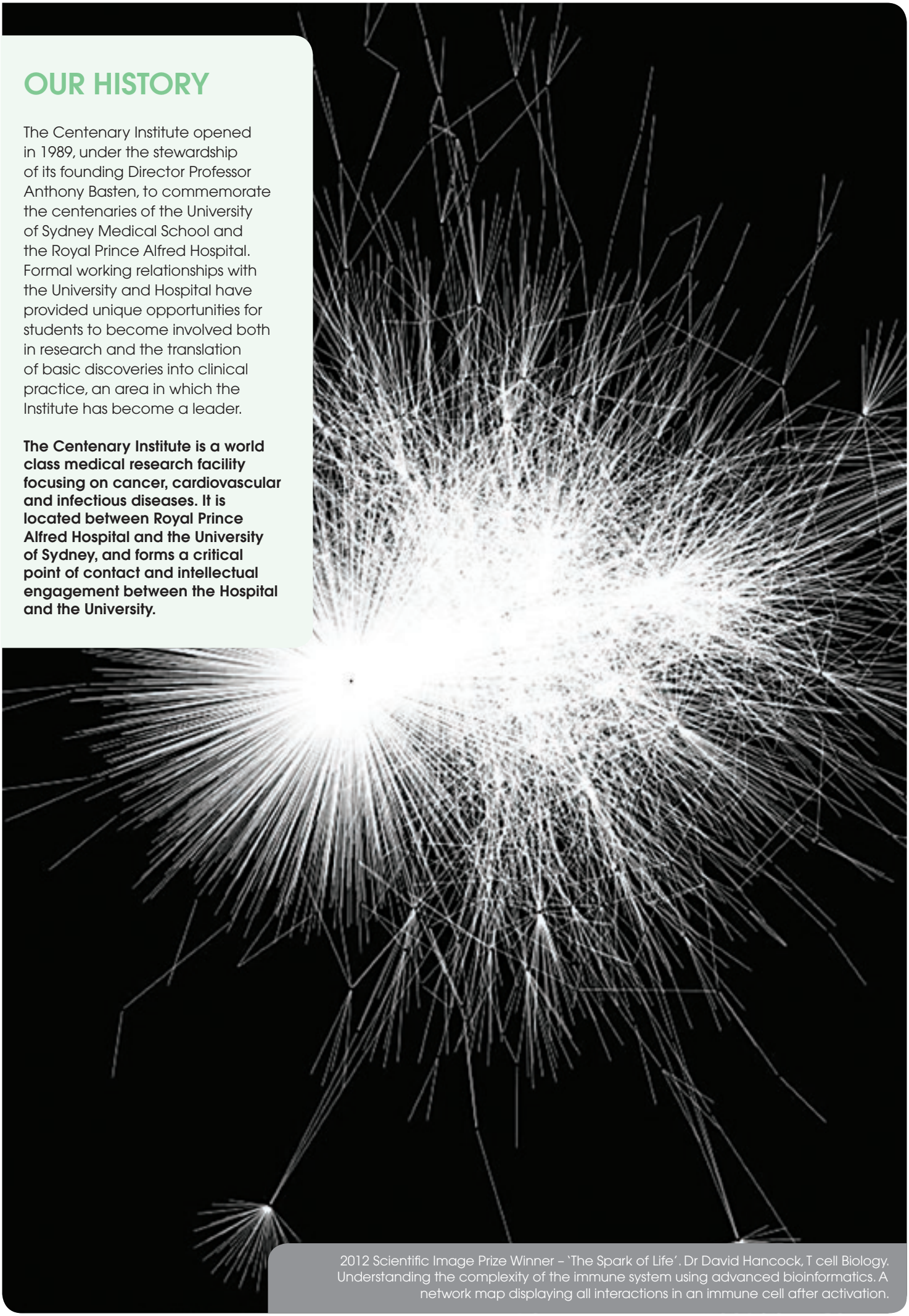
Centenary Institute
research for life

Annual Report 2012

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.

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.



2012 Scientific Image Prize Winner – 'The Spark of Life'. Dr David Hancock, T cell Biology. Understanding the complexity of the immune system using advanced bioinformatics. A network map displaying all interactions in an immune cell after activation.

Centenary Institute Annual Report 2012

Contents

The Honourable Michael Egan

Chairman's Report

The past year has seen the Institute grow in stature on all fronts, but especially in the way it reaches into the lives of people all over the world. For instance, our excellent work in tuberculosis continues in Vietnam and China, our research into sudden cardiac death is expanding in rural areas of Australia, and we continue to be recognised as a leader in liver transplant research.

The Centenary Lawrence Creative Prize is a prize awarded for creativity to Australian young scientists who are under 8-years in their post-doctoral career. In its second year, nominations were received from researchers all over Australia. I wish to congratulate Dr Jian Yang from the Diamantina Institute at the University of Queensland for being the 2012 winner of this increasingly prestigious $25,000 prize.

Talking about young people, our group of wonderful benefactors, the Young Centenary Foundation, continues to amaze us with their energy and enthusiasm. They are not only enormously helpful in our fundraising efforts, but they also organise exciting events that put Centenary in contact with a fantastic group of interested young people.

This year we were visited by our Scientific Advisory Board (SAB) members, who were most helpful in refining the research direction of our Institute and providing invaluable feedback to our scientists. I especially want to thank the Chair of the SAB, Professor Sir Marc Feldmann, who gave the keynote address at our 2012 Annual Meeting in the presence of our patrons, Her Excellency Professor Marie Bashir and Sir Nicholas Shehadie.

The year also marked the inauguration of the 'Diseases of the Aorta' laboratory. This was a wonderful collaboration between our Institute, and cardiologists Professor David Richmond and Professor Richmond Jeremy at the Royal Prince Alfred Hospital. The laboratory has begun operations under the direction of Professor Jennifer Gamble and we look forward to its development over the next years.

Earlier in the year, Professor Gamble, a pioneer of endothelium research, was also announced as the inaugural University of Sydney Wenkart Chair in Endothelium Medicine at the Centenary Institute.

