Plibersek a few days after she took on her new portfolio of Minister for Health. The Hon Jillian Skinner, Minister for Health and Medical Research in the NSW Government, was the Guest of Honour at our Annual General Meeting last year. Both levels of government have instituted major reviews of medical research, which will guide and prioritise our research strategies for the next 10 years.

The Centenary Institute is unique, because it connects dreams with reality. Our Faculty, many of whom are clinicians, understand reality because they are connected to the real problems of patients. Our scientists, who have expertise in the basic aspects of medical enquiry, provide the innovation and dreams needed for discoveries. In this report you will find many examples of how we go about this exciting journey.

The challenge for the Institute is to make sure it invests wisely in the future. One of the most important problems facing Australia, and indeed the world, is a rapidly ageing population. But we do not understand ageing at all well. For this reason Centenary has started a new laboratory devoted to the study of ageing, under the direction of Dr Masaomi Kato. Dr Kato, who was recruited from Yale, is discovering the genes and gene-regulators that govern the process of ageing. His dream is that ageing, like cancer, will eventually be able to be treated with specific drugs capable of reversing the process.

Many people contribute to our success. This year, however, I especially want to thank our science support team, whose work underpins everything that our scientists do. And with their help, the Institute had a 56% success rate in its NHMRC grant applications this year. The average success rate is about 20%.

Congratulations to Professor Chris Semsarian who was honoured in a new NHMRC publication *10 of the Best Research Projects 2010*; to Professor Jennifer Gamble who received the 2011 National Heart Foundation Ross Hohnen Award, and has become the inaugural Wenkart Chair of Endothelium at the University of Sydney; and to Professor John Rasko who won the 50th annual Eric Susman Prize of the Royal Australasian College of Physicians for his work in improving bone marrow transplants.

Finally, I welcome you to our new-look Annual Report. Because our research connects dreams with reality, we want to ensure that it does not stay locked inside the Institute. One way of assisting this process is to interest the community in what we doing, and invite people to join us on our exciting journey.

So this year, we have decided to make our Annual Report more readable. After all, at the Centenary Institute we have great stories to tell of how, with the support of the community, our dreaming can improve life for everyone.

The Centenary Institute is unique, because it connects dreams with reality. Our Faculty, many of whom are clinicians, understand reality because they are connected to the real problems of patients.

Board of Governors

The Honourable Michael Egan (Chairman)

The Hon Michael Egan (Chairman)

Reappointed Chair in October 2008
Mr Egan, a former Treasurer of NSW (1995-2005), is Chancellor of Macquarie University, Chairman of the Australian Fisheries Management Authority Commission, and a member of the NHMRC. During his 25-year parliamentary career Mr Egan held several ministerial positions.

Mr John Samaha (Deputy Chairman)

Appointed Governor in 2003
Mr Samaha is a leading Sydney litigation lawyer. Before establishing his own specialist practice in 2009, he was a senior partner at Mallesons Stephen Jaques, where he acted for a wide range of institutional and corporate clients, predominantly industry sector leaders.

Dr Teresa Anderson

Appointed Governor in 2007
Dr Anderson is Chief Executive of the Sydney Local Health District and has over 30 years' experience as a clinician and manager in the public health system, including General Manager, Liverpool Hospital and Director, Clinical Operations, Former Sydney South West Area Health Service. Dr Anderson is a Board member of the Ingham Health Research Institute, Anzac Research Institute, Centre for Primary Health Care and Equity, and Inner West Sydney Medicare Local.

Mr Ken Cahill

Appointed Governor in 2009
Mr Cahill is the Executive Director of Royal Prince Alfred Hospital and was previously General Manager of the Central Coast Health Service. He was Chief Radiographer at Royal Prince Alfred Hospital from 1990 to 1997. Mr Cahill has a Master of Public Health from the University of Western Sydney.

Mr Joseph Carrozzi

Appointed Governor in 2008
Mr Carrozzi is a National Managing Partner at accounting firm PricewaterhouseCoopers, managing relationships with some of the largest organisations in Australia. He is admitted as a Barrister at Law in NSW, a member of the Institute of Chartered Accountants in Australia and a Fellow of the Tax Institute of Australia. He is also on the Board of the Italian Chamber of Commerce and Industry in Australia.

Mr Alastair Davidson

Appointed Governor in 2004
Mr Davidson has held executive positions in the banking and financial services industry for 24 years in the UK, US and Australia. He is Managing Director of Aurora Funds Management in Sydney. Prior to this, Mr Davidson was at Citibank, Australia, in Sydney, where he spent eight years as co-head of its new product group. He is also a non-executive Director of Biotech Capital, an ASX-listed investment company.

Professor John Horvath AO

Appointed Governor in 2007
Professor Horvath was the Commonwealth Chief Medical Officer from 2003 to 2009 and continues to advise the Department of Health & Ageing. He holds the position of Honorary Professor of Medicine at the University of Sydney. Professor Horvath is a Fellow of the Royal Australasian College of Physicians, a member of the Council of the NHMRC and Chairman of the Healthcare Committee.

Mr Graham Kelly

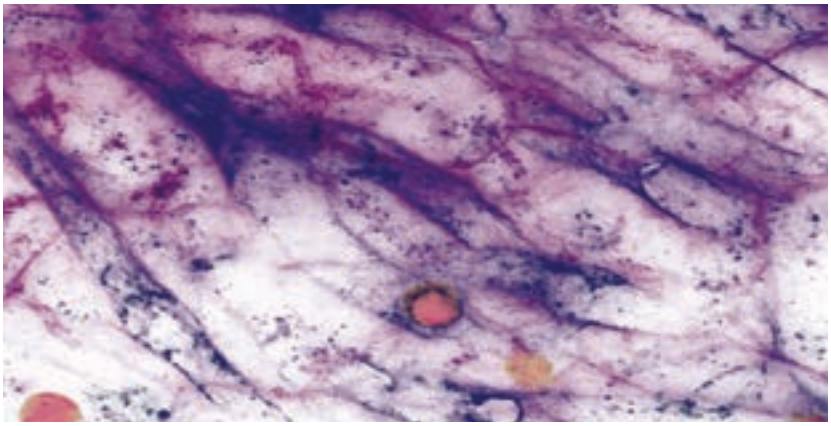
Appointed Governor in 2006
Mr Kelly is non-executive Chairman of Tishman Speyer Office Trust and other companies and a non-executive Director of several more. He is a consultant to the Freehills law firm, and was until recently the Inspector of the Independent Commission Against Corruption and a Director of the Medical Research and Compensation Foundation.

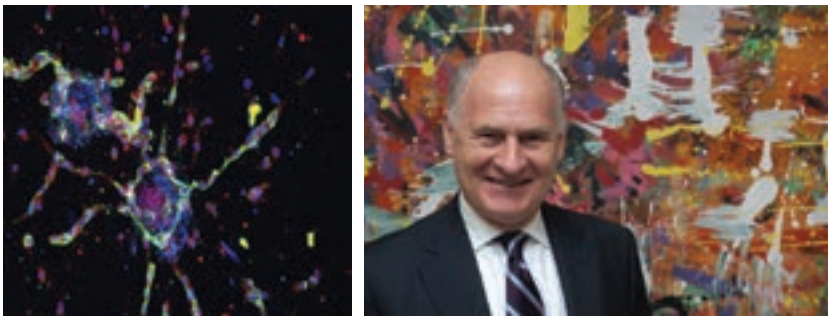
Mr Neil Lawrence

Appointed Governor in 2006
Mr Lawrence is the founder of Lawrence Creative Strategy, as well as the Executive Creative Director of STW, Australia's largest communications group. He was recognised as Australian Marketer of the Year in 2007 for the Australian Labor Party's *Kevin 07* advertising campaign. Mr Lawrence has represented Australia as the Chairman of Judges at the Irish International Advertising awards and on the film jury at Cannes.

Dr Susan Pond AM

Appointed Governor in 2009
Dr Pond was Chairman and Managing Director of Johnson & Johnson Research Pty Limited from 2003 to 2009. A specialist physician, Dr Pond has held positions at the University of California, San Francisco, and the University of Queensland. She has also been Chairman of the Australian Drug Evaluation Committee and non-executive Director and Chairman of AusBiotech Limited, and now serves on the board of Commercialisation Australia.





From top left to right: Mr John Samaha (Deputy Chairman); Dr Teresa Anderson; Professor John Horvath AO; Mr Graham Kelly; Mr Neil Lawrence; Professor Bruce Robinson AM; Image by Frederic Sierro, Liver Immunology; Mr Joseph Carrozzi; Dr Susan Pond AM; Mr Ken Cahill; Mr Alastair Davidson; Ms Josephine Sukkar; Image by Garry Chang, PhD Scholar, Vascular Biology; Professor Mathew Vadas AO

Professor Bruce Robinson AM

Appointed Governor in 2007
Professor Robinson is Dean of the Faculty of Medicine, University of Sydney, and Head of the Cancer Genetic Laboratory at the Kolling Institute. In 2003, he was awarded the Daiichi Prize by the Asia and Oceania Thyroid Association. Professor Robinson is the Founding Chairman of the Hoc Mai Australia Vietnam Medical Foundation and a Fellow of the Australian Institute of Company Directors.

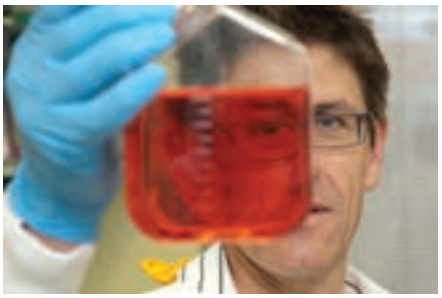
Ms Josephine Sukkar

Appointed Governor in 2011
Ms Sukkar is co-owner and Principal of Buildcorp Australia Pty Ltd and a Director at The Trust Company. She is an active and keen philanthropist who is Co-President at YWCA, NSW, a Director of Opera Australia and of the University Football Club Foundation, and involved with other community and charitable organisations.

Professor Mathew Vadas AO

Appointed Governor in 2007
Professor Vadas followed his medical training with a PhD at the Walter and Eliza Hall Institute in Melbourne and postdoctoral work at Harvard. He then built up a significant research enterprise in Adelaide, where he was the Inaugural Director of the Hanson Centre for Cancer Research (now Hanson Institute). He serves on the Board of Governors of the Sydney Institute of Health and Medical Research.

Research Perspective



Associate Faculty, Dr Chris Jolly
DNA Repair

"The Centenary Institute is dedicated to helping all Australians live longer, healthier lives. Its researchers work across a diverse spectrum of scientific investigation focusing on three areas—cancer, cardiovascular disease and infectious diseases."

Faculty, Dr Patrick Bertolino, Dr Eamon Breen, Research Officer, Bharvi Maneck, Research Assistant, Claire McGuffog,Technical Officer, Liver Immunology

CANCER

Half of all Australians will be diagnosed with cancer before the age of 85. So cancer remains a major concern for most people.

While cancer survival rates have certainly improved through screening, early detection and better treatment, there is still a long way to go.

To overcome the immense challenges presented by cancer, the Centenary Institute is working hard to answer four fundamental research questions:

- What causes cancer?
- Why does cancer spread?
- Why does cancer regress?
- How can we improve cancer treatment?

CARDIOVASCULAR DISEASE

Cardiovascular disease accounts for over a third of all deaths in Australia. More than 45,000 Australians lose their lives to a cardiovascular disease each year. While death rates have declined in the past decade, more than 3 million Australians are still affected each year by cardiovascular disease.

To reduce the impact of cardiovascular disease on Australian families, the Centenary Institute is seeking answers to three crucial questions:

- What are the genetic causes of heart disease?
- How do signals that communicate between and within cells go awry, leading to disease?
- How does blood vessel development proliferate unnecessarily, causing cardiovascular disease?

INFECTIOUS DISEASES

Tuberculosis (TB) is a worldwide pandemic—more than two billion people are infected and almost 1.7 million people die each year from the disease.

Chronic liver damage affects up to 20% of our population. It has many causes, including infections with the hepatitis B and C viruses. Liver cancer is often caused by chronic liver damage and is one of the fastest growing cancers in our community.

The Centenary Institute is hoping to decrease the impact of these infectious diseases on the community by answering these four questions:

- Why does TB infection progress to active disease?
- How can we improve vaccines against TB?
- How does liver damage cause liver failure or liver cancer?
- What properties of the liver result in successful organ transplantation?

Vascular Biology: Piping out good health

Faculty, Professor Jennifer Gamble, Vascular Biology and Executive Director & Faculty, Professor Mathew Vadas

We each have within us some 80,000 km of pipelines that carry the essential supplies needed by cells to all parts of our body. The endothelium that lines this network of blood vessels is essentially a hidden organ in the body weighing about a kilogram. But the workings of this internal transport infrastructure are largely unknown.

You prick your finger on a rose thorn—within the hour the wound is inflamed and itching as your body mobilises to fight infection. That's the endothelium in action.

These same endothelial cells are implicated when things go wrong, in atherosclerosis or hardening of the arteries, for instance; in the complications associated with diabetes; or in ageing. In addition, tumours need new blood vessels in order to grow. So they must stimulate endothelial cells to construct these vessels.

We hope that, over the next decade or two, we will be able to understand and control the endothelium in disease conditions—especially those associated with ageing.

The goal of the Vascular Biology research group is to be able to manipulate blood vessels as an avenue of disease control. For instance, there is an increase in heart disease with age. Understanding what age means to the functioning of endothelial cells will potentially allow us to identify individuals at greatest risk of heart disease and to develop new treatments.

Many diseases are associated with leaky blood vessels and this leakiness can exacerbate the condition. Understanding why these blood vessels become leaky may allow us to develop new therapies targeting this aspect of disease.

— Professor Jennifer Gamble & Professor Mathew Vadas AO

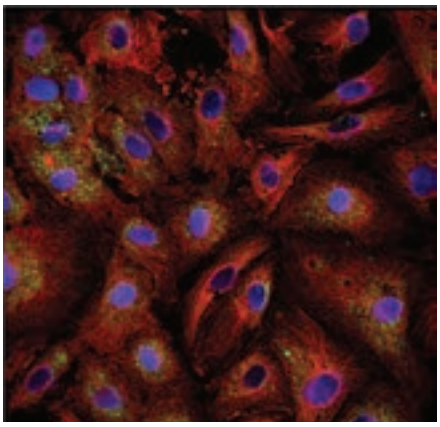
RESEARCH PROGRAM

The Vascular Biology program is focused on understanding how mature endothelial cells maintain their anti-inflammatory and non-leaky surfaces.

We also want to know about the signals essential for promoting the growth of new blood vessels. Our studies can provide insight into the changes that occur in the vessels with ageing and disease. We have already identified the gene SENEX as being important in signalling ageing and decline in endothelial cells.

The program comprises four major projects:

- unravelling the structure of the SENEX protein, and the molecular events that govern its activity, regulation and interactions
- understanding how SENEX regulates inflammation
- understanding how small genetic regulatory elements, known as microRNAs, control endothelial cell functions
- developing drugs to inhibit blood vessel permeability.



Top to bottom: PhD Scholar, Garry Chang, Research Assistant, Jia Li, Research Officer, Dr Joshua Moses; Image: Michael Lovelace & Paul Coleman

Highlights 2011

- Inaugurating the Wenkart Chair of Endothelium at the Centenary Institute and the University of Sydney.

T Cell Biology: Discovering why so many people have puffers

Faculty, Professor Barbara Fazekas de St Groth, T Cell Biology

"The number of people with autoimmune and allergic diseases, such as asthma, hay fever and type 1 diabetes, has more than doubled in the past 20 years. Such a rapid rise in these immune system-mediated diseases must have been caused by changes in environmental factors, because the frequencies of genes within populations take generations to change."

The T Cell Biology research group—which concentrates on the network managers of the immune system, T cells—aims to understand how the immune system usually prevents these diseases and which environmental factors are required to maintain normal immune function.

One of the theories that seek to explain this epidemic of immune disease is known as the hygiene hypothesis. This suggests that too much cleanliness in early life can cause disease because it reduces crucially important contact between the immune system and microorganisms.

Recent evidence points to the harmless microorganisms that populate our gut and skin, collectively termed the 'human microbiome', as an important regulator of immune function via a small but crucial population of T cells called regulatory T cells (T regs).

We are investigating how T regs influence immune function in humans and in animal models, particularly how they control the threshold of stimulation at which the immune system becomes activated.

Allergic reactions and autoimmune diseases arise when this threshold is set too low.

We have discovered a set of peacekeeper cells—immune cells in the outer layers of our skin that stop us from attacking friendly bacteria. Known as Langerhans cells, they have resisted every attempt by us to get them to generate an immune response. The work could open the way to new therapeutic options for immune-mediated diseases such as inflammatory bowel disease, of which Australia has some of the world's highest rates.

But the immune system is a layered defence¬—and the next layer of skin has different kinds of immune cells, which program ongoing responses against bacteria. If bacteria penetrate deeply enough to meet these cells, the immune response will kill them.

— Professor Barbara Fazekas de St Groth

RESEARCH PROGRAM

The T Cell Biology research group has been using mice as models to investigate how T regs work.

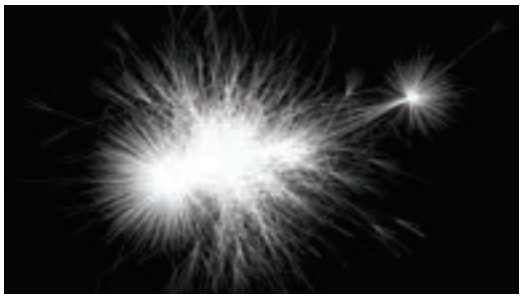
Mice lacking T reg cells are particularly prone to autoimmune diseases and allergies. We have shown that this tendency can be reversed by administering T regs, and that the crucial effect of T reg administration is to control the levels of stimulatory molecules that trigger the immune system into action.

In a mouse asthma model, we have shown that administering T regs prevents allergic sensitisation. But once the mouse has an established allergy, T regs are no longer effective in stopping acute asthma attacks. In organ transplantation, T regs can prevent rejection but, once again, they must be administered before the organ graft is performed.

Conversely, T regs can hinder the natural immune response to tumours. We have shown that otherwise fatal tumours can be killed by T cells if the T regs are inactivated.

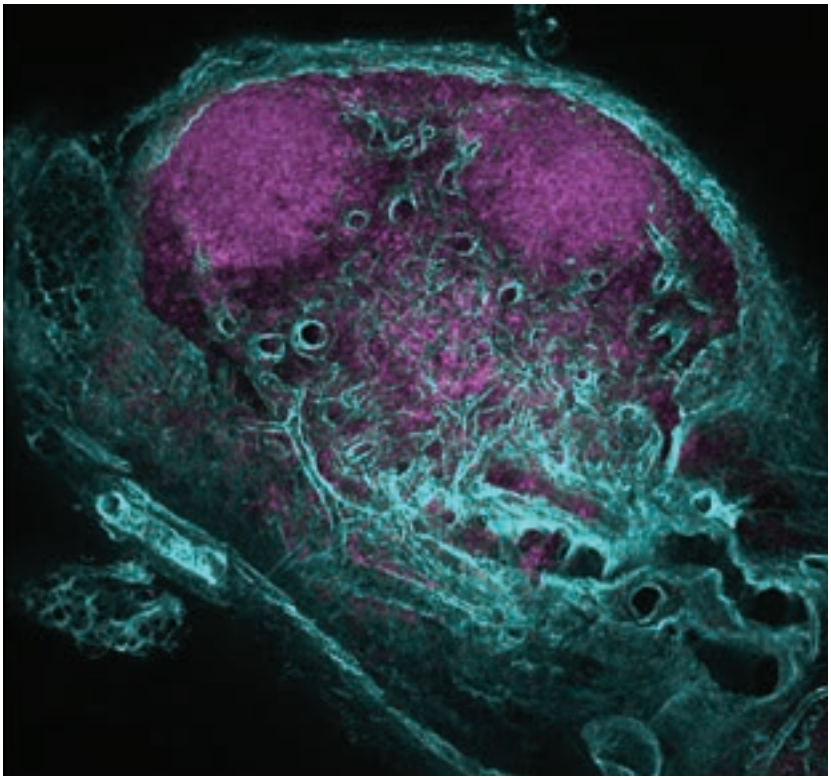
These animal studies have indicated that manipulation of T regs is likely to be more effective for prevention rather than treatment of immune system-mediated disease.

To investigate the contribution of T reg abnormalities to human disease, we are pursuing two different approaches. First, the abnormalities in patients with a range of diseases, including inflammatory bowel disease, multiple sclerosis, Graves' disease, psoriasis and lupus, are being studied in detail. Second, we are monitoring the differences in T regs between human



David Hancock, PhD Scholar, T Cell Biology. "The spark of life" is the winner of the 2011-2012 Centenary Institute Scientific Image Prize

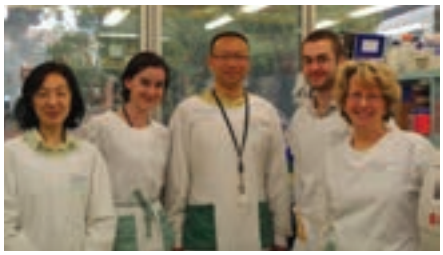
populations living under conditions of high versus low incidence of autoimmune and allergic disease. By correlating these differences with changes in the microbiome in different environments, we will determine which microbiome components are important in maintaining resistance to immune-mediated diseases.



Thomas Guy, PhD Scholar, T Cell Biology

Highlights 2011

- Publishing a paper on Langerhans cells, the peacekeepers of the immune system, in the *Proceedings of the National Academy of Sciences*. This paper shows for the first time that some immune cells are pre-committed to stopping immune responses against friendly bacteria.
- Establishing a new mouse model to investigate the individual and combined contributions of the many different immune system cells (T cells, T regs, B cells, dendritic cells) to the natural anti-tumour response.
- Establishing the first initiative in the world to standardise T reg detection and analysis in clinical settings across multiple sites. This initiative is supported by the Transplantation Society of Australia and New Zealand (TSANZ) Tolerance Working group. It coordinates and teaches methods of conducting flow cytometry analysis of T regs, based on those discovered and used by Professor Barbara Fazekas de St Groth. T reg analysis is a new technology in the immune assessment of renal transplant patients.
- Beginning to study how ageing affects immune responses to influenza vaccination. Professor Barbara Fazekas de St Groth is part of a US consortium that received five years of National Institutes of Health/Broad Agency Announcement funding towards this project.