Arrangements for the establishment of joint laboratories with the Chris O'Brien Lifehouse at RPA and Centenary has also gained ground, with space becoming available in the new Charles Perkins Centre (CPC). The construction of the CPC has moved very fast over the last year with researchers expected to move into the building in 2014.

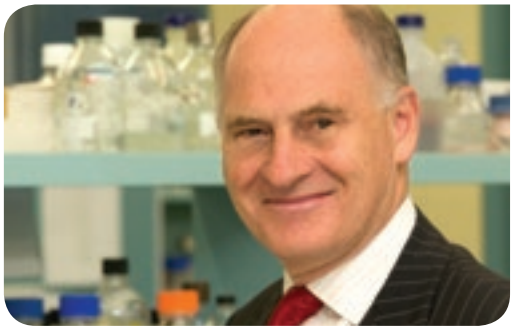
I want to congratulate our Executive Director, Professor Mathew Vadas and the Head of the Gene and Stem Cell laboratory, Professor John Rasko for being honored by the Australian Government as Officers of the Order of Australia (AO). My congratulation are also extended to one of our Governors, Professor Bruce Robinson who was appointed a Member of the Order of Australia (AM).

I also extend my thanks to Mr Ken Cahill for his wonderful service during his time on the Board.

Finally I thank all the Board of Governors, our hard working colleagues at the Institute and the Foundation, and especially our Executive Director Mathew Vadas, for all their work during the year.

"The past year has seen the Institute grow in stature on all fronts, but especially in the way it reaches into the lives of people all over the world."

Executive Director's Report



Executive Director, Faculty,
Professor Mathew Vadas AO

Creativity is often an individual effort and there is much an Institute like ours can do to allow the creative research genius to flourish.

In 2012, Centenary has continued to strive to create an environment that recognises and applauds researchers' innovative imagination. Our seminar series, our meetings, our Scientific Advisory Board are all focused around this. In addition, the Centenary Lawrence Creative Prize, about which you can read more in the Chairman's report, has become a hugely recognised national celebration of the Australian creative potential.

But there is also a well-recognised structural or architectural component to creativity, which maximises the chance meetings, the accidental exposures to new influences or the after-work conversations that fire a new idea. Happily, the University of Sydney's Charles Perkins Centre (CPC) is being erected adjacent to the Centenary and much thought has gone into how best the two entities should interact to maximise creative synergy. The new cafeteria adjacent to Centenary will give scope to social interactions and our advanced plans for a joint venture with Lifehouse in creating the Centenary-Lifehouse Cancer Research Centre (CLCRC) in the CPC will allow for the physical interactions that are so important.

Showcasing Our Excellence

As is evident in this report, 2012 has been outstanding for all our scientists, but I want to highlight five areas.

The opening of a highly secure PC3 laboratory for our Tuberculosis research group in 2012 was a key milestone. Professor Warwick Britton, who heads up this research group, was awarded $2.49 million towards establishing a Centre of Research Excellence on Tuberculosis control. The new prestigious Centre brings together international expertise in public health, epidemiology, basic science, ethics, law and clinical medicine, to address this complex public health problem. It was particularly gratifying to see our Tuberculosis research group highlighted in the press for their truly outstanding work to help combat this infectious disease in the Asia-Pacific region.

There are further exciting achievements in the Molecular Cardiology program led by Professor Chris Semsarian. Genetic studies of over 600 hypertrophic cardiomyopathy (HCM) families in 2012 has enabled the development of new transgenic mouse models which will ultimately help to develop better diagnostic and therapeutic measures to treat patients suffering from HCM. Strong partnerships with Royal Prince Alfred Hospital and Sydney University have enabled the group to become an increasingly prominent and productive research group.

Two of our strongest scientists have decided to join their groups to further enhance their interactions. Dr Chris Jolly and Professor Wolfgang Weninger will now operate jointly as the Immune Imaging group. This group is now a central source of our research and creativity, and also in generating extraordinary scientific images, some of which are highlighted in this report.

Our efforts to build a prominent bioinformatics team under the leadership of Dr William Ritchie have also borne fruit. During the past year, the lab became fully functional and is already providing a superb support service throughout our Institute and to the wider research community. It is also excelling in its own cutting edge research. A winning combination!

Much of the work of the Institute centres on understanding the inflammatory response. The inflammatory response underlies many diseases including cancer and ageing. With the recruitment of Dr Masaomi Kato to head our Ageing Research and our plans for CLCRC, our expertise in inflammation is becoming even more germane. To further exploit this synergy we have begun to organise the inaugural international 'Future of Experimental Medicine Conference – Inflammation in Disease and Ageing' that will be held in Sydney in March 2014. We believe this conference will forge new research collaborations and attract leading scientists to the Institute.

Finally, I want to thank each of our researchers, staff, partners, board and supporters who have made 2012 such a fruitful year, upholding our core values of excellence, relevance and prominence.

As we continue to mature and expand as an Institute, we look forward to creative sparks flying to fuel the discoveries that will benefit all Australians, enabling us all to live longer and healthier lives.

"Creativity is often an individual effort and there is much an Institute like ours can do to allow the creative research genius to flourish."

Board of Governors

The Hon Michael Egan (Chairman)

Appointed Chair in 2005

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 leads the Australian litigation and contentious regulatory practice of global law firm Allen & Overy. He has represented many leading financial institutions and corporations as well as executives who operate in a wide range of sectors, especially banking, wealth management, financial markets, resources, real estate development, IT and telecommunications.

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, Sydney South West Area Health Service. Dr Anderson is a Board member for nine organisations including 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 Cahill stepped down from the board October 2012.

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 an Executive Director of Aurora Funds Limited, a listed asset manager, 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, and Australasian Wealth Investments, which are ASX-listed investment companies.

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, was a member of the Council of the NHMRC from 2003 to 2009, and Chairman of the Healthcare Committee, from 2009 to 2012. Professor Horvath is Chair of the Prosthesis Listing Committee advising the Commonwealth Minister of Health, a member of the Garvan Medical Research Institute Board and a member of the Crown Limited Board.