Top to bottom: Professor Barbara Fazekas de St Groth and team; Senior Research Officer, Dr Elena Shklovskaya, T Cell Biology

Structural Biology: Working to understand cellular bouncers

Associate Faculty, Dr Mika Jormakka, Structural Biology

"Like passport control, cell membranes are an important checkpoint in our bodies. In a very real sense the impact of infection, disease or poisoning depends on what is allowed through cell membranes—in the form of atoms, molecules, viruses and other organic entities. "

Membrane proteins play a critical role in normal cellular processes. Alterations in the function of membrane proteins can cause many human diseases and disorders. A protein's function is determined by its structure or shape. Thus, an intricate understanding of protein structures is a critical objective for biological and pharmaceutical research. By understanding membrane protein anatomy, structure and function, the Structural Biology research group hopes to develop drugs tailored for better outcomes with fewer side effects.

Our long-term aim is to provide high-resolution structures to assist drug development. We want to move away from the trial-and-error process of drug discovery to a process where we first identify a critical structure so we can then design a `perfect' drug to fit. This would potentially provide drugs that hit the target with more precision, reducing unwanted side-effects. Structure-based drug design would also lead to far cheaper drugs and lessen the time from discovery to use in therapy.

To develop precise and detailed models of membrane proteins, the Structural Biology research group uses synchrotron radiation and the technique known as X-ray crystallography. This allows us to visualise the cell's smallest machines (proteins) at the atomic level which, in turn, provides details of how they function and a 3D blueprint to use for structure-based drug design. It's like mapping out the design of a lock so you can generate the matching key, as opposed to a lengthy, imprecise trial-and-error process to find a key that works.

— Dr Mika Jormakka

RESEARCH PROGRAM

Members of the Structural Biology research group are involved in two major research projects.

One is concerned with drug resistance. Specific membrane proteins pump molecules into and out of cells—and they are often the basis of drug resistance, by emptying cells of the compounds used to regulate or poison them. We are focusing our studies on the multi-drug resistance transporters, which are responsible for antibiotic drug resistance in bacteria and chemotherapy drug resistance in cancer patients.

A second major project targets prostate cancer, where the normal balance of absorbing nutrients into the cell is thrown into disarray by increased levels of particular transport proteins. This subsequently allows cancer cells to develop. Of special interest to our group is the increase in leucine transporters, which enable cells to grow rapidly in prostate cancer.

Together with Dr Jeff Holst from the Origins of Cancer research group (within Gene and Stem Cell Therapy), we are conducting structural studies on two transporters found to be important in the development and progression of prostate cancer. Determining the structures of these transporters will provide a platform for designing drugs to regulate them, and thus stop progress of the cancer.

Highlights 2011

- Beginning structural studies of the membrane transporters involved in prostate cancer development and progress, including setting up the infrastructure for membrane protein expression, which has been a major hurdle in the field.
- Initiating drug discovery, in collaboration with Dr Jeff Holst, targeting these transporters.
- Identifying functionally important amino acids allowing us to understand important aspects of the operation of multi-drug transporter NorM, a protein responsible for antibiotic drug resistance in bacteria.
- Determining the structure of the catalytic core of a protein responsible for pumping out chemotherapy drugs from cancer cells. This provides detailed insight to the function and mechanism of the protein.

Signal Transduction: Communication is at the heart of good health

Faculty, Associate Professor Pu Xia, Signal Transduction

Our bodies consist of up to 75 trillion cells, and every one of them must function in a highly cooperative way. So, good communication between cells is essential for good health. Such communication, also known as signal transduction, is conducted by means of the hundreds of thousands of biochemical reactions that make up the specific languages of cells. To decode these languages, or signalling pathways, is a core objective of the Signal Transduction research group.

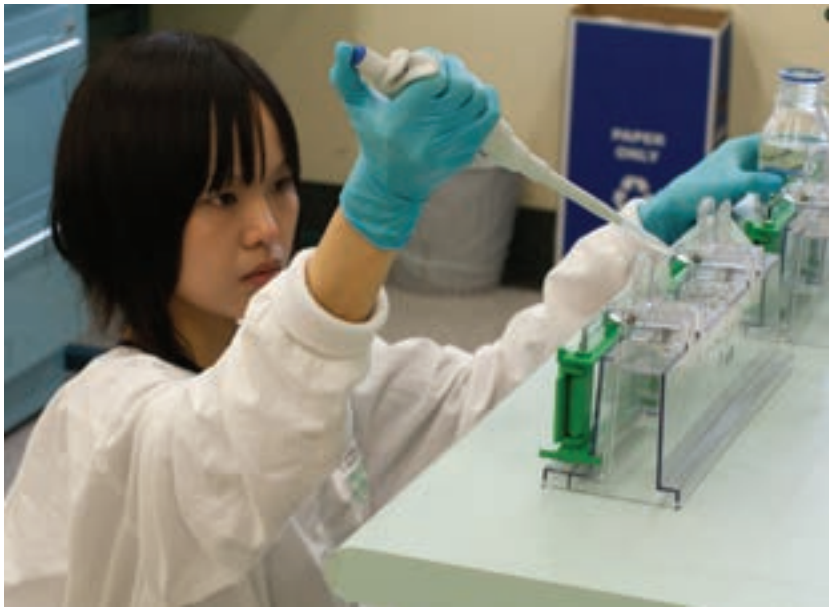
By understanding how cells communicate, researchers can find the faults or switches in the signalling networks that cause or control diseases, such as cancer, diabetes and cardiovascular disorders. This will help identify molecular targets so that we can develop more effective therapies that shut down the disease-causing signals and treat or prevent diseases at their root.

We have identified a key signalling pathway, important for cell survival and growth, built around the enzyme sphingosine kinase (SphK). We found that SphK is often overproduced by cells when they become inflamed or cancerous. Blocking the enzyme with chemical or genetic inhibitors significantly reduces inflammation and slows down or stops cancer cell growth.

The group has also been studying the pancreatic beta cells that produce insulin. Diabetes occurs when beta cells are damaged, and insufficient insulin is produced. Interestingly, we discovered that SphK is used by beta cells as an essential signal for survival under stress, especially in people who are clinically obese.

We are now exploring these findings in clinically relevant settings to develop new drugs to allow us to treat cancer, diabetes and inflammation-associated diseases.

— Associate Professor Pu Xia



PhD Scholar, Mei Li Ng, Signal Transduction

RESEARCH PROGRAM

Liver cancer is the fifth most common cancer in the world, and its prognosis is very poor. Fewer than one patient in 11 survives more than five years after diagnosis of liver cancer.

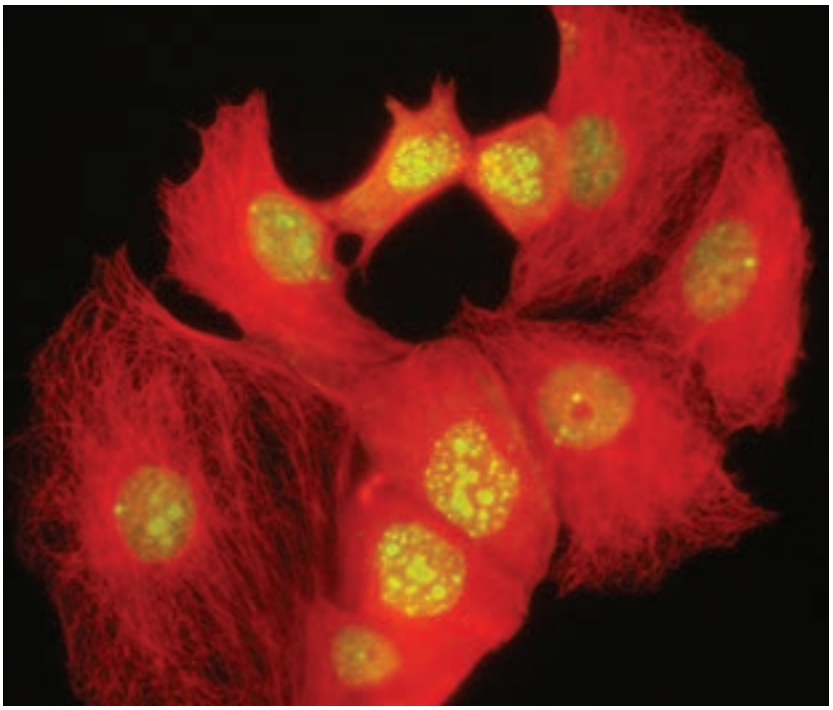
Apart from genetic influences, inflammation is typically the first stage on the path to liver cancer. So, using molecular and genetic tools, the Signal Transduction research group is working with colleagues in the Liver and Vascular Biology research groups to understand this progression and thereby explore new strategies to prevent and treat liver cancer.

Insulin resistance, a condition where the hormone insulin becomes less effective than normal at reducing the level of sugars in the blood, occurs in nearly one in five Australians, and is a common feature of obesity. The liver is a major target of insulin and plays a central role in controlling the metabolism of sugars, fats and proteins. Thus, insulin resistance in the liver is the most important cause of diabetes. At present there is no effective way to prevent or treat liver insulin resistance because the underlying mechanisms are poorly understood. The Signal Transduction research group is investigating how and why insulin resistance takes place in the liver, aiming to find a new way to manage both obesity and diabetes.

Cell suicide, known as apoptosis, of pancreatic beta cells plays a fundamental role in the onset of diabetes. Protecting beta cells against death and rescuing their insulin-making function is emerging as a new strategy for treating diabetes. Another project of the research group is examining how pancreatic beta cells communicate in order to survive, especially under stressful conditions such as high levels of blood sugar or lipids. The researchers are

using mice, specially fed a high-fat diet, to investigate how insulin-producing cells are damaged by obesity, and how such damage can be prevented. This research could help develop a new therapeutic strategy for the prevention and treatment of diabetes.

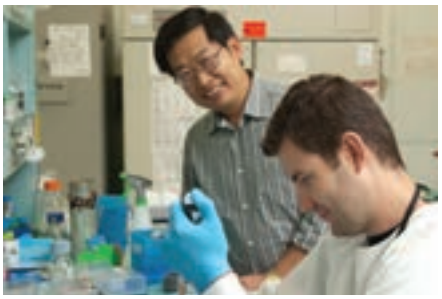
S-nitrosylation is a chemical modification which affects the function of a wide array of proteins. High glucose environments lead to significantly fewer S-nitrosylated proteins. The Signal Transduction research group is investigating the effect of S-nitrosylation on proteins critical to cell movement and survival. Low levels of S-nitrosylation have been implicated in many disease states including cancer and diabetes. The study aims to identify that signalling pathways are disrupted by low S-nitrosylation.



The Kiss, Breast cancer by Research Fellow, Eileen McGowan, Signal Transduction

Highlights 2011

- Uncovering a new signalling mechanism that leads to pancreatic beta-cell death under a stressful condition where cells are exposed to high levels of lipids. Such conditions are often observed in obese people, so the findings could help to create new strategies to prevent diabetes.
- Identifying S1P, a key lipid that is required for pancreatic beta-cell survival under the lipid-induced cellular stress and cell death. This suggests a new molecular target for drug development in prevention and treatment of diabetes.
- Finding that SphK is an important signalling molecule that regulates insulin action in controlling sugar production by the liver. This will help us to understand the molecular mechanisms of insulin resistance in the liver, leading to a new way to fight diabetes.
- Developing a new animal model that mimics obesity-associated inflammation conditions in the human liver. Further investigations using this model will allow us to explore the mechanisms underlying the development of chronic fatty liver disease and liver cancer.



Faculty, Associate Professor Pu Xia, and Research Assistant Dominik Kaczorowski, Signal Transduction

Molecular Cardiology: Getting to the heart of sudden death

Assistant Director, Faculty, Professor Christopher Semsarian, Molecular Cardiology

Cardiovascular disease affects one in six Australians and two out of three families. To come to grips with a problem of such large scale there are several lines of integrated research within the Molecular Cardiology program. The unifying focus is the study of those cardiovascular disorders that are caused by underlying genetic abnormalities. More than 40 cardiovascular diseases have now been identified as directly caused by primary genetic abnormalities.

The most common cause of sudden death in young people, including competitive athletes, is hypertrophic cardiomyopathy (HCM), which affects up to one in 500 people. HCM is a genetic abnormality that causes the heart muscle to thicken abnormally, leading to problems of the rhythm and function of the heart. Tragically, genetic heart diseases like this are often silent; the individuals suffering from them often display no symptoms. In fact, sudden death can be the first sign of the problem in up to half the young people who are its victims.

Our approach to conditions like HCM includes identifying the gene defects that can cause sudden death through heart disease; understanding the underlying mechanisms that lead from gene defect to disease; and translating the acquired knowledge into improved diagnosis, treatment and prevention of heart disease. In the case of HCM, our research program has collected clinical information and DNA for genetic studies from more than 600 HCM-affected families around Australia. To complement the studies in humans, our laboratory has developed two unique transgenic mouse models of HCM, as well as cell culture models to evaluate the cellular effects of specific gene mutations.

Many other genetic causes of heart disease remain unknown. Our early research is showing promise, but we still have a long way to go.

Over the next five years, our research will lead to improved diagnosis of patients with genetic heart disease. Since diagnoses will be based on detection of abnormal genes, any problem should be able to be identified earlier in life, providing a greater window for starting treatment or prevention strategies.

Our work will also be used to identify the people in our community who have a higher risk of developing heart disease, such as heart failure and sudden death, thereby enabling better targeted, personalised therapy. The studies we undertake should also identify new targets for drug therapy.

— Professor Chris Semsarian

RESEARCH PROGRAM

In the spirit of the Institute, the Molecular Cardiology program led by Professor Chris Semsarian aims to integrate molecular biology, the latest genetic technologies and clinical medicine to reduce problem heart conditions and prolong life.

The unifying focus is the study of cardiovascular disorders that are caused by underlying genetic abnormalities.

The aims of the research program are to identify new genetic abnormalities in patients with heart disease, understand the molecular basis of the disease, and investigate what factors influence these disease-causing mechanisms, and how. The research program uses three concurrent sets of studies: in humans with inherited cardiovascular disorders attending the Genetic Heart Disease Clinic at Royal Prince Alfred Hospital; in genetically modified mice; and in isolated cells.

Several diseases are being studied, ranging from structural heart disorders such as cardiomyopathies to primary arrhythmia-generating diseases, such as long QT syndrome.

Highlights 2011

- Emily Tu and Jodie Ingles being awarded PhDs from the University of Sydney for their studies in genetic heart diseases.
- Professor Chris Semsarian receiving a three-year NHMRC project grant to study the clinical and genetic basis of familial valve diseases.
- Dr Jodie Ingles receiving the 2011 Cardiac Society of Australia and New Zealand Allied Health Affiliates Prize for her health economic studies focused on the cost effectiveness of genetic testing.
- Publishing 20 articles in peer-reviewed scientific journals; which is recognition of the program's quality and productivity.
- Receiving an International Program Development Grant from the University of Sydney that enabled the program to undertake a field study in rural Cambodia evaluating more than 500 children at risk of genetic and rheumatic heart diseases.

Gene and Stem Cell Therapy: Seeking cures by tweaking genes

Faculty, Professor John Rasko AO, Gene and Stem Cell Therapy

"The revolutionary technologies using gene therapy and stem cells could provide cures for many human diseases—heart disease, organ failure and some cancers, as well as genetic diseases such as haemophilia and thalassaemia. The hope is to provide regenerative medicines based on a firm foundation in scientific evidence."

Centenary Executive Director Professor Mathew Vadas, The Hon Tanya Plibersek, MP, Federal Minister for Health, Professor John Rasko and Steven Allen, Tech Support Officer

The Gene and Stem Cell Therapy research program is looking at overcoming the barriers to introducing such technologies; at developing models to understand the biology of adult stem cells; and at finding the causes of diseases including specific cancers, leukaemias and genetic disorders.

The outcomes can be both practical and dramatic. By discovering ways in which to increase cell numbers prior to transplantation, for instance, we have not only been able to help my patients at the Royal Prince Alfred Hospital, but also the more than 25,000 other people around the world each year who receive a bone marrow transplant.

Our work on blood-forming stem cells could increase the effectiveness and safety of treatments for diseases such as leukaemia, lymphoma and multiple myeloma, since these cells are the critical component of bone marrow and cord blood transplants.

The group works in five areas—gene therapy, stem cell biology, molecular mechanisms of gene control, genetic disorders, and cancer biology.

We are particularly interested in those molecules and mechanisms that regulate genes—the microRNAs and transcription factors. These are the triggers that switch genes on and off, and that fine tune them, turning their activity up and down. The overwhelming complexity of molecular circuitry that we have been successful in dissecting relies on our use of computer programming and the growth of our bioinformatics group.

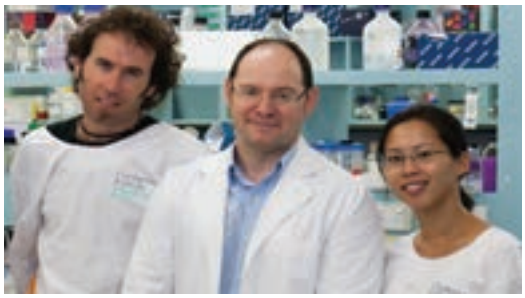
— Professor John Rasko AO

RESEARCH PROGRAM

A major project of the Gene and Stem Cell Therapy research program is developing, in collaboration with groups in Texas and at the University of Sydney, the best environment for growing blood-forming, bone marrow stem cells. An ability to be able to handle and culture stem cells outside the body is an essential first step in studying and manipulating them for therapeutic purposes.

The Gene and Stem Cell Therapy program is responsible for characterising and identifying the genes involved in three of the five known human disorders of amino acid transport. The recognition that these amino acid transport mechanisms are also increased in various cancers led directly to the establishment of the Origins of Cancer laboratory led by Dr Jeff Holst, which seeks to characterise and target amino acid transport in cancer.

There is ongoing collaboration with researchers at the National Institutes



Senior Research Officer Dr Chuck Bailey, Faculty, Professor John Rasko and Research Assistant Cynthia Ng

Associate Faculty, Dr Jeff Holst, Gene and Stem Cell Therapy

of Health in the US studying two closely related genes involved in regulating cancer—both triggering and suppressing it. Our discoveries involving the pumps required for cellular uptake of nutrient amino acids have led to further research in the Origins of Cancer laboratory designed to 'starve' cancer cells.

And we are also studying the differences in the role of RNA and of microRNAs in healthy white blood cells and in leukaemia. We were successful in receiving an NHMRC grant with internationally-acclaimed colleagues in Adelaide to study practical approaches to treating chronic myeloid leukaemia. Our work involves closely collaborating with the Bioinformatics research group to build online resources available to all scientists worldwide.

Dr Jeff Holst , Gene and Stem Cell Therapy

Highlights 2011

- Professor John Rasko winning the 50th annual Eric Susman Prize of the Royal Australasian College of Physicians for the most outstanding contribution to the knowledge of any branch of internal medicine. The award recognises his discoveries in relation to adult stem cells used to treat leukaemias.
- Two students—Jessica Vanslambrouck and Jessamy Tiffen—graduating with PhDs at the University of Sydney. Both joined prestigious laboratories for postdoctoral studies: The Institute for Molecular BioSciences in Queensland and The Wellcome Trust Sanger Institute in Cambridge, UK, respectively.
- Discovering that the human kidney disorder 'dicarboxylic aminoaciduria' is caused by the cell surface pump SLC1A1 (published in the *Journal of Clinical Investigation*) and so determining the genetic basis of three of the five principal human amino acid kidney diseases. This discovery was widely reported in the media as it may have implications for obsessive compulsive disorder in humans.
- Publishing two papers in the Annals of Internal Medicine—which is distributed to more than 132,000 members of the American College of Physicians and many more worldwide—in which we explored the promises and ethical challenges of stem cell research for regenerative medicine.
- Dr Jeff Holst receiving a fellowship from the National Breast Cancer Foundation to study micronutrient uptake in breast cancer progression.
- Professor John Rasko receiving a Sir Zelman Cowen Universities Fund Blue Sky Research Grant.
- Fiona Guan winning a Young Investigator Award for research into leukaemia at the International Society for Cellular Therapy Conference.

Bioinformatics: Calculating a path through biological complexity

Dr William Ritchie, Bioinformatics

"One obvious lesson from the many years of research into conditions such as cancer, TB, liver and heart disease is that there is no one single cause or cure. The systems of the human body—and biology in general—are simply too complex, and we are only just now becoming able to deal with them."

That's what the emergence of computers and bioinformatics in medical research is all about. Computers allow us to make progress in an era of trawling through genomes, simulating biological systems, and undertaking increasingly sophisticated clinical trials.

Bioinformatic approaches are used to understand the multiple complex interactions that are the basis of most diseases. They revolve around the analysis of large complex data sets and the representation of data in new and unique ways to enable researchers understand the intricate basis of human diseases.

Initially funded in 2009 from the Centenary Institute Foundation's fundraising efforts, and led until the middle of 2011 by Dr Nicholas Shackel, the Bioinformatics research group uses sophisticated computing techniques to examine the complex interactions within the whole human genome to determine, for instance, how cardiac disease results in sudden cardiac death or how liver cancer develops.

The computational requirements of modern bioinformatic approaches are considerable. Today practically every laboratory at Centenary is generating gigabytes of data. So the Bioinformatics research group has established computer infrastructure to support the needs of all researchers within the Institute.