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

Neil Lawrence is the founder and CEO of Lawrence Creative Strategy and the Executive Creative Director of STW Group, 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 and has represented Australia as the Chairman of Judges at the Irish International Advertising awards and on the film jury at Cannes. Mr Lawrence is a regular contributor to The Australian newspaper.

Dr Susan Pond AM

Appointed Governor in 2009

Dr Pond AM, FTSE is Chair of the Australian Initiative for Sustainable Aviation Fuels and Adjunct Professor in Sustainability at the United States Studies Centre at the University of Sydney, Chair of the Australian Government's Clean Technology Innovation Program Committee, Vice President of the Academy of Technological Sciences and Engineering and Board Member of the Australian Nuclear Science and Technology Organisation, Innovation Australia and Biotron Ltd. Previously, Dr Pond was Chair and Managing Director of Johnson & Johnson Research Pty Limited, held positions in Medicine at the University of California, San Francisco, and the University of Queensland and as Chair of the Australian Drug Evaluation Committee and AusBiotech.

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.

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 Institute for Creative Health and supports the Contemporary Collection Benefactors of the Art Gallery of NSW. He is on the Medical Research Advisory Board of the Australian Cancer Research Foundation, and on NHMRC committees.

Joseph Carrozzi, Foundation Chair and Governor

Centenary Institute Medical Research Foundation

FOUNDATION COMMITTEE MEMBERS

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

FOUNDATION SUPPORT STAFF

Head Fundraising, Communications, Marketing Suzie Graham
Philanthropy Coordinator Laura Beth Albanese
Fundraising & Database Coordinator Barbara Smith
Communications and Donor Relations Katherine Finch
Digital Marketing and Fundraising Coordinator Felix Daniel (from Sept)
Fundraising and Marketing Specialist Darshan Parmar (May-Aug)
Corporate Partnerships Consultant Leonie Walton (from Oct)
Fundraising Coordinator Leisl Hotterman (until March)
Donor Services Assistant Maria Krikelis (from March)

The Centenary Institute Medical Research Foundation serves to encourage the community to support the vital research being done by the Institute's brilliant scientists. Our supporters are the cornerstone of our fundraising program. Without their time, talent, and financial contributions, our scientists would not be able to see their research projects through to fruition and achieve lifesaving results.

Supporters of the Institute come from all walks of life, and give generously in a variety of ways. We are eternally grateful to each of of them, and continue to be inspired by their kind and generous spirit of giving and support.

Community fundraising is an important part of our fundraising success. These committed individuals raise money for Centenary through the help of supporters, volunteers and their family, friends and neighbours. They may fundraise for different reasons, but they all share in a passion that engages their communities. Their support ranges from events such as trivia nights, bake sales, fashion parades, and concerts, and can also include sponsored events such as marathons and fun runs.

We are truly grateful to each of our FUNdraisers for their extraordinary effort in 2012.

The Foundation's appeals have also been a major source of funding. We are grateful for our regular givers and supporters, whose continued support ensures that our scientists will have the resources they need to ensure their projects' success.

Bequests play a vital part in our ability to plan long term, and we really value these benefactors and this income received by the Foundation from these extraordinary gifts.

Fundraising events also give supporters a chance to further engage with our work and our scientists in a social setting.

In May, the 4th Annual Centenary Foundation Fundraising Dinner was held at PricewaterhouseCoopers (PwC), and saw the who's who of the business community, politicians, and philanthropists join together in an evening to support the Institute. A special thank you goes to our generous sponsors who made this evening possible. The event featured a live and silent auction and fine art sale which raised over $160,000 in support of the Foundation Fellowship in Bioinformatics.

In October, the Foundation held a cocktail party at the home of members, Simon and Julie Ford and Tintilla Estate sponsored the evening. Guests were updated on the progress of modern medicine and the promise of personalised medicine by Centenary Director, Professor Mathew Vadas AO.

The Young Centenary Foundation (YCF) continued to work with young people to gain their investment into medical research and embed philanthropy into youth culture. In 2012, they held art, music and comedy events, which raised over $30,000. This funding will be used for the first annual YCF grants – funding young scientists to deliver creative and innovative projects to support their research goals.

A special thank you to each one of our Foundation committee members for their generous time and financial commitment to the organisation which made so many of our achievements possible in 2012.

— Joseph Carrozzi, Chair, Centenary Institute Medical Research Foundation

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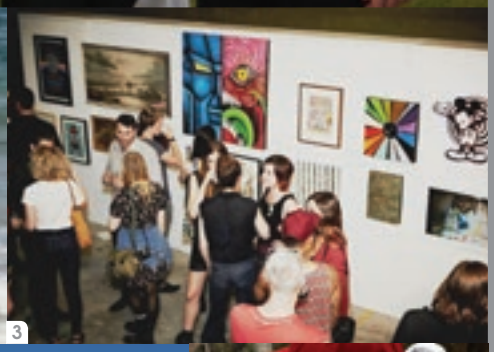

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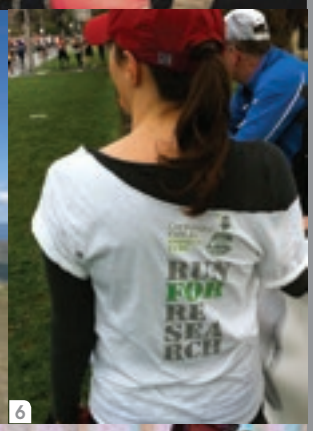

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FUNDRAISER HIGHLIGHTS

City2Surf had a dedicated Run4Research Team of over twenty runners – raised + $17,000 (1, 6)

Centenary scientist Dr Josep "Pep" Font raced in The Coolangatta Gold - raised +$2,500 for the Structural Biology lab in which he works (2)

Young Centenary Foundation's (YCF) Art, Music & Comedy events raised + $30,000 (3)

Meg Taylor movie night raised $7,500 to support the Molecular Cardiology Program

The Bamford Family event raised + $5,000 to support the Molecular Cardiology Program