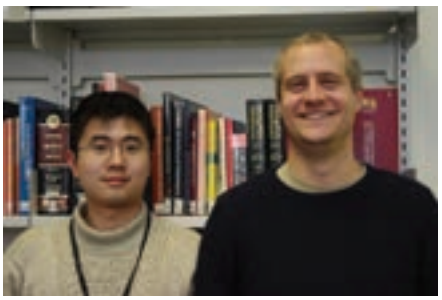
— Dr William Ritchie

RESEARCH PROGRAM

The Bioinformatics research group assists nearly every other laboratory in the institute. As such it is involved in projects such as:

- helping to identify genes involved in blood cell development with the Gene and Stem Cell Therapy program. The particular genes the group uncovered were not known to do anything until computer analysis found the connection. The work could help us understand mechanisms of leukaemia and provide new approaches to therapy
- helping the Molecular Cardiology program find the microRNAs connected with sudden cardiac arrest. In this case, a 20-minute computer experiment has saved years of research
- setting up a server that allows researchers to see quickly if anyone in the world has already done certain kinds of experiments in the organ or tissues in which they are interested.

The group also is pursuing its own work in two main areas. The first is determining the genetic signatures of diseases to enable the prediction of outcomes. It has become more and more apparent that disease conditions can take different paths depending on the genetic environment, and this may well demand different treatments—what is now called personalised medicine.



PhD Scholar Dadi Gao and Dr William Ritchie

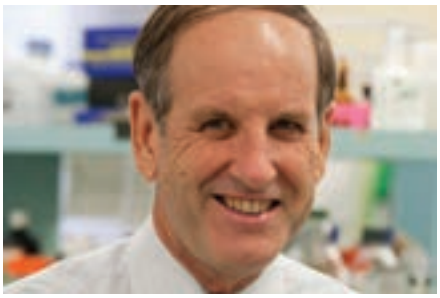
Adding sugars to proteins, in the process known as glycolysation, can change the body's metabolism. We are studying how it can contribute to the development of pathogenic processes such as liver cirrhosis or cancer.

Highlights 2011

Project highlights Bioinformatics 2011

- Assisting Professor John Rasko's Stem Cell group to identify genes involved in building blood cells.
- Assisting Professor Chris Semsarian's Molecular Cardiology group to uncover microRNAs connected with heart attacks

Mycobacterial: The killer on our doorstep



Faculty, Professor Warwick Britton, Mycobacterial

In the late 19th Century tuberculosis (TB) was the leading cause of death in Australia—20 times deadlier per capita than all cancer conditions today put together. Then the discovery that the cause of TB was the parasitic bacterium *Mycobacterium tuberculosis* enabled Australia and other developed countries to combat the disease with massive public health, screening and treatment programs.

But TB never went away. Today two billion people worldwide carry TB and 10% of them—200 million people—will die of it. In Australia, TB still infects around 1,200 people each year. Our nearest neighbour, Papua New Guinea, with a one-third the population of Australia, registered more than 14,000 new cases and almost 3,000 deaths in 2010. And multi-drug-resistant strains have been reported there. So it is important for us not only to assist the global fight against this deadly disease, but also to be prepared against an invasion of our own country.

The Centenary Institute's contribution to the war against TB is broad and deep. We are working to understand how the bacterium infects us and can hide so successfully from our immune defences for decades; why only 10% of infected people become ill; and how to stop the spread of TB by carefully managing infected people. In addition, we are applying what we learn to develop new ways of fighting TB, potential new drugs to treat TB, and new vaccines to protect us.

M. tuberculosis also provides an important general model of bacteria that invade cells. So the discoveries we make about TB provide new information on how the immune system controls many different types of infections in humans.

Our team has great depth. In the program I lead are three research laboratories which work together closely on different approaches to stopping the disease—based on immunology, the response of hosts to the bacteria, and the search for new drugs and vaccines. We obtain significant funding from the NHMRC and Britain's Wellcome Trust, and collaborate widely with other research groups in Australia and overseas. We even have two young researchers working against the disease on the front line. One is based in Vietnam and the other is in Sydney but working closely with researchers in China.

In addition, the Institute itself has made big investments in TB research. It is currently installing a new high biosecurity TB laboratory that will allow the researchers in our labs to work safely with TB bacteria as they crack open the secrets of this deadly disease.

— Professor Warwick Britton

RESEARCH PROGRAM

The TB research program comprises three inter-related research groups: Mycobacterial, Host Response to Tuberculosis, and Vaccine Development.

Mycobacterial

Professor Warwick Britton's group examines how immune responses in the lung control mycobacterial infections, and how to use this information to make more effective vaccines against TB. In a newly funded project, Dr Manuela Florido is exploring the interaction of Influenza A and mycobacterial infection in the lung, and has already discovered that co-infection reduces the protective cellular immune response to mycobacteria and thus control of the infection. We are now examining the impact of influenza on chronic mycobacterial infection in the lung. In collaboration with Associate Professor Jamie Triccas, a Research Affiliate of the Centenary Institute, we are studying how to improve the current BCG vaccine or use attenuated strains of the tuberculosis bacterium itself as a vaccine. It is important that these new vaccines stimulate prolonged immunity to TB, and we have found that one such live vaccine, an attenuated PhoP-deficient strain of *M. tuberculosis* developed by collaborators in Spain, is highly protective and stimulates a sustained T cell memory response. The alternative approach is to use one, or a restricted number, of *M. tuberculosis* proteins as subunit vaccines. Dr West and Professor Britton have compared the effectiveness of different *M. tuberculosis* proteins, either alone or in combination, as well as a variety of delivery systems. One secreted TB lipoprotein, MPT83, is very promising, as it is widely recognised in TB patients and stimulates strong protection against TB.

As part of this group, two researchers are working with colleagues overseas. Dr Magda Ellis is collaborating with molecular biologists from the Chinese National Human Genome Centre, analysing the genes of 6,000 people in North-West China to identify what makes some individuals particularly susceptible to contracting TB while others are protected. Dr Greg Fox is based in Vietnam where he is working to reduce the risk that family members face when a relative has active TB. Dr Fox is coordinating a major randomised control trial of active case finding in the contacts of TB patients, a joint project with the Woolcock Institute that was rolled out to 70 districts across Vietnam in 2011. He is also working with Dr Bernadette Saunders to analyse genetic variation in TB patients and control subjects in Hanoi in a study that parallels Dr Ellis' hunt for genetic markers of TB risk.

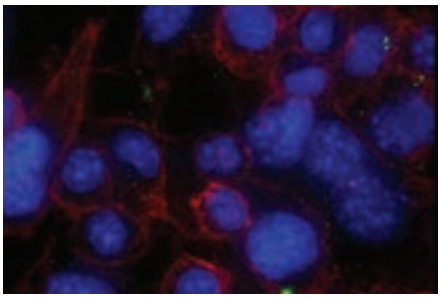
Host Response to Tuberculosis

Dr Bernadette Saunders leads a group studying how the host responds to infection with TB bacteria. In collaboration with Professor Chris Goodnow of ANU, her group is endeavouring to identify new susceptibility genes for TB infection. Mice with randomly induced genetic variation are tested for susceptibility to *M. tuberculosis* infection. Her group has isolated a number of susceptible mouse strains and used the powerful technique of next generation sequencing of the whole genome to identify the single causative mutation in several of them. It is investigating how these single variations in the genetic code cause profound susceptibility to TB. The group is also studying the ways in which the white blood cells known as macrophages control TB infection. Living inside macrophages is one way in which *M. tuberculosis* evades the immune system. Gene activity induced in human macrophages by TB infection has been identified by microarray analysis. Dr Saunders' group has shown how one such highly induced gene, encoding the enzyme Indoleamine 2,3 dioxygenase-1, influences the response of macrophages to TB infection in humans and mice.

Associate Faculty Dr Bernadette Saunders, Associate Faculty Nick West, Faculty Professor Warwick Britton

Vaccine Development

Dr Nick West's group is leading the hunt for potential new drugs and vaccines against TB. Dr West has developed a library of 15,000 different mutants of *M. tuberculosis,* and this is a powerful tool to investigate how the bacterium responds to different growth conditions during infection of the host compared to growth in the test tube. Members of the group have identified genes that are essential for the bacterium to gain a foothold in the lung and then spread to other organs, and are now studying which genes are necessary for persistence of infection. These 'essential' genes should make good drug targets. We continue to collaborate with Dr Richard Payne, a synthetic chemist at the University of Sydney, to develop and test new inhibitors of these essential mycobacterial enzymes. The *M. tuberculosis* protein, Rv3802c, is a secreted enzyme that breaks down fats and is shared with *Mycobacterium leprae,* the cause of leprosy. We have identified this protein as the target for the lipase inhibitor, tetrahydrolipstatin. This is a drug used for treating obesity, which also inhibits mycobacterial growth. We have now developed more potent inhibitors of this essential cell wall lipase that kill *M. tuberculosis.* The group is investigating how to use proteins, proven to be protective against TB, as dry powder vaccines that could be delivered into the lung to stimulate immunity at the site of TB infection.



Mycobacteria infect macrophages, macrophages make microparticles in response. These microparticles are then taken up by other macrophages, internalized within the cell

Highlights 2011

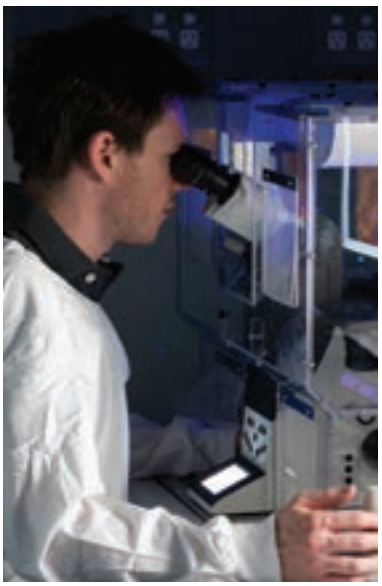
- Dr Magda Ellis being awarded NHMRC funding to track genetic susceptibility to TB in rural China.
- Obtaining funding for a new cell sorter to expand research in the new TB high-biosecurity laboratory, which is nearing completion.
- Demonstrating that *M. tuberculosis* infection of macrophages induces potent activation of IDO-1—an enzyme which breaks down the essential amino acid tryptophan—and that it has different effector roles in human and mouse macrophages.
- Developing a new and more effective inhibitor of *M. tuberculosis* cell wall lipase as potential TB drug.
- Proving that the secreted lipoprotein MPT83 stimulates protective immunity against TB infection.
- Developing new collaborations in TB vaccine development with the US Aeras Foundation and the European NEWTBVAC consortium.
- Rolling out a randomised control trial of 'active case' finding in the contacts of TB patients to 70 districts across Vietnam.

Immune Imaging: Probing the outer layers of the body's defences

Assistant Director, Faculty, Professor Wolfgang Weninger, Immune Imaging

The cornerstone of our health is our immune system. It's our defence against viruses and bacteria, parasites and tumours. When it does not function properly we become vulnerable. When it turns against us, conditions known as autoimmune diseases emerge. They include some of the most devastating human diseases.

So it's not surprising that the Centenary Institute has several research groups working on different aspects of the immune system. They are a diverse collection but, because they all study the immune system, they tend to work on the skin and the gut—the parts of the body that are most exposed to the outside world, and from which pathogens and the bulk of toxins emerge.



Research Officer Dr Ben Roediger, Immune Imaging and his image "Harmonious Muscle", finalist in the 2012 Scientific Image Prize

The Immune Imaging research program, which I head, comprises four groups whose common feature is that they all employ similar technology—multiphoton microscopes—which can be used to track immune events as they occur in living tissue. This novel imaging approach provides a new way of studying fundamental questions about how the immune system defends us against microbes and cancer cells. Studies of targeted treatments and vaccines also help us understand their mode of action so we can improve therapeutic strategies for patients.

I am a trained dermatologist. One of the attractions of coming to the Centenary Institute has been the ability to mix research and clinical work, something I could not do in the US or Austria where I was trained.

The immune system is so complex and all-pervasive that, with improvements in technology, it is still possible to make fundamental discoveries of huge importance to therapy. In the past year, within this research area several key discoveries have been made at the Institute. My own group, for instance, has found immune cells in the deeper layers of the skin that are specifically tuned to respond to the bacteria that invade that far. Dr Paul Mrass has identified a molecule on the surface of killer T cells that allows them to move around and kill tumours, and Dr Chris Jolly has shown a mechanism by which DNA repair can lead to cancer. Dr Nikolas Haass has discovered a means of making melanoma cells more sensitive to therapy.

— Professor Wolfgang Weninger

RESEARCH PROGRAMS

The four laboratories in the immune imaging program are able to track interactions with the immune system using multiphoton microscopes. Proteins of interest are labelled with fluorescent tags, which are then stimulated to release light under the microscope using lasers. The technique is termed multiphoton because it takes two or more packets of light energy to trigger the fluorescence. This means that infrared lasers with very short, high energy pulses can be used. This has two advantages—the light energy does not damage living cells and it also penetrates deeper into the tissue.

The laboratory, led by program head Professor Wolfgang Weninger, is investigating how the cells of the innate immune system, the first responders, interact with pathogens in skin tissue. These researchers are challenging the tissue with different viruses, bacteria and

parasites to test a variety of different models of infection. The studies have implications for the development of vaccines. This laboratory collaborates with many other groups, in Australia and overseas.

The major goal of the laboratory led by Dr Paulus Mrass is to define the rules coordinating T cell migration and interaction within live organisms. To study these processes within a model site of inflammation, the researchers are using a unique imaging system that enables them to track killer T cells within live tumours in real time. By finding ways to improve the capacity of T cells to search for target cells, the group aims to develop strategies that enhance the protective function of T cells against cancer and other diseases.

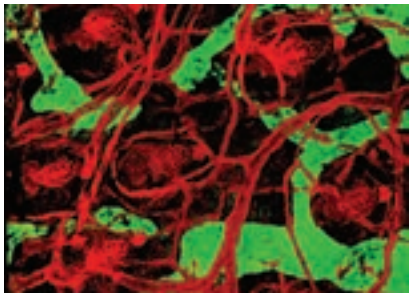
Associate Faculty, Dr Paulus Mrass, Assistant Director Faculty, Professor Wolfgang Weninger, Immune Imaging

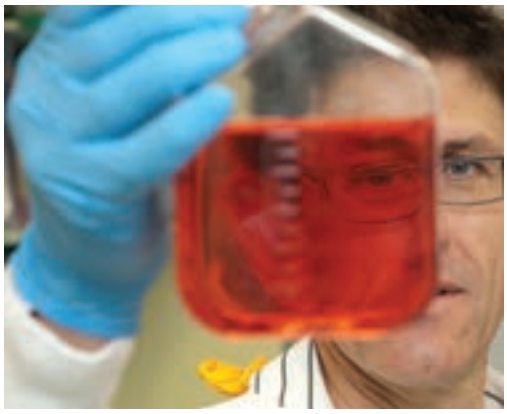
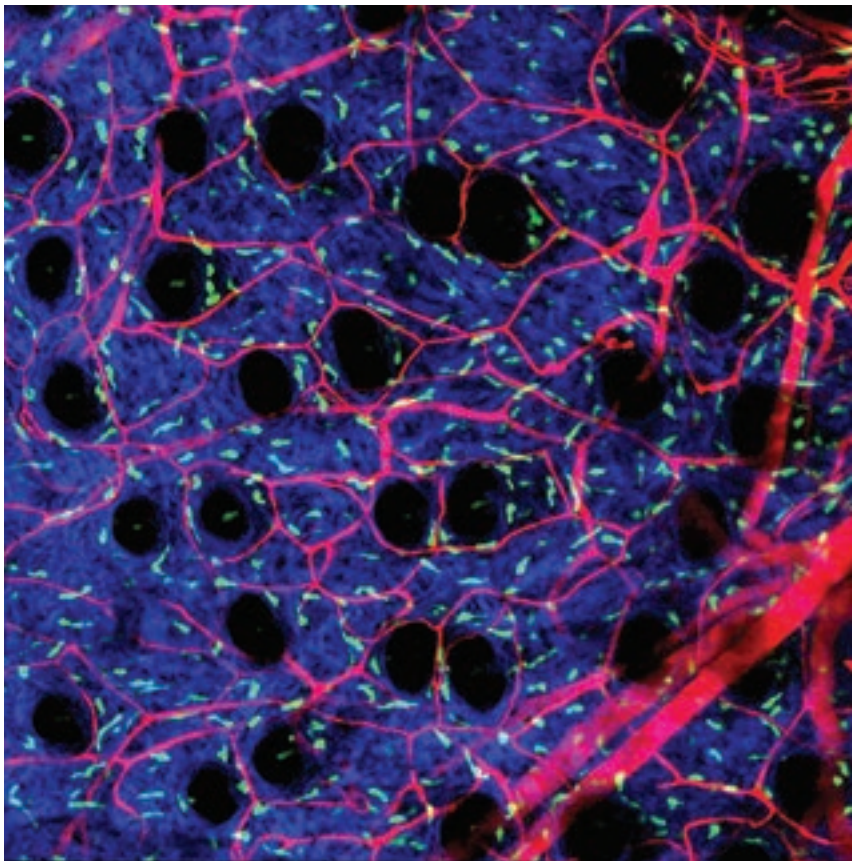
Highlights 2011

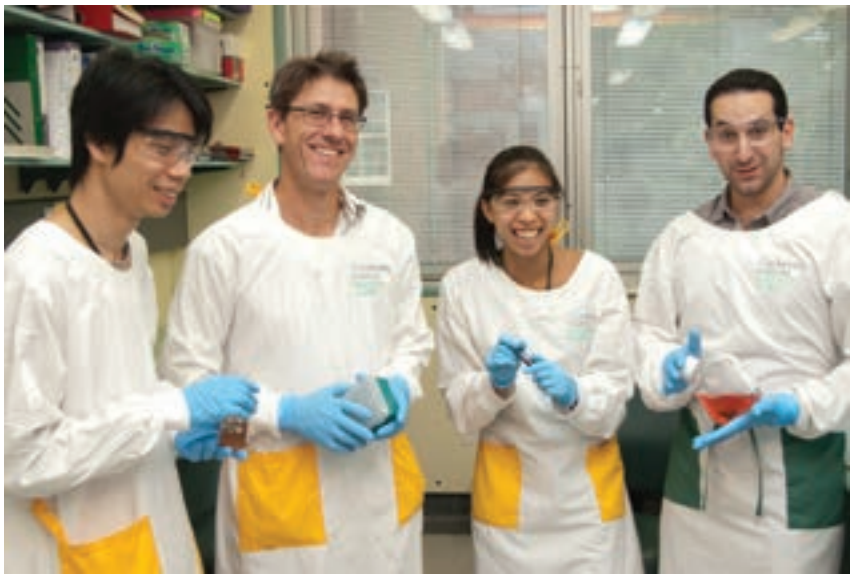
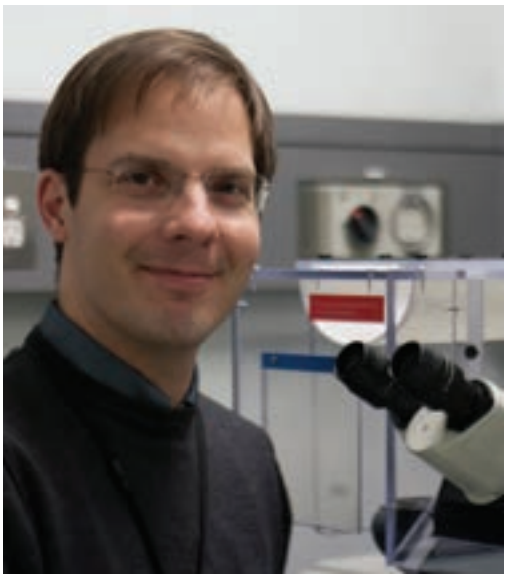
- Professor Wolfgang Weninger being awarded a grant by NSW Cancer Institute to investigate how anti-tumour cells are generated and operate.
- Professor Wolfgang Weninger being awarded a grant to investigate the behaviour of neutrophils at sites of tissue inflammation.
- Professor Wolfgang Weninger publishing a paper on a novel pathway allowing effector T cells to home in on inflamed tissues.
- Professor Wolfgang Weninger publishing a paper on a new layer of defence in the body—gamma delta T cells in the dermis.
- Dr Paulus Mrass being awarded an ARC Grant to design novel image-analysis approaches that analyse migration and geometry of tumour-infiltrating T cells.
- Dr Nikolas Haass publishing a paper on how melanomas can be made more sensitive to anti-cancer drugs.
- Dr Nikolas Haass publishing a collaborative paper on induction of cell cycle arrest in breast cancer.
- Dr Nikolas Haass winning the Adrian Johnson Memorial Prize 2011 of the Australasian College of Dermatologists for the best paper published in the *Australasian Journal of Dermatology.*
- PhD student Nethia Mohana-Kumaran being awarded best oral presentation by a young investigator by the Australasian Society for Dermatology Research.
- Dr Kimberley Beaumont and Andrea Anfosso winning the 2nd and 3rd places of the Centenary Institute Scientific Image of the Year Prize.
- Dr Christopher Jolly submitting a paper on the regulation of faithful versus mutagenic (cancer-causing) DNA repair by the cell division cycle.
- Student George Sharbeen being awarded his PhD.

Dr Nikolas Haass and his group work on therapies for the aggressive skin cancer known as melanoma, the most common cancer of young adults in Australia. They are investigating the characteristics and resistance to drugs of the different types of cells in melanomas, so that treatment can be better targeted in future. Using a sophisticated imaging system, the researchers are examining behaviour of melanomas in real time during proliferation and invasion. Dr Haass and his team are testing potential new drugs and approaches to the treatment of melanoma, as well as how cells interact in the tumour environment.

Dr Christopher Jolly is studying DNA repair mechanisms, and how the body generates antibodies. These two turn out to be significantly linked. In fact, understanding DNA repair pathways should enable us to prevent early stage cancer from progressing. Dr Jolly and his team have developed a powerful model in which they can manipulate and analyse DNA damage and repair during particular phases of the cycle of the B cells of the immune system. Dr Jolly and his collaborators have also identified a novel gene that seems to be specifically required for multi-potent stem cell function in at least two independent tissues. This gene may influence therapies based on stem cells.

From top left to right: Associate Faculty, Dr Nikolas Haass; Three dimensional rendering of blood vessels (red) and lymphatic vessels (green) in the mouse ear skin; Dr Ben Roediger, Research Officer; Immune Imaging Team; Faculty Dr Chris Jolly, DNA Repair, image of mast cells (green) distributed evenly throughout the skin, with blood vessels shown in red and the collagen matrix depicted in blue; Image by PhD Scholar, Edwin Lau, Faculty, Dr Chris Jolly, Research Assistant, Christine Yee and PhD Scholar George Sharbeen; Director Faculty, Associate Faculty, Dr Paulus Mrass

Liver Immunology, Injury and Cancer: The fight against liver disease is far from won

Assistant Director, Faculty, Professor Geoff McCaughan, Head of Liver Injury & Cancer

"Liver cancer is the fastest growing cancer condition in the Western world and the third most common solid tumour. The Centenary Institute is at the forefront of dealing with the problem, as it has been since our liver unit was established more than 15 years ago."

The liver is our largest solid organ. About the size of a football in adults, it contains over 300 billion cells which perform hundreds of essential tasks including cleaning our blood of toxins and waste; storing fats and sugars so they're available for rapid use; and acting as a factory—producing bile, clotting factors, immune factors and much more. If the liver shuts down we can survive for no more than a day or two. Fortunately the liver is tough—capable of working and regrowing if as much as 75% is removed. It can also modulate or adjust the body's immune system. A transplanted liver can turn off rejection of kidneys and hearts transplanted into the same animal.

But we work our livers hard and as a consequence we're seeing a growth in serious liver diseases and liver cancer. About half a million Australians are chronically infected with the hepatitis B virus (HBV) or hepatitis C virus (HCV). These viruses are the driving force behind an upsurge in chronic liver damage which now affects up to one in five Australians. New vaccines and other treatments are helping us get on top of these liver viruses. But now we face a new challenge—the combination of diabetes and obesity looks as if it will trigger another significant increase in serious liver disease through the conditions known as fatty liver and non-alcoholic steatohepatitis (NASH).

And serious liver disease leads to cancer. Unlike other cancers which appear to arise almost from nowhere, about 90% of liver cancers result from disease and damage. These lead to fibrosis or scarring that greatly increases the chances of liver cancer and failure. The initial damage can occur as a result of viral infection, abuse of alcohol, diabetes and obesity, or autoimmune or genetic conditions. So liver disease encompasses a whole spectrum of ages and causes. It is a complex area and grossly under-recognised as a public health issue.

There are two major research programs in the liver area at the Centenary Institute—in liver immunology and in liver injury and cancer.

The Liver Immunology program is focused on understanding why liver transplants are not rejected in the same way as other solid organ transplants. The findings will help in the design of new strategies to prevent rejection and disease. They may also shed light on ways to improve the transplant acceptance rates of other solid organs.

The Liver Injury and Cancer program is aimed at understanding how liver damage occurs, and will help us improve diagnosis and develop new strategies to treat liver disease and stop its progression into liver cancer.

In 2011, researchers at the Institute provided the first gene profile of a damaged human liver; showed that immune cells within the liver can be removed by the liver itself thus promoting acceptance of liver transplants; and discovered and cloned novel enzymes that play a role in liver damage and in fatty liver related to diabetes.

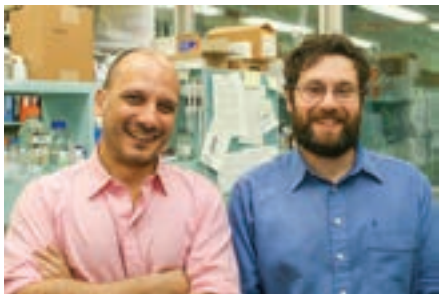
The Liver research unit at the Centenary Institute is one of only two in Australia with a program grant from the NHMRC. Our approach is distinctive in two ways—we study liver disease at the most fundamental level and we link the research directly to treatment.

For instance, as well as heading research into liver disease and damage at the Institute, I am also the Director of the Royal Prince Alfred Hospital's (RPAH) liver transplant program, which is the largest in the country. This direct link between laboratory and clinic means that research at the Institute begins not with experiments and test tubes, but in the clinic with actual diseased human liver tissue that patients allow us to take back and study in the laboratory. The experience of what we learn can then be applied directly in the clinic.

The Centenary Institute was one of the first places in the world to try to come to grips with liver damage at the molecular level, leading to a greater understanding of the role of genes and also to the discovery of potential drug targets.

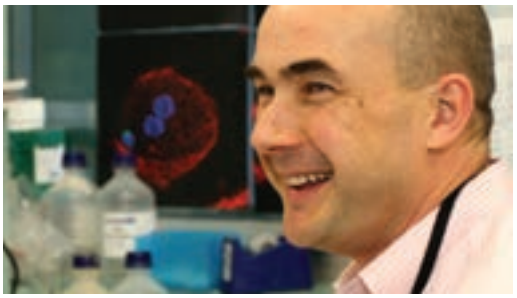
I now lead an international working party of experts convened by the Asian Pacific Association for the Study of the Liver which sets and publishes guidelines for the study, prevention, diagnosis, management and treatment of hepatitis C in keeping with the most recent research.

– Professor Geoff McCaughan



Faculty, Dr Patrick Bertolino, Head of Liver Immunology with Associate Faculty Dr David Bowen

Associate Professor Mark Gorrell, Group Head Molecular Hepatology Group, Liver Injury & Cancer



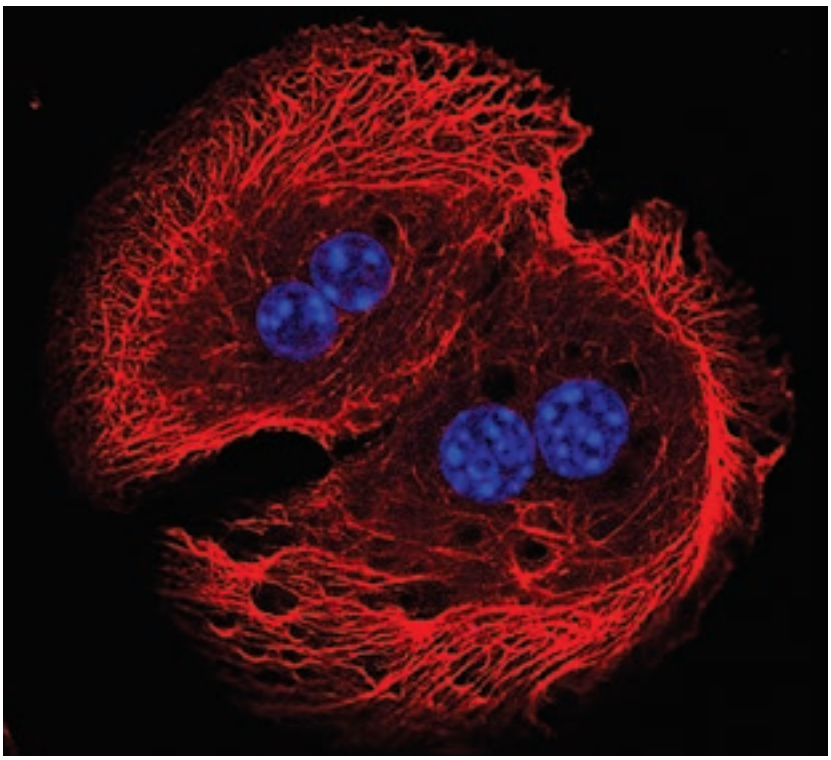
Dr Nick Shackel, Head Liver Cell Biology Group, Liver Injury & Cancer

RESEARCH PROGRAM

There are two broad liver research programs in the Centenary Institute–Liver Immunology and Liver Injury and Cancer

Liver Immunology

The Liver Immunology program, led by Dr Patrick Bertolino and Dr David Bowen, is studying the unique relationship between the liver and the immune system. Livers damp down immunity to such an extent that they can be transplanted without rejection in some cases. Having already shown that the liver, like the lymph nodes, can activate and instruct the T cells of the immune system, this year the immunology research group demonstrated that liver cells can engulf and destroy T cells.



Two liver cells (DNA in blue) Photo: Michelle Vo, PhD Scholar

The group is continuing to use mouse models to examine how the liver induces tolerance in the immune system and is investigating how to manipulate these mechanisms to allow the induction of a persistent immune response. Exploring the mechanism of how the liver regulates immunity could not only lead to better transplantation therapy through turning the immune system down, but also to more effective prevention and treatment of liver disease by strengthening its action.

The research group is also collaborating with Professor Ian Alexander of the Children's Medical Research Institute, NSW, to develop technology to activate or silence genes of interest in liver cells, and to inactivate T cells that recognise proteins made in the liver. This is particularly important for gene therapy, to avoid immune-mediated destruction in treated patients of liver cells that have activated a gene previously missing. It will not only give the researchers powerful tools to identify and analyse the molecules critical for tolerance, but could also provide some important clues to improve the success of human gene therapy.

Linking back to the clinic, the group is examining people undergoing liver transplantation for disease related to HCV reinfection of the transplanted organ. By studying the immune response to HCV in this group of patients, the researchers hope to gain important insights into factors that could improve treatment outcomes both in liver transplantation and in early infection.

Liver injury and Cancer

The Liver Injury and Cancer program, headed by Professor Geoff McCaughan, comprises four projects. His own research centres on the triggers of liver damage, the development of liver cancer at a molecular level and the management of liver transplantation. His research group was one of the first in the world to try to understand how liver disease occurs at a molecular level. Currently the group is studying the role of the hedgehog signalling pathway, which has been implicated in cancer, and of a novel microRNA in causing liver injury and cancer.

Professor McCaughan also collaborates in a research project on alcohol-based liver disease (ALD) with Dr Devanshi Seth and Professor Paul Haber. They have discovered a key protein, osteopontin, involved in liver injury. Dr Seth heads an international team that is now studying the genetic basis of why some patients develop alcohol-related liver injury and others do not.

Associate Professor Mark Gorrell is studying the proteins that will provide many of the targets for drug-related therapy and may well be the key to unlocking fatty liver disease and NASH. In particular the project focuses on the dipeptidyl peptidase (DPP) family of proteins and fibroblast activation protein (FAP), which he and Professor McCaughan discovered 25 years ago. These proteins provide a link with diabetes and NASH.

The Liver Cell Biology team of bioinformatician Dr Nicholas Shackel is investigating the role of the main cells of the liver, hepatocytes, during liver inflammation and scarring. In particular they have been studying the role of the molecule EMMPRIN in scarring and how liver stem cells contribute to the development of cancer. Dr Shackel also leads a team that is working to discover genes that may contribute to HCV-related liver injury and is also investigating the role of novel liver stem cell pathways in liver injury.

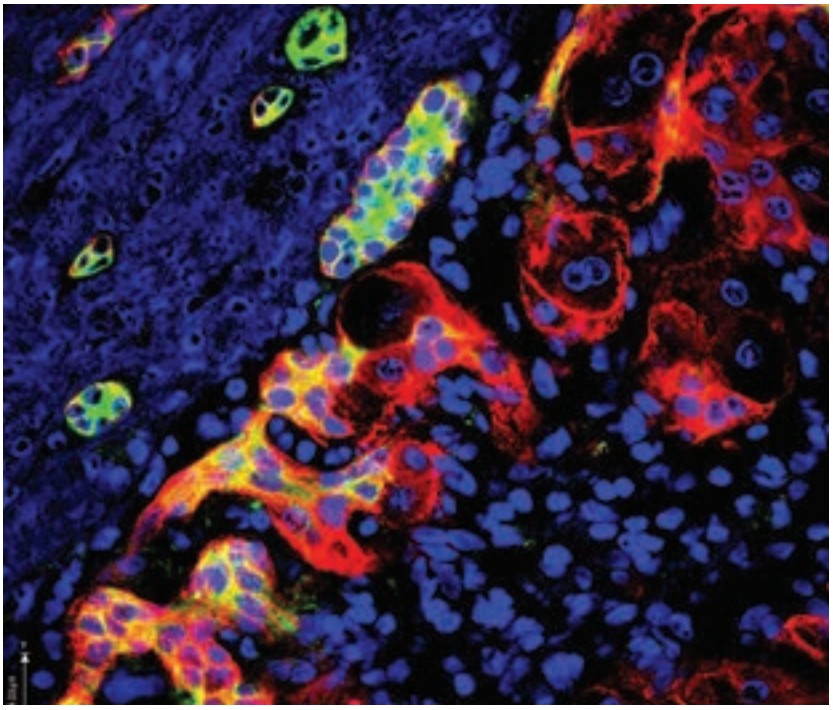


Image by PhD Scholar, Dr Emilia Prakoso, Liver Immunobiology. Image 9-EP. Liver progenitor cells (green=ck19, red=EpCAM) in human cirrhosis (blue=DAPI, nuclei)

Highlights 2011

- Publishing the first direct evidence of liver cells engulfing immune T cells.
- Demonstrating that manipulating genes in the liver can induce tolerance.
- Showing that the hedgehog protein is a driver of the progression of liver disease. This work resulted in Candice Grezelak winning the Young Investigator Prize at National Gastroenterology Week.
- Identifying a novel microRNA as a modulator of TGFB-induced liver injury.
- Being awarded a US National Institutes of Health grant for a major genetic study of ALD.
- Publishing guidelines for dealing with hepatitis C for the Asia-Pacific Region.
- Publishing a new model of NASH via the induction of diabetes.
- Identifying substrates for a key enzyme that causes liver injury.
- Being awarded a NSW Cancer Council grant to investigate the molecular signatures of primary liver cancer.
- Demonstrating the role of EMMPRIN in liver cell biology and how it contributes to liver injury.
- Documenting complex stem cell phenotypes in hepatitis-related liver injury.

Dr Devanshi Seth, Alcoholic Liver Disease, Liver Injury & Cancer

All of this work feeds back into the treatment of liver disease. For instance, whereas monitoring the replication of the virus is a standard part of treatment for HBV-related disease, RPAH is one of only a few hospitals in the world to do the same thing for HCV. It is this sort of collaboration with Centenary that has earned RPAH its reputation as a centre for liver disease therapy.

In the next five to ten years, Professor McCaughan hopes collaboration with the Institute's Vascular Biology (endothelium) research group led by Professors Jennifer Gamble and Mathew Vadas will lead to better therapies for liver repair, and that some of the enzyme-based work will result in improved drug treatments. One potential treatment, based on a compound involved in diabetes known as DPP-IV, is relatively close to testing.

Core Facilities

Cytometry, Imaging and IT Manager, Dr Adrian Smith, Scientific Support

Flow Cytometry

Flow cytometry—measuring the characteristics of cells—and cell sorting are key technologies used extensively by most research groups at the Centenary Institute. Our cytometry facility is well-equipped with four cell sorters and five flow cytometry analysers.

In 2011, we added a laser to our nine-laser analyser, making it the first instrument in the world with ten lasers and a blueprint for other cutting edge facilities around the world.

Furthermore, Centenary received close to $1 million from the Cancer Institute NSW and the NHMRC to help purchase a next-generation ten-laser high-speed cell sorter, another world-first.

The Facility Manager, Dr Adrian Smith, was re-elected as President of the Australasian Flow Cytometry Group and facility staff presented at the national cytometry conference in Hobart. Dr Smith also attended and presented at the International Society for the Advancement of Cytometry's international congress in the United States. Mr Steven Allen (Cytometry Technical Support) attended the 34th Annual Advanced Cytometry Course in New Mexico, USA.

Imaging

Centenary operates two multiphoton microscopes that give researchers unprecedented access to the operation of living tissues at the cellular and molecular level. Late in 2011 Centenary purchased an additional custom-designed multiphoton microscope; expected to arrive in mid-2012.

The Institute is equipped with a multi-laser, spectral, confocal microscope for imaging cells and tissues with high-resolution 3D images and videos.

In 2011, Centenary purchased two deconvolution microscopes with funding from the Cancer Institute NSW, Perpetual Trustees and the Ramaciotti Foundation. One of these systems is dedicated to the high-speed imaging of living cells.

Genomics Facility

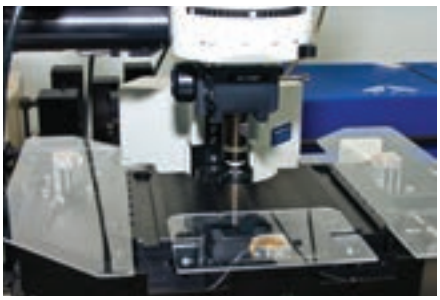
The promise of personalised medicine will be realised using genomics approaches. The Centenary Institute houses the latest Affymetrix Gene Array platform (supported by funding from the Cancer Institute NSW) and NimbleGen Array platform. These platforms will create a better understanding of the molecular basis of cancer, cardiovascular and infectious diseases and will help develop new therapies. We have also used even newer technologies profiling microRNA expression as well as 'deep sequencing' which increases accuracy.

Mouse Cardiac Physiology and Function Facility

In evaluating the cardiac characteristics of genetically engineered mice, the Agnes Ginges Centre for Molecular Cardiology at the Centenary Institute has developed a facility which allows in vivo analysis of cardiac measurements, including during exercise.

PC3 Laboratory

The Centenary Institute houses the only Physical Containment 3 (PC3) facility in Australia that permits experimental work with tuberculosis (TB) infection. This facility is essential for its ongoing studies



Top to bottom: The Centenary Institute unveils a powerful multiphoton microscope with unique features unlike any other in Australia; Equipment in the new PC3 laboratory.

of the immunological and inflammatory response triggered by *Mycobacterium tuberculosis* infection and of the genetic factors that control resistance and susceptibility to TB.

In 2011, construction began on a new $1.2 million PC3 facility, jointly financed by the Australian and NSW governments, which will be the biggest of its kind in Australia.

Animal Facility

Genetically modified mouse lines are bred under Level 2 Specific Pathogen-Free conditions in the Animal Facility. The PC2 approved facility, approved by the Australian Quarantine and Inspection Service, offers differing levels of containment with dedicated areas for immune-deficient mice, infectious studies and quarantine.

Centenary Institute Medical Research Foundation

PhD Scholar, William d'Avigdor, Liver Cell Biology, Liver Injury & Cancer and Her Excellency, Professor Marie Bashir AC CVO, The Governor of New South Wales

"People support the Centenary Institute for a range of reasons. We are grateful for every donation and offer of support. These funds are vital to the achievement of our vision of a world where lives are not cut short or their quality diminished by chronic disease and poor health. "

Professor Warwick Britton, Mary Lusby, Dr Nicholas Shackel, Dr Patrick Bertolino and Suzie Graham at the Races for research fundraiser for the Centenary Institute 2011

The Centenary Institute Medical Research Foundation's purpose is to inspire the community to support the Institute's great scientists in their important work. We are extraordinarily grateful for the incredible commitment of our long-term supporters and of new donors to Centenary.

We were honoured to welcome a new Foundation member, Elizabeth Dibbs, who devotes her considerable legal experience and strategic expertise to charitable causes. More talent has come on board from a new generation of philanthropists led by Neil Lawrence's daughter Anna who, following in her father's footsteps as inaugural Chair of the Centenary Foundation, this year became the first Chair of the Young Centenary Foundation.

The Foundation's quarterly appeals continue to be a major source of funding and our regular giving program now includes more than 400 participants. We would also like to acknowledge those who chose to leave a gift in their will. Bequests were responsible for 26% of the income for the Foundation for 2011. These funds are essential for the long-term funding and sustainability of research and programs.

Making a difference through events

Events provide people with the opportunity to become actively involved in Centenary's work and meet its scientific leaders.

The Third Annual Foundation Dinner and Art sale, expertly coordinated by LauraBeth Albanese, was held in June and once again was a great success, raising more than $130,000 to support the Bioinformatics Fellowship at Centenary Institute.

We are grateful to our sponsors for contributing to a stunning event attended by corporate Sydney, representatives of the major media groups, both sides of government and their friends.

Top to bottom: Chairmen of the Foundation present and past, Joseph Carrozzi with Neil Lawrence and inaugural Chair of the YCF, Anna Lawrence; Dr Nick Shackel talks on Bioinformatics

Foundation member Elizabeth Dibbs

Centenary does Movember

Professor Warwick Britton and Julie Ford at the Races for research fundraiser for the Centenary Institute 2011

Julie and Simon Ford invited Centenary supporters and appreciators of fine art to their beautiful Greenwich home in October to raise money at our Races for Research event. Dr Nick Shackel introduced guests to the wonders of bioinformatics. Proceeds from the event went towards the Bioinformatics unit. Professor Robert Lusby, a vascular surgeon and owner of Tintilla Estate, which sponsored the event, explained how medical research had changed the face of vascular surgery.

It was a record Run for Research at City2Surf in 2011. The 14.2 kilometres of hills in this race can make or break the toughest of athletes. But even Heartbreak Hill and light drizzle did not deter the 33 fundraisers who ran for the Centenary Institute. Together they raised an amazing $16,165.

Community fundraising forms an integral part of our efforts. Thanks to all our committed fundraisers and their supporters. They include Albert Milne, Holly Burt, Meron Wolde, Alex Tresilian, Jack Dow, Michelle Vo, Amar Flora, Jack O'Donnell, Dr Nikolas Haass, Anna Lawrence , Katrina Maximova, Oddy Graham, Ben Goldsmith, LauraBeth Albanese, Peter Chen, Ben Roediger, Professor Jennifer Gamble, Samantha Lu, Camille Vadas, Jesse Todd, Steven Chung, Conita Hung, Kathy Jones, Sebastian Perhauz, Corinne Hodson, Mathew Hocking, Vanessa Chau, Gary Lucey, Professor Mathew Vadas, William D'Avigdor, Dr George Wang, Matt O'Donnell, Yee-Fong Lee, Jeff and Jan Cook, Football Media Association, Keep Young Hearts Beating, Meg Taylor, The Peter 'Wally' Bamford Memorial Concert, Richard Daniel, Julia Zuza.