Foundation's annual fundraising dinner raised +$160,000 (4, 7)

Centenary scientist Wil D'Avigdor joined a team of four to race in the Mongol Rally – a dangerous 15,000km drive and raised $3,700 to support Liver Immunology (5)

YCF's Sarah Bornstein shaved her head for Cancer research – raised + $13,000

Roseville Rotary donated $5,000 to the T cell Biology Groups' student travel scholarship

HUGE THANK YOU TO YOU ALL

FOUNDATION DINNER SPONSORS

PricewaterhouseCoopers (PwC)
Hardy's
Seppeltsfield Wines
Mount Mary Vineyard
Peter Lehmann Wines
Paul Sumner and Mossgreen Auctions
Artifix
Rockford Barossa
Jonathan Zwartz Trio performers
Racing NSW
Qantas
Richard Champion de Crespigny
ANZ Stadium

AND HEARTFELT THANKS TO ALL ARTISTS AND LIVE AND SILENT AUCTION CONTRIBUTORS FOR YOUR AMAZING SUPPORT

Research Perspective

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.

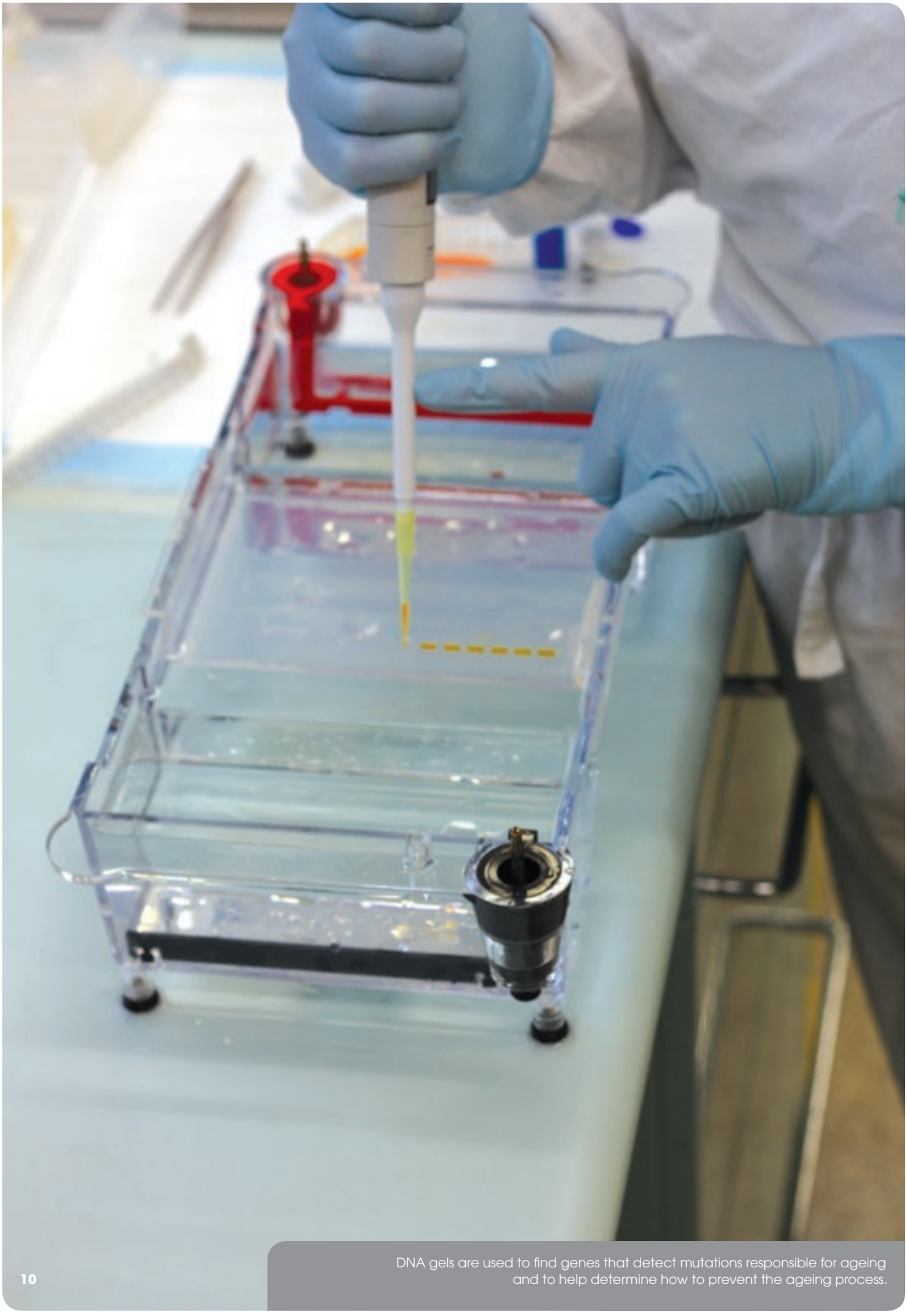
Chronic liver damage affects up to 20% of our population. It has many causes, including infections with the hepatitis B and C viruses. Liver cancer is often caused by chronic liver damage and is one of the fastest growing cancers in our community.

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?

Centenary research is about taking discoveries from the laboratory to the clinic, enabling us all to live longer and healthier lives.

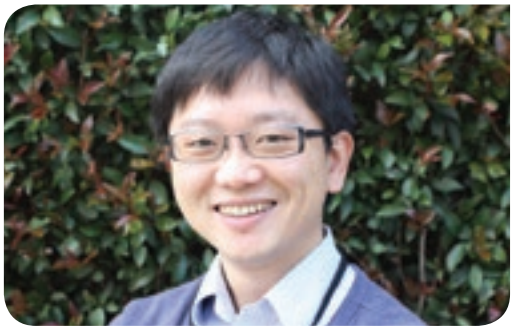
Professor Chris Semsarian consulting his patient, Emily, who has a rare genetic heart disease.