Philanthropy Coordinator, LauraBeth Albanese, Centenary Institute Medical Research Foundation

The Football Media Association (FMA) held its first annual fundraising trivia competition in August 2011, inspired by FMA founding member, Sydney Morning Herald journalist and FOX Sports commentator, Michael Cockerill's battle with leukaemia, raising $6500.

Jan and Geoff Cook held an event for a cause close to their hearts—melanoma research. Jan, her brother and her daughter have all been affected by the disease. One hundred and thirty guests were invited to sample fine Tamburlaine Wines from the Hunter Valley as Jan and Geoff raised a staggering $15,557 in support of Dr Nikolas Haass' research into melanoma at Centenary.

On behalf of the Foundation and the research teams, we thank everyone who has contributed to the work in this 12-month period.

We thank the members of the Foundation for a big personal commitment which made so many of our achievements in 2011 possible.

Justice Margaret Beasley AO
Joseph Carrozzi (Foundation Chair)
Elizabeth Dibbs
Simon Dulhunty
Julie Ford
Simon Ford
Annette Larkin
Caroline Lawrence
Neil Lawrence
John Samaha
Andrew White

– Suzie Graham

Dr Marie-Liesse Asselin-Labat, Research Fellow, Laboratory Head and Faculty Member, Division of Stem Cells & Cancer, Walter & Eliza Hall Institute of Medical Research

Rob Mactier, Chairman, STW Group (Major Sponsor of the Lawrence Creative Prize)

Mr Neil Lawrence & Dr Marie-Liesse Asselin-Labat, WEHI

Inaugural Centenary Institute Lawrence Creative Prize

In August 2011, the Centenary Institute launched the annual Lawrence Creative Prize, a national award of $25,000 to a researcher fewer than eight years out from his or her PhD. The prize is unusual in that it specifically recognises creativity in addition to hard work. It was named for Neil Lawrence, inaugural Chairman of The Centenary Institute Foundation.

The announcement of the prize led to applications from more than 30 of the nation's most talented scientists. The international judging panel included such luminaries as immunologist Professor Sir Marc Feldman of Oxford University and Professor Ian Frazer, a former winner of the Prime Minister's Prize for Science.

They selected as the first winner a brilliant young Melbourne cancer researcher, Dr Marie-Liesse Asselin-Labat. Major sponsors of the award included FOXTEL, Mindshare and the STW grou p, with supporting sponsors The Australian, UBS, Deloitte and Crosby | Textor.

Centenary Institute Lawrence Creative Prize Trophies "Fruit of Knowledge" glass sculptures by Nick Mount.

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Centenary Institute Awards for Excellence in 2011

Dr Nick Pearce, Chief Operating Officer

Professor Wolfgang Weninger, Immune Imaging, won the 2012 Axel Ullrich Award for the highest Impact Factor for a paper published in 2011 by a Centenary Institute researcher.

Dr Jodie Ingles, Molecular Cardiology, won the 2012 Student Paper Award For the highest Impact Factor for a paper published in 2011 by a Centenary Institute student.

Professor Chris Semsarian, Molecular Cardiology, won the 2012 Paper with Highest Citations Award for the highest citations in the preceding five years for a paper published in the past five years by a Centenary Institute researcher.

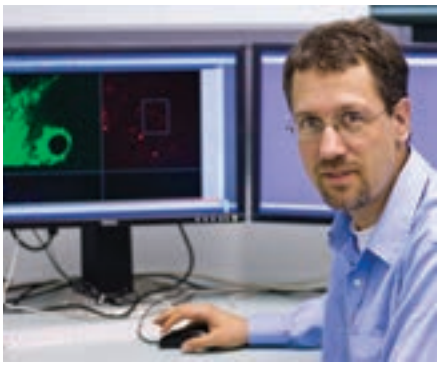
Professor Barbara Fazekas de St Groth, T Cell Biology, won the 2012 Centenary Innovation Award, which recognises individuals who have introduced innovations and process improvements that have made a significant and positive impact on the Centenary Institute, its people and community.

Bob Thorburn, Scientific Support, won the 2012 Centenary Outstanding Service Award, which acknowledges employees who consistently strive to go above and beyond their role and contribute positively to the goals of the Centenary Institute.

David Hancock, T Cell Biology, won the 2012 Scientific Image Prize by a Centenary Institute researcher in 2011.

Ka Ka Ting, Vascular Biology, was a finalist in the 2012 Scientific Image Prize by a Centenary Institute researcher in 2011.

Ben Roediger, Immune Imaging, was a finalist in the 2012 Scientific Image Prize by a Centenary Institute researcher in 2011.



Top to bottom: Faculty, Professor Barbara Fazekas de St Groth, T Cell Biology; Research Officer, Emily Tu, Assistant Director, Faculty, Professor Christopher Semsarian, Molecular Cardiology, Faculty, Professor Wolfgang Weninger, Immune Imagining

David Hill, Immune Imaging, was a finalist in the 2012 Scientific Image Prize by a Centenary Institute researcher in 2011.

Michael Lovelace and Paul Coleman, Vascular Biology, were finalists in the 2012 Scientific Image Prize by a Centenary Institute researcher in 2011.

2011 Publications

Dr Jodie Ingles, Molecular Cardiology

Ash MR, Maher MJ, Guss JM, **Jormakka M.** *The initiation of GTP hydrolysis by the G-domain of FeoB: insights from a transition-state complex structure.* **PLoS One.** 2011;6(8):e23355.

Ash MR, Maher MJ, Guss JM, **Jormakka M.** *A suite of Switch I and Switch II mutant structures from the G-protein domain of FeoB.* **Acta Crystallogr D Biol Crystallogr.** 2011 Nov;67(Pt 11):973-80.

Ash MR, Maher MJ, Guss JM, **Jormakka M.** *The structure of an N11A mutant of the G-protein domain of FeoB.* **Acta Crystallogr Sect F Struct Biol Cryst Commun.** 2011 Dec 1;67(Pt 12):1511-5.

Bagnall RD, Ingles J, Semsarian C. *Molecular diagnostics of cardiomyopathies: the future is here.* **Circ Cardiovasc Genet.** 2011 Apr;4(2):103-4.

Bailey CG, Ryan RM, **Thoeng AD, Ng C,** King K, **Vanslambrouck JM,** Auray-Blais C, Vandenberg RJ, Bröer S, **Rasko JE.** *Loss-of-function mutations in the glutamate transporter SLC1A1 cause human dicarboxylic aminoaciduria.* **J Clin Invest.** 2011Jan;121(1):446-53.

Balamatsias D, Kong AM, Waters JE, Sriratana A, Gurung R, **Bailey CG, Rasko JE,** Tiganis T, Macaulay SL, Mitchell CA. *Identification of P-Rex1 as a novel Rac1-guanine nucleotide exchange factor (GEF) that promotes actin remodeling and GLUT4 protein trafficking in adipocytes.* **J Biol Chem.** 2011 Dec 16;286(50):43229-40.

Baleriola C, Rawlinson WD, Dore GJ, Chaverot S, Stelzer-Braid S, Yoshihara M, Crawford D, Sievert W, **McCaughan G,** Weltman M, Cheng W, Rizkalla B, Dubois D, Thommes J, Roberts S. *Effect of low-level HCV viraemia at week 24 on HCV treatment response in genotype 1 patients.* **Antivir Ther.** 2011;16(2):173-80.

Beham A, Puellmann K, Laird R, Fuchs T, Streich R, Breysach C, Raddatz D, Schweyer S, Oniga S, Peccerella T, Findeisen P, Kzhyshkowska J, Gratchev A, **Saunders BM,** Wessels J, Möbius W, Kaene J, Becker H, Neumaier M & Kaminski W. *A TNFα-regulated variable macrophage immunoreceptor implicated in tuberculosis granuloma formation. 2011.* **Plos Pathog.** 2011 Nov;7(11):1-16.

Benseler V, Tay SS, Bowen DG, Bertolino P. *Role of the hepatic parenchyma in liver transplant tolerance: a paradigm revisited.* **Dig Dis.** 2011;29(4):391-401.

Benseler V, Warren A, **Vo M,** Holz LE, **Tay SS,** Le Couteur DG, **Breen E,** Allison AC, van Rooijen N, **McGuffog C,** Schlitt HJ, **Bowen DG, McCaughan GW, Bertolino P.** *Hepatocyte entry leads to degradation of autoreactive CD8 T cells.* **Proc Natl Acad Sci USA.** 2011 Oct 4;108(40):16735-40.

Bishop GA, Ierino FL, **Sharland AF,** Hall BM, Alexander SI, Sandrin MS, Coates PT, **McCaughan GW.** *Approaching the promise of operational tolerance in clinical transplantation.* **Transplantation.** 2011 91(10):1065-74.

Boase NA, Rychkov GY, Townley SL, Dinudom A, Candi E, Voss AK, **Tsoutsman T, Semsarian C,** Melino G, Koentgen F, Cook DI, Kumar S. *Respiratory distress and perinatal lethality in Nedd4-2-deficient mice.* **Nat Commun.** 2011;2:287.

Bokil NJ, Totsika M, Carey AJ, Stacey KJ, Hancock V, **Saunders BM,** Ravasi T, Ulett GC, Schembri MA, Sweet MJ. *Intramacrophage survival of uropathogenic Escherichia coli: differences between diverse clinical isolates and between mouse and human macrophages.* **Immunobiology.** 2011 Nov;216(11):1164-71.

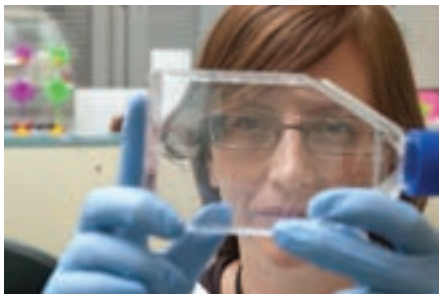
Both G, Alexander I, Fletcher S, Nicolson TJ, **Rasko JE,** Wilton SD, Symonds G. *Gene therapy: therapeutic applications and relevance to pathology.* **Pathology.** 2011 Oct;43(6):642-56.

Bröer A, Juelich T, **Vanslambrouck JM,** Tietze N, Solomon PS, **Holst J, Bailey CG, Rasko JE,** Bröer S. *Impaired nutrient signaling and body weight control in a Na+ neutral amino acid cotransporter (Slc6a19)-deficient mouse.* **J Biol Chem.** 2011 Jul 29;286(30):26638-51.

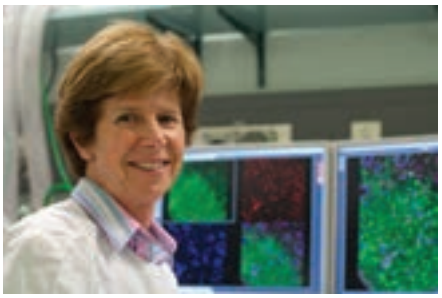
Chang JT, Ciocca ML, **Kinjyo I,** Palanivel VR, McClurkin CE, Dejong CS, Mooney EC, Kim JS, Steinel NC, Oliaro J, Yin CC, Florea BI, Overkleeft HS, Berg LJ, Russell SM, Koretzky GA, Jordan MS, Reiner SL. *Asymmetric proteasome segregation as a mechanism for unequal partitioning of the transcription factor T-bet during T lymphocyte division.* **Immunity.** 2011 Apr 22;34(4):492-504.

Cheung TC, Ware CF. *The canonical and unconventional ligands of the herpesvirus entry mediator.* **Adv Exp Med Biol.** 2011;691:353-62.

Choi PYI, Dunkley S, **Rasko JEJ.** *Immune thrombocytopenia: a diagnosis of exclusion.* **Medicine Today.** 2011; 12(3): 41-46

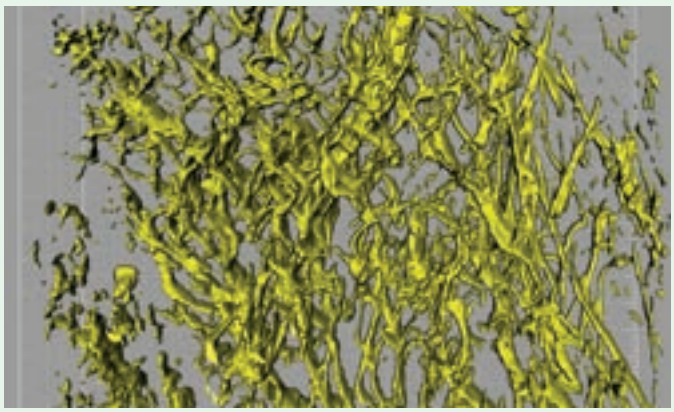


Laura Yates, Cardiovascular Genetics Counselor, Molecular Cardiology



Faculty, Professor Jennifer Gamble, Vascular Biology

Faculty, Professor Barbara Fazekas de St Groth, T Cell Biology



Phillip Tong, PhD Candidate, Immune Imaging

Choi, PY-I, **Rasko JEJ.** *The challenge of investigating thrombocytopenia.* **Medicine Today.** 2011 12(2):26-35.

Engler JR, Zannettino AC, **Bailey CG, Rasko JE,** Hughes TP, White DL. *OCT-1 function varies with cell lineage but is not influenced by BCR-ABL.* **Haematologica.** 2011 Feb;96(2):213-20.

Eshoo S, **Semsarian C,** Ross DL, Marwick TH, Thomas L. *Comparison of left atrial phasic function in hypertrophic cardiomyopathy versus systemic hypertension using strain rate imaging.* **Am J Cardiol.** 2011 Jan 15;107(2):290-6.

Fazekas de St Groth B, Zhu E, Asad S, Lee L. *Flow cytometric detection of human regulatory T cells.* **Methods Mol Biol.** 2011;707:263-79.

Fox GJ, Britton WJ. *Learning from the genetics of enteric tuberculosis.* **J Gastroenterol Hepatol.** 2011 Jul;26(7):1086-8.

Gamble JR, Vadas MA, McCaughan G. *Sinusoidal endothelium is essential for liver regeneration.* **Hepatology.** 2011 Aug;54(2):731-3.

Gardam S, Turner VM, Anderton H, **Limaye S,** Basten A, Koentgen F, Vaux DL, Silke J, Brink R. *Deletion of cIAP1 and cIAP2 in murine B lymphocytes constitutively activates cell survival pathways and inactivates the germinal center response.* **Blood.** 2011 Apr 14;117(15):4041-51.

Gorrell MD, Zekry A, **McCaughan GW,** Lloyd A. *The long and the short of interferon-gamma-inducible protein 10 in hepatitis C virus infection.* **Hepatology.** 2011 54(5):1875-9.

Grant D, Fisher RA, Abecassis M, **McCaughan G,** Wright L, Fan ST. *Should the liver transplant criteria for hepatocellular carcinoma be different for deceased donation and living donation?* **Liver Transpl.** 2011 17 Suppl 2:S133-8.

Gray B, **Ingles J, Semsarian C.** *Natural history of genotype positive-phenotype negative patients with hypertrophic cardiomyopathy.* **Int J Cardiol.** 2011 Oct 20;152(2):258-9.

Gu BJ, **Saunders BM,** Petrou S, Wiley JS. *P2X(7) is a scavenger receptor for apoptotic cells in the absence of its ligand, extracellular ATP.* **J Immunol.** 2011 Sep 1;187(5):2365-75.

Herbert KE, Levesque JP, Mills AK, Gottlieb DJ, Cooney J, Szer J, **Rasko J,** To LB. *How we mobilize haemopoietic stem cells.* **Intern Med J.** 2011 Aug;41(8):588-94.

Hersey P, Smalley KS, Weeraratna A, Bosenberg M, Zhang XD, **Haass NK,** Paton E, Mann G, Scolyer RA, Tüting T. *Meeting report from the 7th International Melanoma Congress, Sydney, November, 2010.* **Pigment Cell Melanoma Res.** 2011 Oct;24(5):989.

Ingles J, Yeates L, Hunt L, McGaughran J, Scuffham PA, Atherton J, **Semsarian C.** *Health status of cardiac genetic disease patients and their at-risk relatives.* **Int J Cardiol.** 2011 Sep 17. (Epub ahead of print).

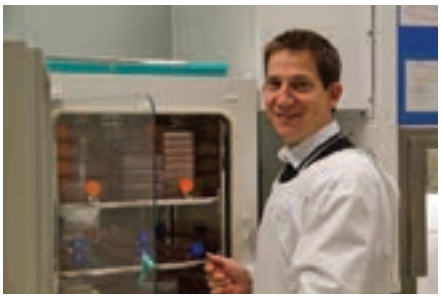
Ingles J, Yeates L, Semsarian C. *The emerging role of the cardiac genetic counselor.* **Heart Rhythm.** 2011 Dec;8(12):1958-62.

Ingles J, Zodgekar PR, **Yeates L,** Macciocca I, **Semsarian C,** Fatkin D; *CSANZ Cardiac Genetic Diseases Council Writing Group. Guidelines for genetic testing of inherited cardiac disorders.* **Heart Lung Circ.** 2011 Nov;20(11):681-7.

John B, Ricart B, Tait Wojno ED, Harris TH, Randall LM, Christian DA, Gregg B, De Almeida DM, **Weninger W,** Hammer DA, Hunter CA. *Analysis of behavior and trafficking of dendritic cells within the brain during toxoplasmic encephalitis.* **PLoS Pathog.** 2011 Sep;7(9):e1002246. Epub 2011 Sep 15.

Keane FM, Nadvi NA, Yao TW, Gorrell MD. *Neuropeptide Y, B-type natriuretic peptide, substance P and peptide YY are novel substrates of fibroblast activation protein-α.* **FEBS J.** 2011 278(8):1316-32.

2011 Publications



Associate Faculty, Dr Nick West, Mycobacterial

Assistant Director, Faculty, Professor Geoff McCaughan, Liver Injury & Cancer

Kelly M, Bagnall RD, Peverill RE, Donelan L, Corben L, Delatycki MB, **Semsarian C.** *A polymorphic miR-155 binding site in AGTR1 is associated with cardiac hypertrophy in Friedreich ataxia.* **J Mol Cell Cardiol.** 2011 Nov;51(5):848-54.

Kilmartin JR, **Maher MJ,** Krusong K, Noble CJ, Hanson GR, Bernhardt PV, Riley MJ, Kappler U. *Insights into structure and function of the active site of SoxAX cytochromes.* **J Biol Chem.** 2011 Jul 15;286(28):24872-81.

Kong CU, **Ng LG, Nambiar JK,** Spratt JM, **Weninger W, Triccas JA.** *Targeted induction of antigen expression within dendritic cells modulates antigen-specific immunity afforded by recombinant BCG.* **Vaccine.** 2011 Feb 4;29(7):1374-81.

Kota BP, **Allen JD,** Roufogalis BD. *The effect of vitamin D3 and ketoconazole combination on VDR-mediated P-gp expression and function in human colon adenocarcinoma cells: implications in drug disposition and resistance.* **Basic Clin Pharmacol Toxicol.** 2011 Aug;109(2):97-102.

Lasaro MO, Sazanovich M, Giles-Davis W, **Mrass P,** Bunte RM, Sewell DA, Hussain SF, Fu YX, **Weninger W,** Paterson Y, Ertl HC. *Active immunotherapy combined with blockade of a coinhibitory pathway achieves regression of large tumor masses in cancer-prone mice.* **Mol Ther.** 2011 Sep;19(9):1727-36.

Lo L, McLennan SV, Williams PF, Bonner J, **Chowdhury S, McCaughan GW, Gorrell MD, Yue DK,** Twigg SM. *Diabetes is a progression factor for hepatic fibrosis in a high fat fed mouse obesity model of non-alcoholic steatohepatitis.* **J Hepatol.** 2011 Aug;55(2):435-44.

Macpherson JL, **Rasko JEJ.** *Cellular therapy in the Asia-Pacific region. A guide for the future pathologist.* **Pathology.** Oct 2011 43(6):616-626.

Maron BJ, Ahluwalia A, Haas TS, **Semsarian C,** Link MS, Estes NA 3rd. *Global epidemiology and demographics of commotio cordis.* **Heart Rhythm.** 2011 Dec;8(12):1969-71.

Maron BJ, **Yeates L, Semsarian C.** *Clinical challenges of genotype positive (+)-phenotype negative (-) family members in hypertrophic cardiomyopathy.* **Am J Cardiol.** 2011 Feb 15;107(4):604-8

Martin JH, Deacon CF, **Gorrell MD,** Prins JB. *Incretin-based therapies – review of the physiology, pharmacology and emerging clinical experience.* **Intern Med J.** 2011 Apr;41(4):299-307.

McCaughan GW, Bowen DG. *Pathogenesis of cholestatic hepatitis C.* **J Hepatol.** 2011 Feb;54(2):392-4.

McCaughan GW, Shackel NA, Bowen DG. *Liver transplantation and hepatitis C: will understanding the interleukin-28B polymorphisms improve outcomes?* **Liver Transpl.** 2011 17(3):219-21.

McGowan EM, Alling N, **Jackson EA, Yagoub D, Haass NK, Allen JD, Martinello-Wilks R.** *Evaluation of cell cycle arrest in estrogen responsive MCF-7 breast cancer cells: pitfalls of the MTS assay.* **PLoS One.** 2011;6(6):e20623. Epub 2011 Jun 3.

Miller CM, Boulter NR, Fuller SJ, Zakrzewski AM, Lees MP, **Saunders BM,** Wiley JS, Smith NC. *The role of the P2X$_7$ receptor in infectious diseases.* **PLoS Pathog.** 2011 Nov;7(11):e1002212. Epub 2011 Nov 10.

Ng DC, Ng IH, Yeap YY, Badrian B, **Tsoutsman T,** McMullen JR, **Semsarian C,** Bogoyevitch MA. *Opposing actions of extracellular signal-regulated kinase (ERK) and signal transducer and activator of transcription 3 (STAT3) in regulating microtubule stabilization during cardiac hypertrophy.* **J Biol Chem.** 2011 Jan 14;286(2):1576-87.

Ng LG, Qin JS, Roediger B, Wang Y, **Jain R, Cavanagh LL, Smith AL,** Jones CA, de Veer M, Grimbaldeston MA, Meeusen EN, **Weninger W.** *Visualizing the neutrophil response to sterile tissue injury in mouse dermis reveals a three-phase cascade of events.* **J Invest Dermatol.** 2011 Oct;131(10):2058-68.

Faculty, Professor John Rasko AO, Gene and Stem Cell Therapy

Dr Ben Roediger, Research Officer, Immune Imaging

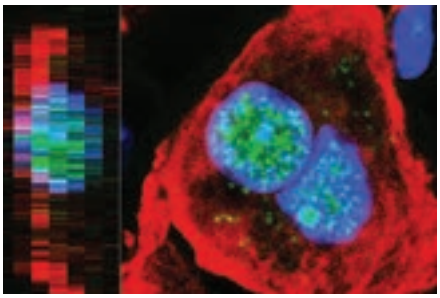


Image by Research Officer, Dr Alison Morgan, Liver Immunobiology

Nguyen LS, Jolly L, Shoubridge C, Chan WK, Huang L, Laumonnier F, Raynaud M, Hackett A, Field M, Rodriguez J, Srivastava AK, Lee Y, Long R, Addington AM, Rapoport JL, Suren S, Hahn CN, **Gamble JR,** Wilkinson MF, Corbett MA, Gecz J. *Transcriptome profiling of UPF3B/NMD-deficient lymphoblastoid cells from patients with various forms of intellectual disability.* **Mol Psychiatry.** 2011 Dec 20. (Epub ahead of print).

O'Sullivan BJ, **Pai S,** Street S, An X, MacDonald KP, Wong M, Strutton G, Gerondakis S, Steptoe RJ, **Fazekas de St Groth B,** Hill GR, Thomas R. *Immunotherapy with costimulatory dendritic cells to control autoimmune inflammation.* **J Immunol.** 2011 Oct 15;187(8):4018-30.

Poustchi H, Farrell GC, Strasser SI, Lee AU, **McCaughan GW,** George J. *Feasibility of conducting a randomized control trial for liver cancer screening: is a randomized controlled trial for liver cancer screening feasible or still needed?* **Hepatology.** 2011 Dec;54(6):1998-2004.

Power C, **Rasko JE.** *Will cell reprogramming resolve the embryonic stem cell controversy? A narrative review.* **Ann Intern Med.** 2011 Jul 19;155(2):114-21.

Power C, **Rasko JE.** *Promises and challenges of stem cell research for regenerative medicine.* **Ann Intern Med.** 2011 Nov 15;155(10):706-13

Prakoso E, Fulham M, Thompson JF, Selby WS. *Capsule endoscopy versus positron emission tomography for detection of small-bowel metastatic melanoma: a pilot study.* **Gastrointest Endosc.** 2011 Apr;73(4):750-6.

Qian L, Wythe JD, Liu J, Cartry J, Vogler G, Mohapatra B, Otway RT, Huang Y, King IN, Maillet M, Zheng Y, Crawley T, Taghli-Lamallem O, **Semsarian C,** Dunwoodie S, Winlaw D, Harvey RP, Fatkin D, Towbin JA, Molkentin JD, Srivastava D, Ocorr K, Bruneau BG, Bodmer R. *Tinman/Nkx2-5 acts via miR-1 and upstream of Cdc42 to regulate heart function across species.* **J Cell Biol.** 2011 Jun 27;193(7):1181-96.

Rasko JE. *Future Path: frontiers of molecular and cellular pathology.* **Pathology.** 2011 Oct;43(6):523-4.

Roediger B, Weninger W. *How nickel turns on innate immune cells.* **Immunol Cell Biol.** 2011 Jan;89(1):1-2.

Semsarian C; CSANZ Cardiac Genetics Diseases Council Writing Group. *Guidelines for the diagnosis and management of hypertrophic cardiomyopathy.* **Heart Lung Circ.** 2011 Nov;20(11):688-90.

Seth D, Haber PS, Syn WK, Diehl AM, Day CP. *Pathogenesis of alcohol-induced liver disease: classical concepts and recent advances.* **J Gastroenterol Hepatol.** 2011 Jul;26(7):1089-105.

Shklovskaya E, O'Sullivan BJ, Ng LG, **Roediger B,** Thomas R, **Weninger W, Fazekas de St Groth B.** *Langerhans cells are precommitted to immune tolerance induction.* **Proc Natl Acad Sci USA.** 2011 Nov 1;108(44):18049-54.

Sievert W, Altraif I, Razavi HA, Abdo A, Ahmed EA, Alomair A, Amarapurkar D, Chen CH, Dou X, El Khayat H, Elshazly M, Esmat G, Guan R, Han KH, Koike K, Largen A, **McCaughan G,** Mogawer S, Monis A, Nawaz A, Piratvisuth T, Sanai FM, Sharara AI, Sibbel S, Sood A, Suh DJ, Wallace C, Young K, Negro F. *A systematic review of hepatitis C virus epidemiology in Asia, Australia and Egypt.* **Liver Int.** 2011 Jul;31 Suppl 2:61-80.

Sievert W, Dore GJ, **McCaughan GW,** Yoshihara M, Crawford DH, Cheng W, Weltman M, Rawlinson W, Rizkalla B, Depamphilis JK, Roberts SK; CHARIOT Study Group. *Virological response is associated with decline in hemoglobin concentration during pegylated interferon and ribavirin therapy in hepatitis C virus genotype.* **Hepatology.** 2011 Apr;53(4):1109-17.

Smith NJ, Chan HW, Qian H, Bourne AM, Hannan KM, **Warner FJ,** Ritchie RH, Pearson RB, Hannan RD, Thomas WG. *Determination of the exact molecular requirements for type 1 angiotensin receptor epidermal growth factor receptor transactivation and cardiomyocyte hypertrophy.* **Hypertension.** 2011 May;57(5):973-80.

Song S, Shackel NA, Wang XM, Ajami K, McCaughan GW, Gorrell MD. *Discoidindomain receptor 1: isoform expression and potential functions in cirrhotic human liver.* **Am J Pathol.** 2011 178(3):1134-44.

Stanley AC, de Labastida Rivera F, Haque A, Sheel M, Zhou Y, Amante FH, Bunn PT, Randall LM, Pfeffer K, Scheu S, Hickey MJ, **Saunders BM,** Ware C, Hill GR, Tamada K, Kaye PM, Engwerda CR. *Critical roles for LIGHT and its receptors in generating T cell-mediated immunity during Leishmania donovani infection.* **PLoS Pathog.** 2011 Oct;7(10):e1002279. Epub 2011 Oct 6.

2011 Publications

Faculty, Associate Professor Pu Xia, Signal Transduction

Sumaria N, Roediger B, Ng LG, Qin J, Pinto R, Cavanagh LL, Shklovskaya E, Fazekas de St Groth B, Triccas JA, Weninger W. *Cutaneous immunosurveillance by self-renewing dermal gammadelta T cells.* **J Exp Med.** 2011 Mar 14;208(3):505-18.

To LB, Levesque JP, Herbert KE, Winkler IG, Bendall LJ, Hiwase DK, Antonenas V, Rice AM, Gottlieb D, Mills AK, **Rasko JE, Larsen S,** Beligaswatte A, Nilsson SK, Cooney JP, Cambareri AC, Lewis ID. *Mobilisation strategies for normal and malignant cells.* **Pathology.** 2011 Oct;43(6):547-65.

Tran AT, Cergol KM, **West NP, Randall EJ, Britton WJ,** Bokhari SA, Ibrahim M, Lapthorn AJ, Payne RJ. *Synthesis and evaluation of potent ene-yne inhibitors of type II dehydroquinases as tuberculosis drug leads.* **ChemMedChem.** 2011 Feb 7;6(2):262-5.

Triccas JA, Winter N, Feng CG, **West NP.** *Immunity to mycobacterium tuberculosis.* **Clin Dev Immunol.** Epub 2011.

Tu E, Bagnall RD, Duflou J, **Semsarian C.** *Post-mortem review and genetic analysis of sudden unexpected death in epilepsy (SUDEP) cases.* **Brain Pathol.** 2011 Mar;21(2):201-8.

Tu E, Waterhouse L, Duflou J, **Bagnall RD, Semsarian C.** *Genetic analysis of hyperpolarization-activated cyclic nucleotide-gated cation channels in sudden unexpected death in epilepsy cases.* **Brain Pathol.** 2011 Nov;21(6):692-8.

Vohra J, Skinner J, **Semsarian C.** *Cardiac genetic investigation of young sudden unexplained death and resuscitated out of hospital cardiac arrest.* **Heart Lung Circ.** 2011 Dec;20(12):746-50.

Wang C, Cordoba S, Hu M, **Bertolino P, Bowen DG, Sharland AF,** Allen RD, Alexander SI, **McCaughan GW,** Bishop GA. *Spontaneous acceptance of mouse kidney allografts is associated with increased Foxp3 expression and differences in the B and T cell compartments.* **Transpl Immunol.** 2011 24(3):149-56.

Wang Q, **Bailey CG, Ng C, Tiffen J, Thoeng A,** Minhas V, Lehman ML, Hendy SC, Buchanan G, Nelson CC, **Rasko JE, Holst J.** *Androgen receptor and nutrient signaling pathways coordinate the demand for increased amino acid transport during prostate cancer progression.* **Cancer Res.** 2011 Dec 15;71(24):7525-36.

Warren A, **Benseler V,** Cogger VC, **Bertolino P,** Le Couteur DG. *The impact of poloxamer 407 on the ultrastructure of the liver and evidence for clearance by extensive endothelial and kupffer cell endocytosis.* **Toxicol Pathol.** 2011 39(2):390-7.

West NP, Cergol KM, Xue M, **Randall EJ, Britton WJ,** Payne RJ. *Inhibitors of an essential mycobacterial cell wall lipase (Rv3802c) as tuberculosis drug leads.* **Chem Commun (Camb).** 2011 May 14;47(18):5166-8.

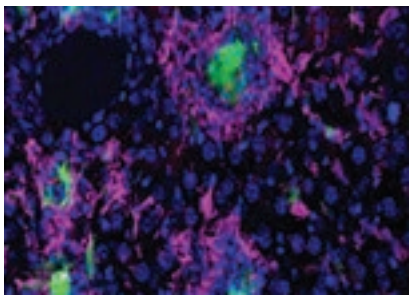
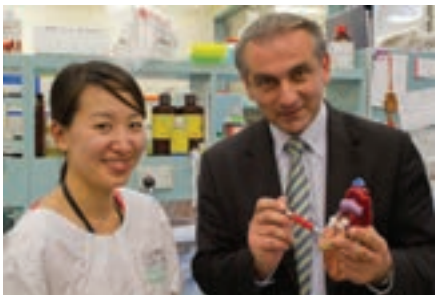
West NP, Thomson SA, **Triccas JA,** Medveczky CJ, Ramshaw IA, **Britton WJ.** *Delivery of a multivalent scrambled antigen vaccine induces broad spectrum immunity and protection against tuberculosis.* **Vaccine.** 2011 Oct 13;29(44):7759-65.

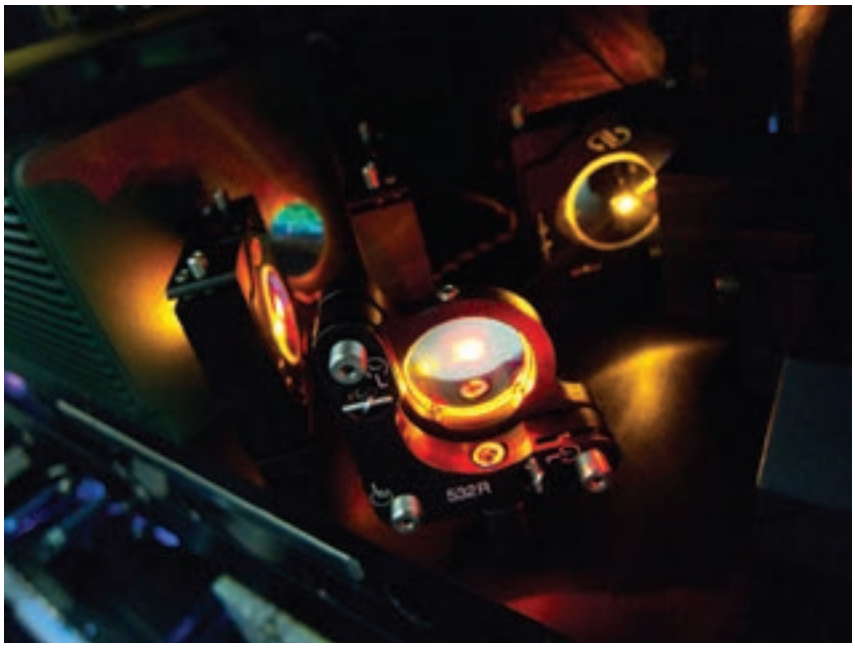
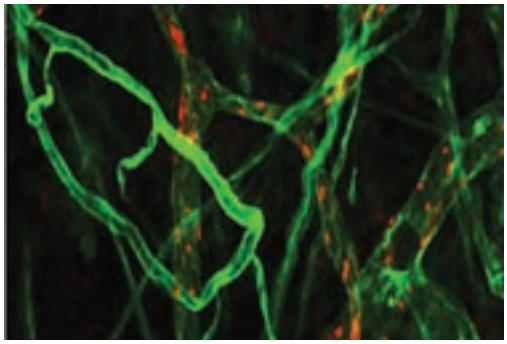
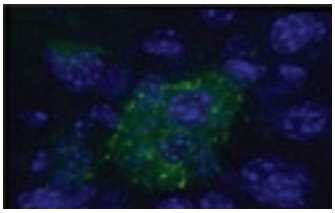
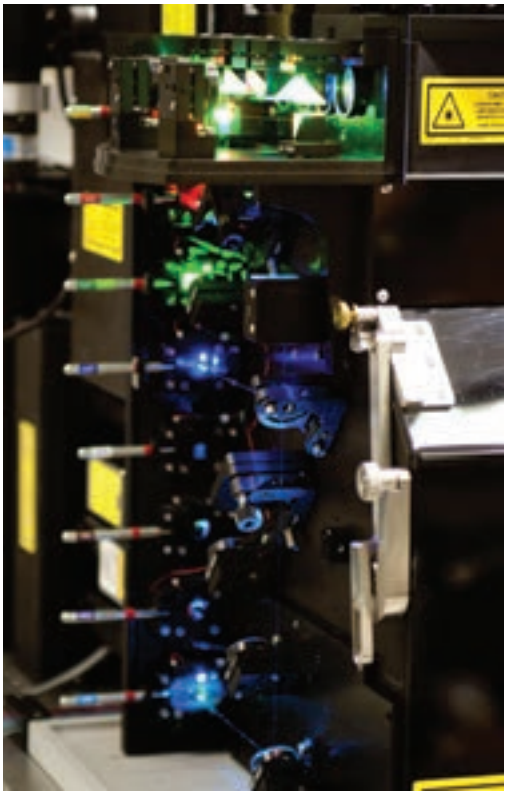
Wood NA, Linn ML, Bowen DG. *Exhausted or just sleeping: awakening virus-specific responses in chronic hepatitis C virus infection.* **Hepatology.** 2011 54(5):1879-82.

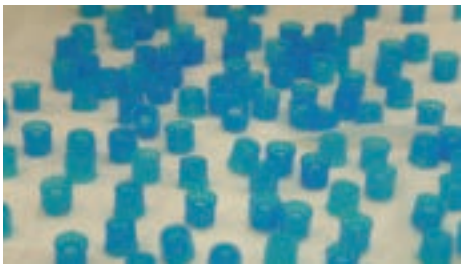
Xia P, Wadham C. *Sphingosine 1-phosphate, a key mediator of the cytokine network: juxtacrine signaling.* **Cytokine Growth Factor Rev.** 2011 Feb;22(1):45-53.

Yao TW, Kim WS, **Yu DM, Sharbeen G, McCaughan GW,** Choi KY, **Xia P, Gorrell MD.** *A novel role of dipeptidyl peptidase 9 in epidermal growth factor signaling.* **Mol Cancer Res.** 2011 9(7):948-59.

Yu DMT, Gysbers V, Riekhoff AG, Kähne T, Knott HM, De Meester I, Abbott CA, **McCaughan GW, Gorrell MD.** *Soluble CD26/dipeptidyl peptidase IV enhances human lymphocyte proliferation in vitro independent of dipeptidyl peptidase enzyme activity and adenosine deaminase binding.* **Scand J Immunol.** 2011 Feb;73(2):102-11.

Top to bottom: Research Assistant Angel Pang, PhD Scholar Erin Shanahan & Associate Faculty, Dr Nick West, Mycobacterial; Research Officer Emily Tu, Assistant Director, Faculty, Professor Christopher Semsarian, Molecular Cardiology; Dr Szun Tay, Faculty Dr David Bowen, Michelle Vo, PhD Scholar, Liver Immunology

2011 Invited Presentations

Research Officer, Emily Tu, Assistant Director, Faculty, Professor Christopher Semsarian, Molecular Cardiology

International

Holst J, ISREC Hallmarks and Horizons of Cancer Conference, September 2011, Lausanne, Switzerland

Holst J, INSERM, Villejuif, September 2011, France

Holst J, Regina Elena Cancer Centre, September 2011, Rome, Italy

Haass N, Loss of Noxa delays melanomagenesis in a genetically-defined, pre-disposed mouse melanoma model (presenter: **Nethia Mohana-Kumaran**), Florida International University, November 2011, Miami, USA

Haass N, MITF expression dictates the subcompartment-specific distribution of differentially cycling tumor cells in melanoma, 8th International Melanoma Research Congress, November 2011, Tampa, USA

Haass N, Real-time cell cycle analysis in 3D and in vivo Melanoma Symposium, Moffitt Cancer Center, November 2011, Tampa, USA

Haass N, Melanomas are composed of differentially cycling tumour cells in a subcompartment-specific distribution, Singapore Immunology Network, A*STAR, July 2011, Singapore

Haass N, Novel imaging techniques to study cell cycle regulation in melanoma, Experimental Dermatological Oncology Workshop, XXXVIII Arbeitsgemeinschaft Dermatologische Forschung (ADF) Annual Meeting, February 2011, Tübingen, Germany

Rasko J, New Developments in Cellular Therapy, HSA Academy Symposium Scientific Advances and Regulation in Blood and Cellular Therapy, July 2011, Singapore

Rasko J, The Promise of Prometheus: The Past and Future of Regeneration Research, Brocher Foundation Seminar Series, September 2011, Geneva, Switzerland

Rasko J, Down Under Dinner: CML for starters and HSC microenvironment for entrée, University of Chicago, October 2011, Chicago, USA

Rasko J, An Elastic Microenvironment Preserves Primitive Haemopoietic Cells, Weill Cornell Stem Cell Research and Regenerative Community Seminar Series, Cornell University, October 2011, New York, USA

Vadas M, Dynamic phenotypes of endothelium: inflammation, angiogenesis and senescence, Nara Inst of Science & Technology, February 2011, Japan

Britton W, Improving BCG the APC way, JALMA Medical Research Institute, May 2011, Agra, India

Britton W, Infectiologie Animale et Santé Publique, June 2011, INRA Centre de Tours Nouzilly, France

Britton W, Laboratoire Immunologie et Embryologie Moléculaires, CNRS, June 2011, Orleans, France

Britton W, Institut Pasteur, June 2011, Paris, France

Britton W, National Institute for Medical Research, Mill Hill, June 2011, London, UK

Britton W, Influenza A virus infection impairs BCG-specific T cell responses and mycobacterial clearance during pulmonary infection with BCG and influenza A virus, Eighth International Conference on the Pathogenesis of Mycobacterial Infections, Saltsjobaden, June 2011, Stockholm, Sweden

Britton W, Tuberculosis vaccines: Status and Path Forward, September 2011, Beijing, China

Britton W, Genetic susceptibility to Tuberculosis, role of P2X7, Shenzhen-Hong Kong Institute of Infectious Diseases, September 2011, Shenzhen, China

Gorrell M, Novel role of fibroblast activation protein in energy metabolism, 7th International Proteolysis Society General Meeting, October 2011, San Diego, USA

Gorrell M, Novel role of fibroblast activation protein in an experimental model of obesity and liver steatosis, Asian Pacific Association for the Study of the Liver, Hepatology International, Vol. 5: p. 37, February 2011, Bangkok, Thailand

Xia P, Targeting sphingosine kinase 1 for cancer treatment, The 4th World Cancer Congress, May 2011, Dalian, China

Xia P, Understanding the mechanism of pancreatic beta cell survival—towards to translating from benches to bedsides, Peking Union Hospital, Beijing, China

Xia P, Targeting sphingolipid metabolic pathway for anti-cancer drug development, Guangdong Pharmaceutical University, Guangzhou, China

Xia P, The 14th Convention of Overseas Chinese Scholars in Science and Technology, December 2011, Guangzhou, China

Semsarian C, Double or compound mutations in hypertrophic cardiomyopathy, American Heart Association Scientific Meeting, November 2011, Orlando, USA

Semsarian C, State of postmortem genetic testing for inherited heart diseases, Scientific Sessions of the Heart Rhythm Society, May 2011, San Francisco, USA

Semsarian C, Utility of HCM gene testing in children, Scientific Sessions of the Heart Rhythm Society, San Francisco, USA

Ingles J, Key role of genetic counselling in cardiac genetic diseases, Scientific Sessions of the American Heart Association, November 2011, Orlando, USA

Ingles J, Yeates L, Hunt L, McGaughran J, Scuffham PA, Atherton J, **Semsarian C**, Health status of cardiac genetic disease patients and their at-risk relatives, Heart Rhythm Society's 32nd Annual Scientific Sessions, May 2011, San Francisco, USA

McCaughan G, Indication and Timing of Liver Transplant. APASL. Bangkok, Thailand. February 2011

McCaughan G, Post-transplant HBV prophylaxis – What is best and how can we minimize it? APASL. Bangkok, Thailand. February 2011

McCaughan G, Treatment of Decompensated HBV with the new drugs. New Zealand viral hepatitis meeting. Auckland, New Zealand. June 2011'

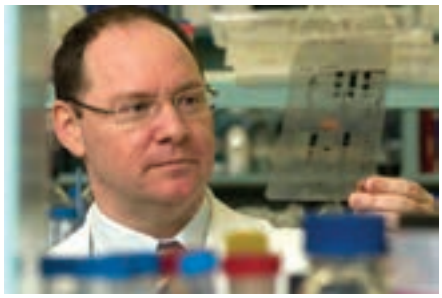
McCaughan G, Antiviral Therapy for HCV: Impact of Retransplantation. ILTS. Valencia, Spain. June 2011

McCaughan G, Outcomes in Liver Transplantation : Alcoholic Liver Disease. Seoul, Korea. September 2011

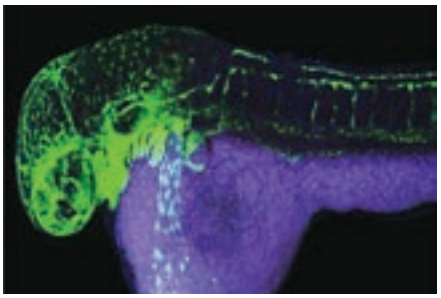
McCaughan G, Long-term HBV Recurrence – The case for no HBIG. CAST. Seoul, Korea. September 2011

McCaughan G, Prevention of HBV recurrence post liver transplant. ILTS Satellite meeting. Istanbul, Turkey. October 2011

Fazekas de St Groth B, Workshop speaker, Keystone Symposium on Immunoregulatory Networks, Breckenridge, USA, 2011



Faculty, Professor John Rasko AO, Gene and Stem Cell Therapy



Ka Ka Ting, Research Officer, Vascular Biology, "Pisci lucidem viridis", finalist in 2012 Centenary Institute Scientific Image Prize

Associate Faculty, Dr Nikolas Haass, Immune Imaging

Saunders BM, Eighth International Conference on the Pathogenesis of Mycobacterial Infections. Sweden June 2011.