DNA gels are used to find genes that detect mutations responsible for ageing and to help determine how to prevent the ageing process.

Ageing Research

Toward Prevention of Ageing



Research Officer, Dr Masaomi Kato, Ageing Research

Overview

There is an overwhelming global epidemic of an ageing population. More than 20% of the population will be over 60 years of age by 2050. The understanding of the biology of ageing and the discovery of therapeutics to control the process is of increasing importance. Although ageing appears to be a passive process, genetic studies in model organisms have demonstrated that ageing is partly under genetic control which means it can be manipulated, treated and delayed. Our group is interested in elucidating the underlying mechanisms that cause ageing and limit lifespan. We want to learn how these molecular, biochemical processes influence not only lifespan, but also health-span. Our model organism, the nematode *C. elegans*, is ideal for testing our hypotheses as it has relatively a short lifespan, provides powerful genetics and shares many age-related issues with humans. Our group's ultimate goal is to develop a 'cure' for ageing by investigating key genetic pathways in age-associated diseases such as diabetes, cancer and neurodegenerative disorders.

— Masaomi Kato

Research program

Understanding how the genetic machinery can extend lifespan
Reducing food intake (but keeping with adequate nutrition) can delay the ageing process and attenuate age-associated pathologies, including metabolic disorders. We are currently studying the role of the genetic machineries that involve microRNAs, to determine their role in dietary restriction mediated longevity. By understanding the molecular basis of longevity and the metabolic changes induced by dietary restriction, we can provide new insight into metabolic diseases in humans.

FOXO in lifespan determination
The forkhead box O (FOXO) is an evolutionarily conserved transcription factor. FOXOs are functionally silent under normal conditions but activated in response to metabolic or environmental stress and regulate downstream stress resistance and metabolic genes, suggesting its role as a homeostasis regulator. Recent data across multiple human cohorts have shown an association with FOXO genetic variants and lifespan, suggesting the importance of FOXO in lifespan determination in humans. We have identified novel factors affecting FOXO activity in our model organism, *C. elegans*, and are now studying their function in stress response and lifespan regulation.

Leading the way in ageing research
With a global ageing population, society everywhere faces an urgent and expensive public health issue: how to provide for and manage health and well-being. The Centenary Institute is planning the inaugural international symposium 'Future of Experimental Medicine' looking at the central mechanisms of the ageing process: inflammation. The meeting will be in Sydney, early in 2014. Importantly, the meeting will bring together clinicians and researchers – experts in microbiome, nutrition, cell signalling, senescence, genetics and bioinformatics – to enhance the translational outcomes of this research.

STAFF

Research Officer
Masaomi Kato (from May)
Research Assistant
Swas Kumar (fom July)

RESEARCH HIGHLIGHT OF THE YEAR

Our group has introduced a model system, the nematode *C. elegans*, into Centenary to facilitate ageing research. It is ideal for this type of research due to its short lifespan of only 2-3 weeks and its shared characteristics with human ageing.

We have used *C. elegans* to identify a novel genetic factor necessary for dietary restriction-mediated lifespan extension. Since this genetic component is evolutionarily conserved from *C. elegans* to humans, it may have a role in metabolic control that is common to a diverse range of animal species.

Associate Faculty, Dr William Ritchie, Bioinformatics

Bioinformatics

Virtual maps to decode biological complexity

STAFF

Associate Faculty
William Ritchie

PhD Scholar
Dadi Gao

Visiting Researcher
Julie Cahu (Apr-May)

RESEARCH HIGHLIGHT OF THE YEAR

Our team discovered a novel computational method to detect new microRNAs in human cells. The method was based on computer predictions of how microRNAs fold into specific hairpin shaped structures. We also published a book chapter on how to predict which genes will be altered by inserting microRNAs into cells.