Saunders BM, Walters SB, Kieckbusch J, Grau GE, Britton WJ & Combes V, Mycobacteria infected macrophages release microparticles that modulate inflammation and antigen presentation, Eighth International Conference on the Pathogenesis of Mycobacterial Infections, June 2011, Sweden.

Shackel N, A novel role of CD147 in liver immune cell aggregation and intrahepatic inflammation, International Cells of the Hepatic Sinusoid, 2011, Florence Italy

Bertolino P, Mechanisms of liver transplantation tolerance, Falk Symposium: Immunology and liver, January 2011, Regensburg, Germany

Weninger W, Institute of Molecular Biotechnology Seminar Series, 2011, Vienna, Austria

Weninger W, Department of Dermatology Seminar Series, Medical University of Vienna, 2011, Vienna, Austria

National

Holst J, 12th Australasian Prostate Cancer Conference, August 2011, Melbourne, Vic

Holst J, PACRIM Breast and Prostate Cancer Meeting, May 2011, Kingscliff, NSW

Holst J, NBCF and PCFA Annual Research Update, February 2011, Sydney, NSW

Holst J, SAN Hospital Prostate Cancer Support Group, July 2011, Sydney, NSW

Holst J, Price Waterhouse Coopers, Health and Wellness Month, October 2011, Sydney, NSW

Haass N, Real-time cell cycle imaging in 3D tumour microenvironment and in vivo models, MEPSA, November 2011, Brisbane, Qld

Haass N, 3D tumour microenvironment models for anti-melanoma drug discovery, Centre for Health Technologies, University of Technology, July 2011, Sydney, NSW

Haass N, Real-time cell cycle imaging in 3D and in vivo, Techniques in Cancer Research Workshop, University of Sydney, June 2011, Sydney, NSW

Haass N, Melanomas are composed of differentially cycling tumour cells in a subcompartment-specific distribution, 8th ASDR Annual Scientific Meeting, May 2011, Perth, WA

Rasko J, Substrate elasticity preserves primitive haemopoietic cells, Peter MacCallum Cancer Centre, March 2011, Melbourne, Vic

Rasko J, Substrate elasticity preserves primitive haemopoietic cells, 11th Hunter Meeting, March 2011, Pokolbin, NSW

Rasko J, Disambiguating epigenetics, RCPA Pathology Update, March 2011, Melbourne, Vic

Rasko J, Stem cells and regenerative medicine: prospects for realizing the Prometheus myth, Royal Society of NSW, July 2011, Sydney, NSW

Rasko J, Substrate elasticity preserves primitive haemopoietic cells, Inflammation and Infection Research Centre (IIRC) 2011 Seminar Series, University of New South Wales, August 2011, Sydney, NSW

Vadas M, BIO Innovation, July 2011, Adelaide, Sth Australia

Vadas M, LICR Translational Oncology Conference, October 2011, Melbourne, Vic

Gamble J, Australian Vascular Biology Society Conference, 2011, Bowral NSW

Britton W, How sequencing of mycobacterial genomes has contributed to understanding of pathogenesis, diagnosis and treatment in Leprosy and Tuberculosis, March 2011

Britton W, TB vaccines—practicalities of introduction, Royal College of Pathologists Australasian Annual Scientific Conference, March 2011, Melbourne, Vic

Britton W, Implications of genomics and RNA sequencing for study of host-pathogen interactions in Tuberculosis, Tuberculosis Research symposium, Woolcock Institute for Medical Research, May 2011, Sydney, NSW

Britton W, BCG vaccination and Novel Tuberculosis vaccine strategies, Tuberculosis Course, Woolcock Institute for Medical Research, May 2011, Sydney, NSW

Britton W, Balancing the risks and benefits of anti-TNF therapy, Rheumatology Meeting, July 2011, Canberra, ACT

Britton W, Cellular Communication and macrophage activation in the control of mycobacterial infections, Immunology Group of Victoria Winter Seminar, Burnet Institute, August 2011, Melbourne, Vic

Britton W, Use of Interferon-release assays in the diagnosis of tuberculosis infection, NSW Tuberculosis Day, August 2011, North Sydney, NSW

Gorrell M, Hepatic steatosis and investigating incretin-based type 2 diabetes therapeutics for preventing NASH, Liver Down Under, December 2011, Perth, WA

Gorrell M, A novel action of dipeptidyl peptidase 9 in Akt dependent epidermal growth factor signalling and apoptosis, Australian Liver Association, May 2011, Kiama, NSW

Gorrell M, Neuropeptide Y, B-type natriuretic peptide, substance P and peptide YY are novel substrates of fibroblast activation protein-α, Australian Liver Association Conference, May 2011, Kiama, NSW

Gorrell M, Novel role of fibroblast activation protein in an experimental model of obesity and liver steatosis, Australian Liver Association, May 2011, Kiama, NSW

Xia P, Death on the Reef, The 1st Australian Workshop on Cell Death, August 2011, Lindeman Island, Qld

Semsarian C, Sudden Death, FRACP BPT Revision Course, Sydney, NSW

Semsarian C, Genes and sudden death, Medical Technology Association of Australia Conference, Sydney, NSW

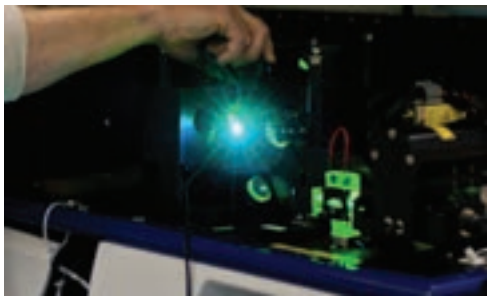
Semsarian C, Genetic basis of cardiac diseases, Australian Vascular Biology Society Annual Scientific Meeting, Bowral, NSW

Semsarian C, Fellowships: What are the benchmarks and how to be competitive, ASMR Professional Development Program, Sydney, NSW

Semsarian C, Personalised approach to sudden death in the young, 20th Annual RBWH Health Care Symposium, October 2011, Brisbane, Qld

Semsarian C, Update on genetic testing in HCM, CSANZ Annual Scientific Meeting, August 2011, Perth, WA

Semsarian C, Screening for sudden cardiac death, CSANZ Annual Scientific Meeting, August 2011, Perth, WA



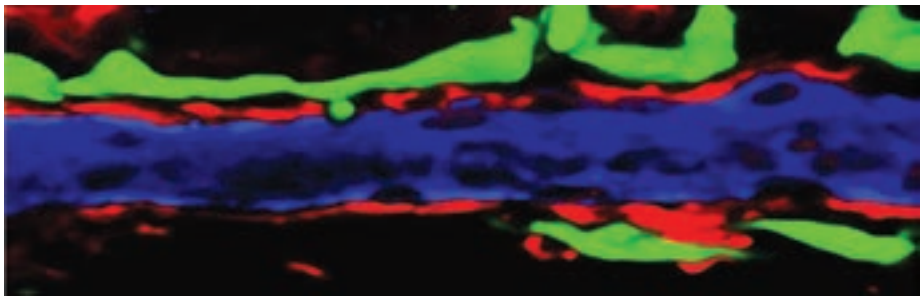


Image by Dr Rohit Jain, Research Officer, Immune Imaging

Semsarian C, Sudden cardiac death in the young, Human Genetics Society of Australasia, July 2011, Gold Coast, Qld

Semsarian C, Getting to the heart of sudden cardiac death, ICD Support Group, Kolling Institute, Sydney, NSW

Semsarian C, Forensic challenges in sudden cardiac death in the young, Department of Forensic Medicine, Glebe, Sydney, NSW

Semsarian C, Sudden cardiac death in the young, Victorian Institute of Forensic Medicine, Melbourne, Vic

Semsarian C, Approach to cardiac genetics in Sydney, QLD Health Genetics Workshop, Brisbane, Qld

Semsarian C, Research opportunities in cardiac genetics clinics, QLD Health Genetics Workshop, Brisbane, Qld

Jolly C, Cell cycle regulation of DNA damage and repair in antibody genes, Children's Cancer Research Institute, Westmead, April 2011, Sydney, NSW

Bowen D, Developments in immunosuppression for liver transplantation, Asia-Pacific Hepato-Pancreatico-Biliary Association Congress, September 2011, Melbourne, Vic

Jormakka M, GAGE Ion channels & Transporters Conference, Canberra, ACT

Ingles J, McGaughran J, Scuffham P, Atherton J, **Semsarian C**, A cost-effectiveness analysis of genetic testing in the evaluation of families with hypertrophic cardiomyopathy, CSANZ Annual Scientific Meeting, August 2011, Perth, WA

Ingles J, The Australian National Genetic Heart Disease Registry: An Update, CSANZ Annual Scientific Meeting, August 2011, Perth, WA

McCaughan G, IL28B in the HCV Liver Transplant Setting. National Liver transplant meeting. Gold Coast. May 2011

McCaughan G, Trends in End-Stage Liver Disease in Australia –Australian Hepatology Masterclass. Melbourne June 2011

McCaughan G, Liver disease in the non LTx patient. RNTS. Melbourne. August 2011

Fazekas de St Groth B, 14th Australasian Autoimmunity Workshop "Autoimmunity: Innovation in Pathogenesis and Therapy, 'Immunoregulatory dendritic cells" Brisbane, May 18, 2011

Fazekas de St Groth B, DC Down Under: DC Molecules and Subsets, Sydney, 11 August, 2011. 'Regulatory T cell control of DC function'.

Fazekas de St Groth B, Australian Gastroenterology Week, Brisbane, 14 September, 2011. 'The immunology of inflammatory bowel disease'.

Fazekas de St Groth B, Australasian Society for Immunology Annual Meeting, 'Regulating T cell activation via the costimulatory threshold' and 'Women in Immunology'. 2011, Adelaide

Fazekas de St Groth B, Department of Immunology, Monash University, Melbourne "The western epidemic of immune-mediated disease: is hygiene to blame?" 2011

Shklovskaya E, DC Down Under: DC Molecules and Subsets, 'Regulatory T cell control of DC function' August, 2011, Sydney

Shklovskaya E, 41st Annual Scientific Meeting of the Australasian Society of Immunology, Adelaide, Australia. Tumour Immunology Workshop speaker: Identification and characterisation of dendritic cells priming anti-tumour CD4 T cell immunity in vivo, 2011

Saunders BM, Infection and Immunity Lorne February 2011 Conference Mycobacteria infected macrophages release microparticles to modulate cell migration, inflammation and antigen presentation. February 2011, Lorne, Vic.

Shackel N, Genomics of Biliary Liver Disease, Australian Gastroenterology Week 2011, Brisbane, Qld

Shackel N, New Indications for TIPSS, Clinical Update in Gastroenterology, 2011, Melbourne, Vic

Shackel N, Portosystemic Encephalopathy Case Discussion, Hepatology Master Class, 2011, Sydney, NSW

Shackel N, Bone Marrow Stem Cells and the Liver: Is it Relevant?, Liver Down Under, 2011, Perth, WA

Shackel N, Fungal Infections in Transplantation, NSW Transplantation Update, 2011, Sydney, NSW

Shackel N, Indications for Combined Liver Kidney Transplantation, Transplantation Society of Australia and New Zealand Annual Meeting, 2011, Canberra, ACT

Shackel N, Novel Genes in Cirrhosis and Liver Cancer, Australian Phenomics Facility China Collaborative Meeting, 2011, Canberra, ACT

Shackel N, Bioinformatics in Liver disease, Royal Prince Alfred Hospital Grand Round, 2011, Sydney, NSW

Shackel N, Darling I need some bread, the newspaper and two thirds of your liver …, Royal Prince Alfred Hospital Grand Round, 2011, Sydney, NSW

Saunders BM, Mycobacteria infected macrophages release microparticles to modulate cell migration, inflammation and antigen presentation, Infection and Immunity Lorne Conference, February 2011, Lorne, Vic

Saunders BM, Regulation of macrophage activation and inflammation during tuberculosis infection, iThreeInstitute, University of Technology Sydney, 2011, Sydney, NSW

Saunders BM, Macrophages and Microparticles, unravelling the mechanisms that control Tuberculosis, Walter and Eliza Hall Institute, 2011, Melbourne, Vic

Saunders BM, Macrophages and Mycobacteria, dissecting the dance of old foes, Burnet Institute, 2011, Melbourne, Vic

Bertolino P,, Invasion of CD8 T cells in hepatocytes leads to their degradation in lysosomal compartments, Liver Down Under meeting, November –December 2011, Perth, WA

Bertolino P,, Suicidal emperipolesis: a novel mechanism to explain CD8 T cell tolerance in the liver, Children Medical Research Institute, March 2011, Sydney, NSW

Bertolino P, Hepatocyte entry leads to degradation of autoreactive CD8 T cells, Annual meeting Australian Society of immunology, December 2011, Adelaide, SA

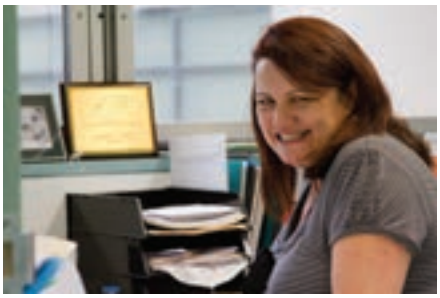
Weninger W, 11th Hunter Cellular Biology Meeting, 2011, Pokolbin, NSW

Weninger W, Monash Institute for Medical Research Seminar series, 2011, Melbourne, Vic

Weninger W, MS McLeod Research Seminars at the Women's and Children's Hospital, 2011, Adelaide, SA

Weninger W, Australasian Society of Immunology Annual Meeting, 2011, Adelaide, SA

Postgraduate Training Program



Dr Bernadette Saunders, Group Leader, Host Response to Infection, Mycobacterial Group

The Centenary Institute maintains its commitment to the development of Australia's next generation of brilliant scientists. Students in the Postgraduate Training Program come from a wide range of ethnic and academic backgrounds to work with Australia's leading medical researchers at the Institute.

The Centenary Institute congratulates the following students for their achievements in 2011.

Doctor of Philosophy (Medicine) (PhDs) Awarded 2011

Student	Supervisor	Thesis Title
Jodie Ingles	Chris Semsarian	Specialised Genetic Heart Disease Clinics: Clinical, Genetic, Psychosocial and Health economic aspects of family management
George Sharbeen	Chris Jolly	Cell Cycle Regulation of Antibody Mutation
Jessamy Tiffen	John Rasko	The Influence of BORIS and CTF on Tumour Development & Metastases in Vivo
Jessica Vanslambrouck	John Rasko	The expression of renal and intestinal amino acid transporters during development and disease
Sarah Ruth Calabro	Nick Shackel	The Role of CD147 in the Extracellular Matrix Remodelling Response to Progressive Liver Injury
Sheena Yao	Mark Gorrell	Functional characterisation of fibroblast activation protein and dipeptidyl peptidase 9
Jennifer Young	Jenny Gamble	Regulation of Angiogenesis by microRNAs
Emily Tu	Chris Semsarian	Pathological and genetic basis of sudden cardiac death in diabetes and epilepsy populations
Megha Rajasekhar	John Rasko	MicroRNA regulation of myeloid differentiation

HONOURS AWARDED 2011

Clea Grace
Elise Laming
Zainab Resland
Ashleigh Swain
Alexandra Terry
Anneliese Tyne
Chiyoko Yagasaki

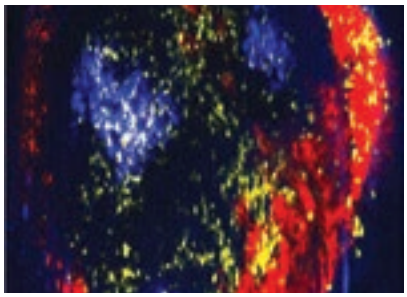
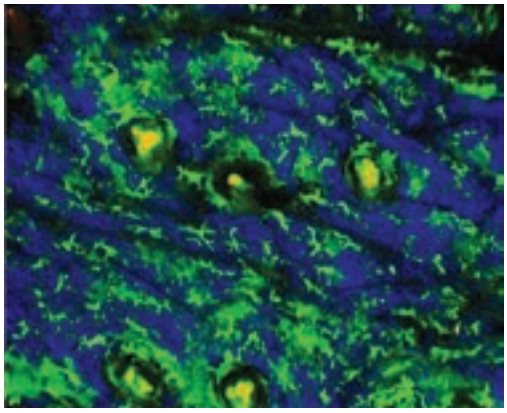
Successful 2011 Grant Recipients

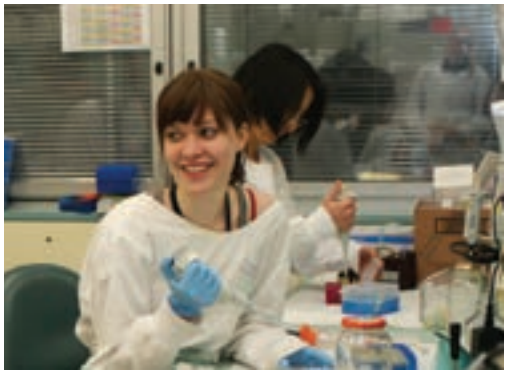
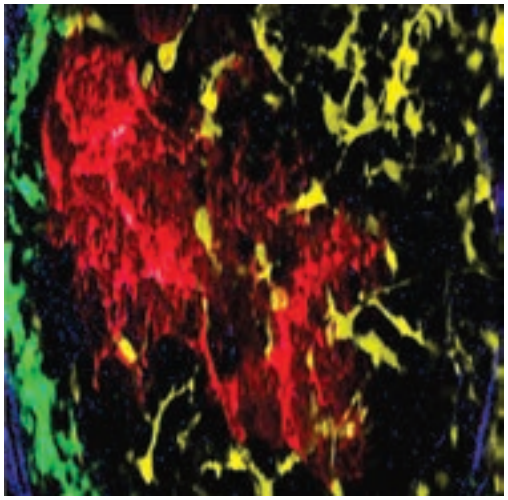
Associate Faculty, Dr Mika Jormakka, Structural Biology

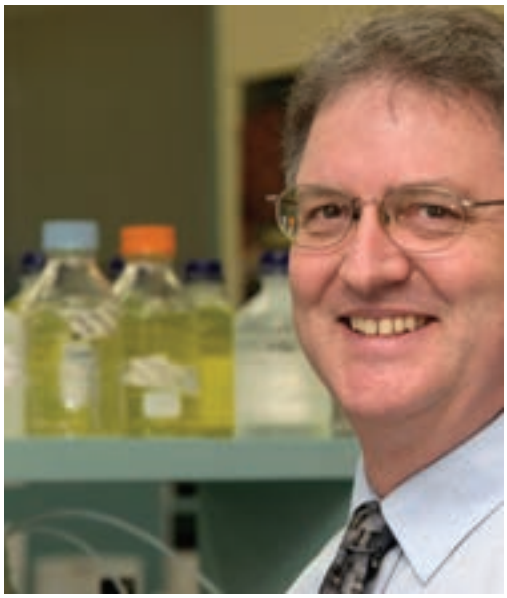
Investigator/s*	Granting Body	Type
Mika Jormakka	NHMRC	Career Development Fellowship
Jodie Ingles	NHMRC/National Heart Foundation	Early Career Fellowship
Chris Semsarian, Richard Bagnall	NHMRC	Project
Magda Ellis, Adrian Hill (Wellcome Trust Centre for Human Genetics), Yurong Yang (QIMR)	NHMRC	Project
Wolfgang Weninger	NHMRC	Project
Wolfgang Weninger, Arby Abtin, Neville Firth (USYD)	NHMRC	Project
Paul Mrass, Wolfgang Weninger	NHMRC	Project
Philip Bird (Monash), Wolfgang Weninger	ARC	Project
Jeff Holst	PCFA	Project
Mark Gorrell, Oliver Schilling (University of Freiburg)	Group of Eight/DAAD	Research Cooperation
Mark Gorrell, Geoff McCaughan, Sumaiya Chowdhury, Stephen Twigg (USYD), Susan McLennan (USYD)	Diabetes Australia Research Trust	Project
Timothy Hughes (University of Adelaide), John Rasko	NHMRC	Project
Joel Mackay (USYD), John Rasko	NHMRC	Project
John Rasko	Sir Zelman Cowen Universities Fund	Bluesky Research Grant
Mark Gorrell, Geoff McCaughan, Andrew Lloyd (UNSW), Amany Zekry (UNSW)	ACH2	Project
Philip Tong	NHMRC	Scholarship
Warwick Britton, Nick King, Georges Grau, Wolfgang Weninger, Geoff McCaughan, Barry Slobedman, Bernadette Saunders, Nick West, Jamie Triccas, Allison Abendroth, Valery Combes, David Bowen, Nick Shackel, Madga Ellis	USYD/NHMRC	Equipment
Warwick Britton, Bernadette Saunders	RL Cooper	Equipment
Chuck Bailey, Jane Gordon	RL Cooper	Equipment
Jenny Gamble, Mathew Vadas	National Heart Foundation	Grant-In-Aid
Chandrika Deshpande	National Breast Cancer Foundation	Fellowship
Jeff Holst	National Breast Cancer Foundation	Fellowship
Wolfgang Weninger	Cancer Institute NSW	Fellowship
David Bowen	USYD Bridging	Project
Bernadette Saunders	USYD Bridging	Project
Bernadette Saunders	Australian Respiratory Council	Project
Barbara Fazekas	Centenary Institute Bridging	Project
Chris Semsarian	HeartKids	Grant-In-Aid
Jane Gordon	Leukaemia Foundation	Scholarship
Michael Kuligowski	USYD ECR	Project
Jeff Holst	Cancer Institute NSW	Fellowship†

* Chief investigator is named first † Declined






From top left to right: Sumaiya Chowdhury, Research Assistant, Liver Immunobiology; Dr Nicholas Sigglekow, Research Officer, Aimei Lee, Phd Scholar, Candice Grzelak Liver Immunobiology; Images Michael Kullgowski; Research Officer Magda Ellis, PhD Scholar Simone Barry, Research Assistant Caitlin Gillis, Research Assistant Brian Chan, PhD Scholar Erin Shanahan, Research Officer Jennifer Huch, Associate Faculty Dr Nick West, Research Officer Shaun Walters, Research Assistant Angel Pang, Research Officer Manuela Florido, Faculty Professor Warwick Britton, Research Assistant Tuyet Tran, Associate Faculty Dr Bernadette Saunders, Mycobacterial lab; PhD Scholar Elizabeth Hamson, Liver Immunobiology; Image Michael Kullgowski; Image Phillip Tong; Associate Professor Mark Gorrell, Molecular Hepatology; The University of Sydney, PhD Scholar, Jodie Ingles, Molecular Cardiology, Centenary Institute – Won the Allied Health Prize, for her presentation on health economics and cardiomyopathy at the Cardiac Society Conference on August 12-13 in Perth

Financial Highlights

Chief Operating Officer, Dr Nick Pearce, Scientific Support

"2011 was an exciting year from a grant perspective with income growing by 19%. Strong growth was seen in both Australian Government (NHMRC and ARC) and non-government grants. The highlight was the outstanding success rate of 56% that our researchers achieved for NHMRC project grant applications."

Centenary purchased a number of machines to strengthen its cytometry and imaging facilities, which are the envy of researchers around Australia and the world.

On behalf of all the researchers and support staff my thanks to our stakeholders and supporters including the Australian Government (Department of Health and Ageing, ARC), State Government (OHMR, Cancer Institute NSW), non-government granting bodies, Sydney Local Health District and the general community for their ongoing support of our research into cancer, cardiovascular and infectious diseases.

Finally my thanks to all the researchers and science support staff for their continued hard work.

— Nick Pearce, Chief Operating Officer

INCOME	2011 IN '000	2010 IN '000	2009 IN '000
Research			
Federal - NHMRC + ARC	7,086	5,989	4,928
NSW Government	1,050	1,331	1,202
Other Research Grants	5,383	3,999	5,475
Total research	13,519	11,319	11,605
Fundraising			
Donations, events + other	1,082	1,198	888
Bequests	364	1,346	657
Total fundraising	1,446	2,544	1,545
Commercial	13	32	86
Other	3,083	3,456	3,742
Total Income	**18,061**	**17,351**	**16,978**
EXPENDITURE			
Research activities	12,694	12,625	11,370
Fundraising	898	870	580
Administration	1,699	1,606	1,602
Building operations	1,982	1,684	1,649
Total Expenditure	**17,273**	**16,785**	**15,201**

Organisational Chart 2011

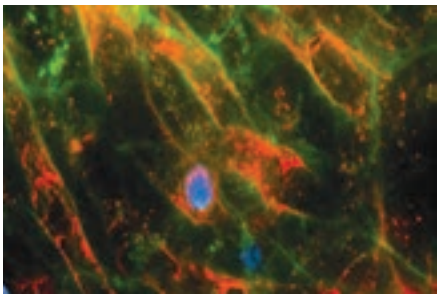


Image by Research Officer Frederic Sierro, Liver Immunology

Board of Governors

Foundation

Scientific Advisory Board

Executive Director

Fundraising and Marketing

Assistant Director

Assistant Director

Scientific Support

Chief Operating Officer

- Administration
- Animal Facility
- Building and OHS
- Cytometry and Imaging
- Finance
- Human Resources
- Information Technology

Research Groups

- Bioinformatics
- Gene & Stem Cell Therapy
- Immune Imaging
- Liver Immunobiology
- Liver Injury and Cancer
- Molecular Cardiology
- Mycobacterial
- Signal Transduction
- Structural Biology
- T Cell Biology
- Vascular Biology

Scientific Support Staff

Nicholas Keilar, Marisa Mourelle, Anna Slowiaczek and Viraf Variava

Executive Director & Faculty
Mathew Vadas

Administration Assistant
Juleigh Langenberg (from September)

HR Assistant
Eric Suchy (until June)

Administration Assistant/Reception
Michael Greensmith

Administration Assistant/Reception
Rachel Wolfenden

Assistant Accountant
Chelsea Wang

Assistant Accountant
David Chow (until February)

Chief Operating Officer
Nick Pearce

Communications Manager
Tanya Sarina (until May)

Director's PA/Office Support Manager
Helen Warwick

Donor Services Assistant
Jeff Wai-Yee (until July)

Donor Services Assistant
Katherine Finch (from June)

Donor Services Coordinator
Barbara Smith

Finance Manager
Tim Neal (from Sept)

Finance Manager
Viraf Variava (until Sept)

Finance Officer
Willie Entona

Fundraising Coordinator
Leisl Holterman

HR Assistant
Anna Slowiaczek (from August)

HR Manager
Nanette Herlihen

IT Development
Nic Barker

Philanthropy Coordinator
LauraBeth Albanese

Fundraising and Marketing Manager
Suzie Graham

Receptionist
Katie Doyle (until August)

Grants Manager
Nicholas Keilar

Volunteer
Bernice Shen

Volunteer
Maria Krikelis

Animal Technician
Danielle Moyes

Animal Technician
David Herne

Animal Technician
Leah Miller

Animal Attendant
Liz Connolly (from September)

Animal Attendant
Megan Kazavos (from July)

Animal Technician
Michael Damjancuk

Animal Attendant
Natalie Littlejohn (from July)

Animal Facility Assistant
Victor Truong

Animal Technician
Carol Juaton

Animal Facility Assistant
Gary Black

Animal Facility Officer
Marisa Mourelle

Veterinary Manager
Maria Wynne

Building Services Assistant
Bob Thorburn

Cytometry Support Coordinator
Robert Salomon

OHS and Operations Manager
Jeff Crosbie

IT Support
Owen Hoogvliet

IT Systems Administrator
Robert Middleton

Microinjectionist
Michelle Brownlee

Microinjectionist
Rain Kwan

Manager – Cytometry, Imaging and IT
Adrian Smith

Technical Support Officer
Steven Allen

Research Staff

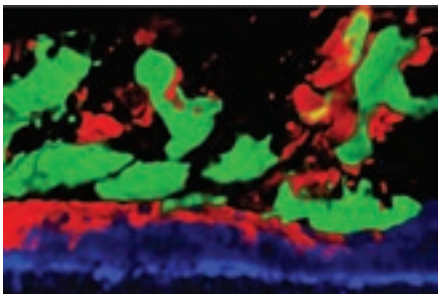


Image by Research Officer, Rohit Jain, Immune Imaging

BIOINFORMATICS

Associate Faculty
Nick Shackel (until October)

Foundation Fellow in Bioinformatics
Mathew Harrison (until October)

Associate Faculty
William Ritchie (from October)

PhD Scholar
Dadi Gao (from October)

CANCER DRUG RESISTANCE

Associate Faculty
John Allen (until July)

GENE AND STEM CELL THERAPY

Faculty
John Rasko

Associate Faculty
Jeff Holst

Research Officer
William Ritchie (from October)

Affiliate Member
Angel Jaramillo (from August)

Affiliate Member
Janet Macpherson (from August)

Affiliate Member
Tony Weiss (from July)

Editorial Research Officer
Carl Power

PhD Scholar
Abram Wassef (from September)

PhD Scholar
Fiona Guan

PhD Scholar
Liane Khoo

PhD Scholar
Dadi Gao (from August)

Research Assistant
Annora Thoeng

Research Assistant
Cynthia Metierre

Research Assistant
Jessamy Tiffen

Research Assistant
Jessica Vanslambrouck (until February)

Research Assistant
Jessica Yang (June - October)

Research Assistant
Kinsha Baidya

Research Assistant
Maria Gonzalez

Research Assistant
Xuebin Dong (until March)

Research Officer
Amy Marshall (from October)

Research Officer
Justin Wong

Research Officer
Kevin Wang

Senior Research Officer
Chuck Bailey

Visiting Scientist
Stephen Larsen

IMMUNE IMAGING

Faculty
Wolfgang Weninger

Associate Faculty
Chris Jolly

Associate Faculty
Paulus Mrass

Associate Faculty
Nikolas Haass

Masters Student
Paula Nascimento (until August)

PhD Scholar
Edwin Lau

PhD Scholar
George Sharbeen (until June)

PhD Scholar
Nethia Kumaran

PhD Scholar
Philip Tong (from February)

Research Assistant
Christine Yee

Research Assistant
Frank Kao (from July)

Research Assistant
George Sharbeen (from July)

Research Assistant
Jenna Langfield

Research Assistant
Jim Qin

Research Assistant
Mary Mouawad

Research Assistant
Andrea Anfosso

Research Officer
Arby Abtin

Research Officer
Ben Roediger

Research Officer
David Hill

Research Officer
Ichiko Kinjo

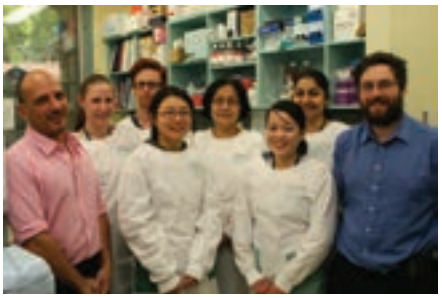
Research Officer
Kimberley Beaumont (from February)

Research Officer
Marcia Munoz (from June)

Research Officer
Rohit Kumar Jain

Research Officer
Saparna Pai

Research Staff



Faculty: Dr Patrick Bertolino and the Liver Immunology team.

Research Officer
Sioh-Yang Tan

Senior Research Officer
Lois Cavanagh

LIVER IMMUNOLOGY

Faculty
Patrick Bertolino

Associate Faculty
David Bowen

PhD Scholar
Michelle Vo

Research Assistant
Bharvi Maneck

Technical Officer
Claire McGuffog

Research Assistant
Nicole Wood

Research Officer
Eamon Breen

Research Officer
May La Linn

Research Officer
Szun Szun Tay

LIVER INJURY AND CANCER

Assistant Director & Faculty
Geoff McCaughan

Associate Faculty
Mark Gorrell

Associate Faculty
Nick Shackel

Honours Student
Chiyoko Yagasaki

Masters Student
Fady Akladios (until January)

PhD Scholar
Aimei Lee (from February)

PhD Scholar
Auvro Mridha

PhD Scholar
Candice Grzelak

PhD Scholar
Carleen Fernandez (until August)

PhD Scholar
Elizabeth Hamson

PhD Scholar
Emilia Prakoso

PhD Scholar
Naveed Nadvi

PhD Scholar
Sarah Richardson (until July)

PhD Scholar
William D'Avigdor

PhD Scholar
Yiqian Chen

Research Assistant
Alastair Duly (from February)

Research Assistant
Alison Potter (March - July)

Research Assistant
Ana Julia Vieira de Rebeiro

Research Assistant
Bharvi Maneck

Research Assistant
Bramilla Patkunanathan

Technical Officer
Christine Yee

Research Assistant
Margaret Gall

Research Assistant
Sumaiya Chowdhury

Research Officer
Nicholas Sigglekow

Research Officer
Alison Morgan

Research Officer
Eamon Breen

Research Officer
Fiona Keane

Research Officer
Jennifer Brockhausen

Research Officer
Victoria Wen (until August)

Senior Research Officer
Fiona Warner

Snr Scientist/Clinical Snr Lecturer
Devanshi Seth

Honours Student
Zainab Reslan (from June)

MOLECULAR CARDIOLOGY

Assistant Director & Faculty
Chris Semsarian

Affiliate Member
Jonathan Arthur (from August)

Clinical Researcher
Caroline Medi (from February)

Cardiovascular Genetics Coordinator
Laura Yeates

Genetics Research Coordinator
Diana Khodr (until June)

PhD Scholar
Jipin Das Kizhakkepatt (from April)

PhD Scholar
Jodie Ingles

PhD Scholar
Matthew Kelly

PhD Scholar
Ratnasari Padang

PhD Scholar
Rhian Shephard

Research Assistant
Angharad Evans

Research Assistant Caitlin Gillis, Mycobacterial

PhD Scholar, Candice Grzelak, Liver Immunobiology

Foundation Fellow, Mathew Harrison, Bioinformatics

Research Officer
Emily Tu

Research Officer
Richard Bagnall

Research Officer
Tatiana Tsoutsman

Registry Coordinator
Tanya Sarina (from June)

MYCOBACTERIAL

Faculty
Warwick Britton

Affiliate Faculty
Jamie Triccas

Associate Faculty
Bernadette Saunders

Associate Faculty
Nick West

Honours Student
Anneliese Tyne

Honours Student
Ashleigh Swain

Honours Student
Clea Grace

PhD Scholar
Carlyn Kong (until January)

PhD Scholar
Claudio Counoupas (from March)

PhD Scholar
Erin Shanahan

PhD Scholar
Frank Kao

PhD Scholar
Gayathri Nagalingam

PhD Scholar
Greg Fox

PhD Scholar
Mercedes Monteleone

PhD Scholar
Samantha Ellis (from August)

PhD Scholar
Simone Barry (from March)

Research Assistant
Angel Pang (from February)

Research Assistant
Caitlin Gillis (from February)

Research Assistant
Lisa Leotta

Research Assistant
Tuyet Tran

Research Officer
Amanda Brown (from August)

Research Officer
Brian Chan (from March)

Research Officer
Jennifer Huch

Research Officer
Magda Ellis (from October)

Research Officer
Manuela Florido

Research Officer
Rachel Pinto

Research Officer
Shaun Walters

Research Officer
Wendy Lin (until February)

Senior Technical Officer
Paul Reynolds

Administration Officer
Lalita Narayan

SIGNAL TRANSDUCTION

Faculty
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Masters Student
Dona Wethsinghe

PhD Scholar
Elise Jackson

PhD Scholar
Jacob Qi

PhD Scholar
Mei Li Ng

Research Assistant
Dominik Kaczorowski

Research Officer
Jinbiao Chen

Senior Research Officer
Carol Wadham

Technical Officer
Lijun Wang

Visiting Scholar
Lan Dai (from November)

STRUCTURAL BIOLOGY

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Mika Jormakka

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Amy Guilfoyle

PhD Scholar
Kimberley Vincent

PhD Scholar
Miriam-Rose Ash

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Samuel Tourle

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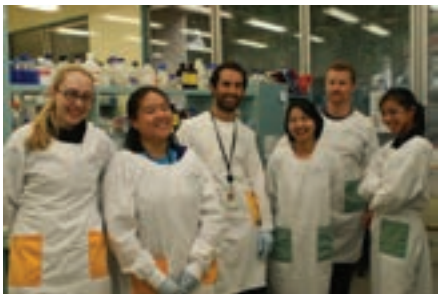
Megan Maher (until August)

Research Officer
Aaron McGrath

Research Officer
Chandrika Deshpande

Research Officer
Josep Font

Research Staff



Dr Alison Morgan, Research Officer, Aimei Lee, PhD Scholar, William D'Avigdor, PhD Scholar, Dr Emilia Prakoso, PhD Scholar, Mathew Harrison, Bioinformatics Foundation Fellow, Christine Yee, Research Assistant, Liver Immunobiology

T CELL BIOLOGY

Faculty
Barbara Fazekas de St Groth

Honours Student
Alexandra Terry

Occupational Trainee
Kathrin Buffin (until February)

PhD Scholar
David Hancock

PhD Scholar
Georgina Kalodimos

PhD Scholar
Holly Bolton

PhD Scholar
Lauren McKnight

PhD Scholar
Loretta Lee

PhD Scholar
Nazri Mustaffa (from November)

PhD Scholar
Thomas Guy

PhD Scholar
Yik Wen Loh

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Cindy Zhu

PhD Scholar
Suzanne Asad

Research Assistant
Wendy Zhang (from February)

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William Hey-Cunningham (until January)

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Michael Kuligowski

Senior Research Officer
Elena Shklovskaya

Visiting Scholar
Xiang Guo Duan (from October)

VASCULAR BIOLOGY

Faculty
Jenny Gamble

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Garry Chang

PhD Scholar
Ilana Lichtenstein

Research Officer
Ka Ka Ting (from June)

Research Assistant
Ann Formaz-Preston (from November)

Research Assistant
Emie Roy

Research Assistant
Jia Li

Research Assistant
Julie Hunter (from March)

Research Assistant
Paul Coleman

Research Assistant
Ying Lu

Research Officer
Angelina Lay

Research Officer
Gabor Hutas (from November)

Research Officer
Joshua Moses

Research Officer
Xiaolang Yan (until May)

Senior Research Officer
Mai Tran

Senior Research Officer
Matthew Grimshaw

Technical Officer
Elena Zaporoshenko

Research Assistant
Georgina Kalodimos (from September)

Acknowledgements

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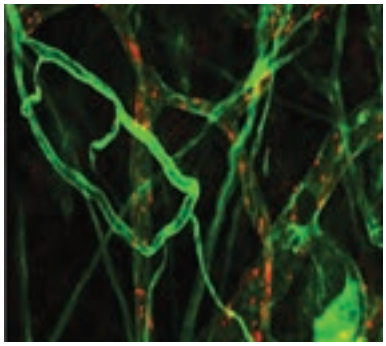
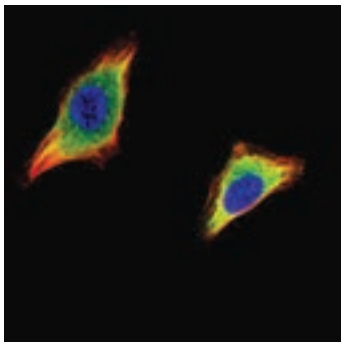
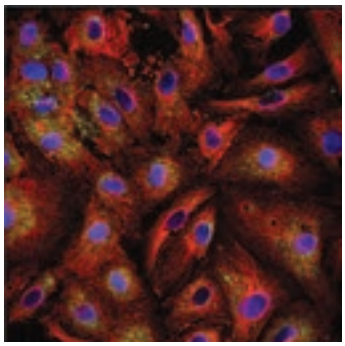


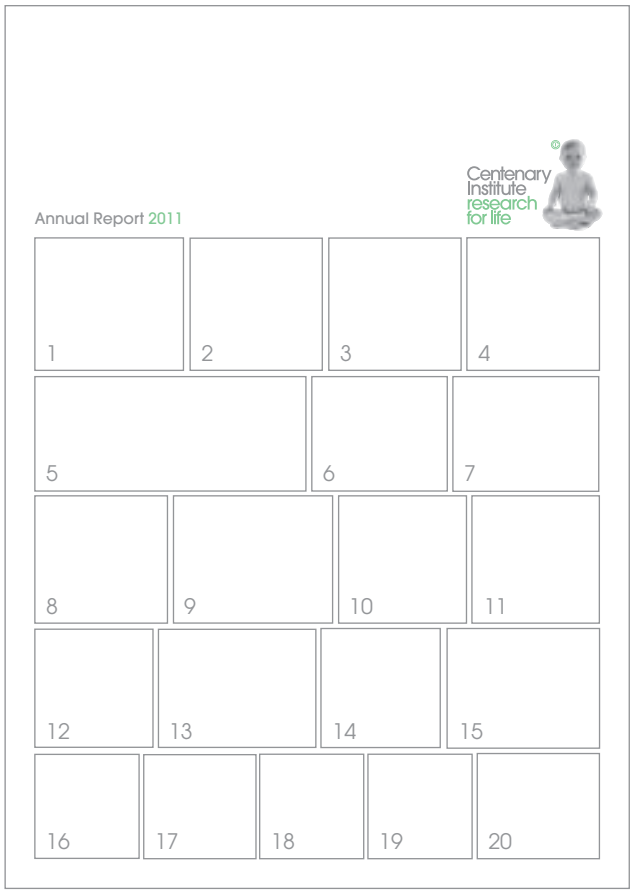

Cover images: 2011-2012 Image Prize entries from Centenary scientists.

1. Rohit Jain
2. Emma Zhang
3. Michael Lovelace and Paul Coleman
4. David Hancock
5. Rohit Jain
6. David Hill
7. Frederic Sierro
8. Michael Kuligowski
9. Frederic Sierro
10. Gary Chang
11. Michael Kuligowski
12. Ka Ka Ting
13. Jim Qin and Sarparna Pai
14. Michael Kuligowski
15. Alex Terry
16. Michael Kuligowski
17. Kim Beaumont
18. Thomas Guy
19. Ben Roediger
20. David Hill

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