Overview

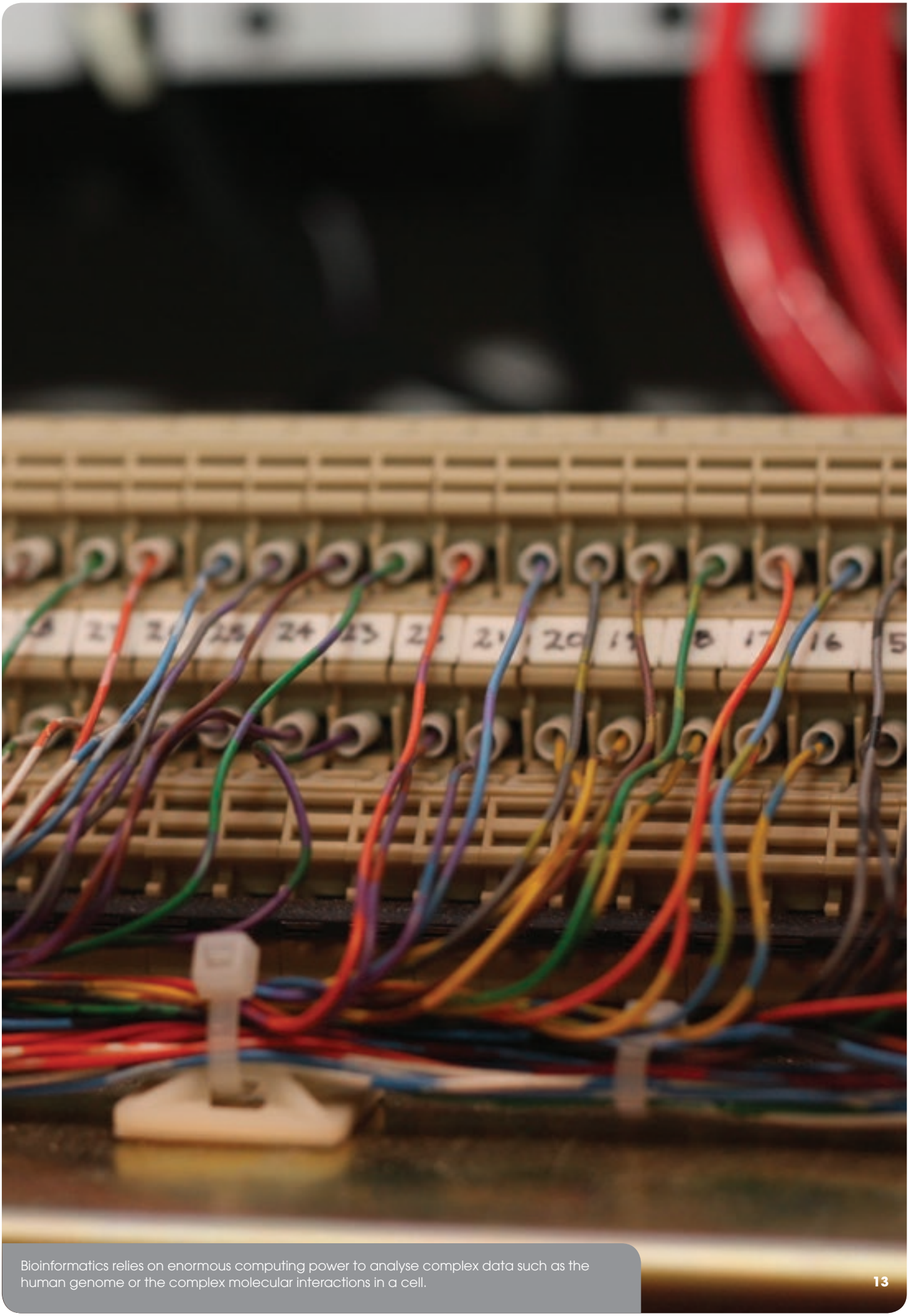
Biological systems like the human body are extremely complex and diverse. The emergence of computers and bioinformatics has been an essential development in dissecting, understanding and analysing these systems quickly and efficiently. Our group uses bioinformatics to understand the multitude of complex interactions in cells forming the basis of disease. Computing power allows these analyses to be conducted within minutes to hours, saving years of research time. We analyse complex data sets including the human genome to determine, for instance, how cardiac disease results in sudden cardiac death. We have established computer infrastructure to support the needs of all Centenary researchers: every group at Centenary has considerable computational requirements, and each generates gigabytes of data. Bioinformatics allows this data to be efficiently probed for valuable information about why disease develops. This information will accelerate basic biological research toward translational medicine, that is, the development of therapeutics and cures for disease.

— William Ritchie

Research program

Micro-managing microRNAs, the micro-managers of disease
MicroRNAs are miniscule pieces of DNA often termed 'micro-managers,' since they are responsible for numerous cancers, neurodegenerative diseases and heart disease. MicroRNAs are arguably the best candidates for novel therapies because they can be easily modified for a beneficial impact on cells. However finding microRNAs is nearly impossible because they are thousands of times smaller than normal genes with completely different sequences. We have applied a code-breaking method called 'Markovian Chains' to find unusually frequent patterns in the DNA code. These sections are likely to be important for the cell, increasing the probability of finding micro-managers by a factor of over 10,000. Having successfully applied this technique to bacteria and viruses, we are going to apply this technique to the much larger mouse and human genomes.

Determining the genetic signature of diseases
If we could identify a unique genetic signature for every disease, it would be possible 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, demanding different treatments – what is now called personalised medicine. We are using bioinformatics approaches to probe for such signatures through our collaborations with Centenary researchers. For example, we were able 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 eventually provide new, personalised approaches to therapy.

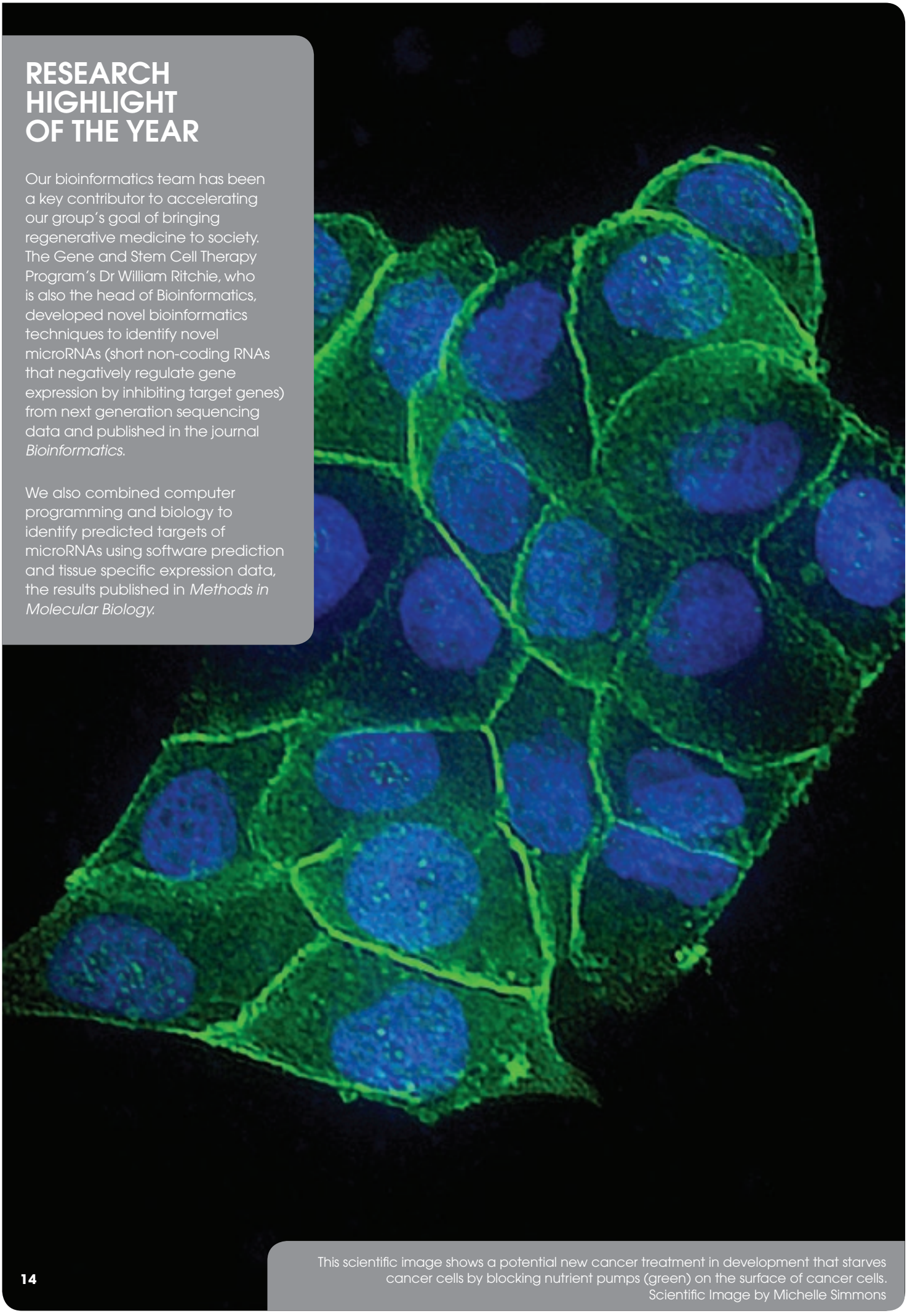


Bioinformatics relies on enormous computing power to analyse complex data such as the human genome or the complex molecular interactions in a cell.

RESEARCH HIGHLIGHT OF THE YEAR

Our bioinformatics team has been a key contributor to accelerating our group's goal of bringing regenerative medicine to society. The Gene and Stem Cell Therapy Program's Dr William Ritchie, who is also the head of Bioinformatics, developed novel bioinformatics techniques to identify novel microRNAs (short non-coding RNAs that negatively regulate gene expression by inhibiting target genes) from next generation sequencing data and published in the journal *Bioinformatics*.

We also combined computer programming and biology to identify predicted targets of microRNAs using software prediction and tissue specific expression data, the results published in *Methods in Molecular Biology*.



This scientific image shows a potential new cancer treatment in development that starves cancer cells by blocking nutrient pumps (green) on the surface of cancer cells. Scientific Image by Michelle Simmons

Gene and Stem Cell Therapy

Seeking cures by tweaking genes

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

Overview

Gene therapy and stem cells can provide cures for a multitude of human diseases including heart disease, organ failure and cancer, and also genetic diseases such as haemophilia and thalassaemia. By discovering ways in which to increase cell numbers prior to transplantation, we have not only been able to help our patients at the Royal Prince Alfred Hospital, but also the tens of thousands of people around the world each year who require a bone marrow transplant. Our five focus areas include gene therapy, stem cell biology, molecular mechanisms of gene control, genetic disorders and cancer biology. By integrating bioinformatics into our research programs, we are able to dissect the overwhelming complexity of molecular circuitry required to identify the triggers that switch genes on and off. Our group's unifying focus is to understand the biology of these regenerative medicines to overcome the barriers to their use in improving human health.

— John Rasko

Research program

Understanding stem cells

Stem cells are capable of forming a wide variety of different cell types and can also self-renew to produce more stem cells. The manipulation of this technology in regenerative medicine has massive application in diseases affecting a variety of cell types. The stem cell differentiation process involves changes at all levels in the cell, from DNA to RNA to protein expression. Within these changes lies the key to understanding what genetic and biochemical factors identify a stem cell, so that we can exploit their potential in human therapies.

Towards novel therapies for cancer

We want to understand the mechanisms by which normal cells are transformed to cause cancer. Just as stem cell differentiation involves changes to DNA, RNA and protein expression, so too does the transition from a healthy cell to a cancerous cell. By directly comparing healthy cells to cancer cells in our laboratory, we can study fundamental cancer cell biology. As the function of important molecules in these processes are dissected, new therapeutic opportunities for human cancers will emerge. Our studies help to define the biochemical pathways and complex molecular machinery implicated in human cancers.

Starving cancer cells

Cancer cells exhibit uncontrolled growth in the body; cellular nutrients must be imported into a cancer cell to sustain this growth. Our group is studying how cancer cells obtain these nutrients. We have discovered that various pumps responsible for nutrient uptake are increased in different cancer types. Our discoveries of different pumps required for nutrient uptake have led to further research in the Origins of Cancer Laboratory into ways to starve and kill cancer cells by blocking these nutrient pumps.

STAFF

Faculty John Rasko
Associate Faculty Jeff Holst
Associate Faculty William Ritchie
Senior Research Officer Chuck Bailey
Research Officer Amy Marshall
Research Officer Kevin Wang
Research Officer Justin Wong
Research Assistant Cynthia Metierre
Research Assistant Kinsha Baidya
Research Assistant Natalia Pinello
Research Assistant Yue Feng (from Feb)
Research Assistant
Katherine Champ (from Jun)
Honours Student / Research Assistant
Michelle Simmons (from Nov)
Editorial Research Officer Carl Power
PhD Scholar Fiona Guan
PhD Scholar Liane Khoo
PhD Scholar Jane Gordon (from Feb)
PhD Scholar Abram Wassef
Visiting Researcher Lyn Moir (from Sept)
Visiting Researcher
Alice Klein (from Sept)
Visiting Researcher
John Doan (from Sept)

Faculty, Professor Wolfgang Weninger, Immune Imaging.

Immune Imaging

Revealing the elegant dance of immune cells to help combat disease

STAFF

Faculty Wolfgang Weninger
Associate Faculty Chris Jolly
Associate Faculty Nikolas Haass
Associate Faculty Paulus Mrass
Senior Research Officer Lois Cavanagh
Research Officer Andrew Mitchell
Research Officer Ben Roediger
Research Officer David Hill (until Jul)
Research Officer George Sharbeen (until Jun)
Research Officer Ichiko Kinjo
Research Officer Kimberley Beaumont
Research Officer Marcia Munoz
Research Officer Mate Biro (from Apr)
Research Officer Rohit Jain
Research Officer Saparna Pai
Research Officer Sioh Yang Tan
Research Officer Szun Szun Tay (from Oct)
Research Assistant Andrea Anfosso (until May)
Research Assistant Jeremy Chou
Research Assistant Jim Qin
Research Assistant Mary Rizk
PhD Scholar Edwin Lau
PhD Scholar Nethia Mohana-Kumaran (until September)
PhD Scholar Philip Tong
Honours Student Timothy Durack
Occupational Trainee Katja Baesler (Jan - Apr)
Visiting Researcher Radjesh Bisoendial

Overview

The skin is the largest organ of our body. It is the outermost surface that is continually exposed to biological factors like bacteria, viruses and parasites, but also physical and chemical factors such as pollution and radiation from sun light. Skin diseases carry a high psychological burden in affected patients. 30% of Australian children suffer from eczema, 3% of Australians suffer from psoriasis, and malignant melanoma is the most common cancer related death in young adults in New South Wales. The immune system plays several major roles in skin health: it is our first line of defence against pathogens and cancer cells, and is a regulator of the wound healing response. On the other hand, overreaction of the immune system underlies most skin diseases. Our group uses cutting-edge imaging approaches to dissect immune system function in a variety of inflammatory skin conditions and skin cancers, with the vision to develop novel therapies.

— Wolfgang Weninger

Research program

Multiphoton microscopes: live tracking of the immune system response
The Immune Imaging program comprises four groups whose common feature is that they all employ a similar technology called multiphoton microscope. We use these specialised microscopes to track immune events as they occur in living tissue – a highly valuable capability for studying disease progression. Critical proteins are labelled with fluorescent tags, which are then stimulated to release light under the microscope using lasers. Using this technology, we can track the behaviour of immune cells, microbes, and cancer cells in real time in the skin and other organs. This allows us to generate a better understanding of the causes of skin diseases.

Massacring melanoma
Melanoma is an extremely aggressive skin cancer and is the most common cancer in young Australian adults. We are investigating the characteristics and resistance to drugs of the different types of cells in melanomas, so that treatments can be better targeted to tumour cells in the future. Multiphoton microscopy allows us to examine in detail the behaviour of melanoma during proliferation and invasion in real time.

DNA repair
When our DNA is damaged, DNA repair mechanisms are activated by the cell to correct the mistakes. DNA repair pathways are linked to the production of antibodies – molecules generated by the immune system that help fight infection and tumours. Our group has developed powerful models to investigate the relationship between DNA repair and antibody production. This allows us not only to generate novel insight into the making of antibodies, but also in the processes that lead to certain cancers of antibody producing cells (lymphomas).

RESEARCH HIGHLIGHT OF THE YEAR

Our international collaborations have formed an invaluable part of our key research contributions this year. We participated in a study with colleagues from Israel that uncovered a new pathway for the entry of key immune system cells, called T cells, into inflamed skin.

Our US collaborations led to a novel discovery into how T cells screen the brain during infection by *Toxoplasma gondii*, a parasite that causes serious illness and in many cases, death. These key findings will influence the development of targeted therapeutics for these and other diseases by revealing the intricate signaling mechanisms employed by the immune system.

Research Officer, Ben Roediger is using a range of specialised microscopes to visualise the dance of immune cells as they occur in living tissue – a highly valuable capability for studying disease progression.

Technical Officer, Claire McGuffog is working to improve the unwanted side-effects of life saving liver transplants to help improve the outcome for patients.

Liver Immunology

The liver and the immune system: a paradoxical partnership

Faculty, Dr Patrick Bertolino, Liver Immunology

Overview

The liver is a tough organ. Made of over 300 billion cells, it is capable of regenerating if as much as 75% is removed. The liver also modulates the body's immune system. For example, livers dampen immunity to such an extent that they can be transplanted without rejection; a transplanted liver can prevent rejection of other organ transplants from the same donor, a phenomenon termed immune tolerance. This phenomenon, however, is detrimental during infections by pathogens such as the hepatitis B virus (HBV), hepatitis C virus (HCV) and malaria, which use immune tolerance to persist leading to chronic infection. The number of Australians with HCV-related liver disease are estimated to triple by 2020, with a significant number developing liver cancer, the third-leading cause of cancer-related death worldwide. Our group investigates how the liver induces immune tolerance for the development of better transplantation treatments, and also for prevention and treatment of chronic liver disease.

— Patrick Bertolino

Research program

The liver and T cells are partners in immune tolerance

Our group has shown that the liver, like the lymph nodes, can activate T cells, a key cell of the immune system. We demonstrated that liver cells can engulf and destroy T cells which produces the dampening effect on the immune system, termed immune tolerance. This research is being continued in mouse models where we are exploring in more depth how the liver induces tolerance, so we can manipulate these mechanisms for the induction of a persistent immune response. Exploring the mechanism of liver regulated immunity will lead not only to better transplantation therapy by turning the immune system down, but also to more effective prevention and treatment of liver disease by strengthening its action.

Improving patient outcomes after liver transplantation

Linking back to the clinic, our group is examining people undergoing liver transplantation for disease related to HCV infection. HCV persists post-transplant, and can cause recurrent liver disease. By studying the immune response to HCV in this group of patients, we hope to gain important insights into how to modulate the immune response to HCV. This will aid in clearing chronic infections, ultimately leading to restoration of liver function and improved treatment outcomes in early infection.

Human gene therapy: regulating important genes in liver cells

We are collaborating with Professor Ian Alexander of the Children's Medical Research Institute to use a gene therapy based technology that allows expression of genes of interest in liver cells. Inactivation of those T cells that recognise proteins newly expressed in the liver is essential in patients treated with gene therapy technology: if T cells were not inactivated they would be free to recognise the new and corrected gene product previously missing as 'foreign', and kill liver cells expressing the gene. This research provides powerful tools to identify and analyse molecules critical for immune tolerance, while providing valuable clues to improve the success of human gene therapy.

STAFF

Faculty Patrick Bertolino
Associate Faculty David Bowen
Senior Research Officer Szun Szun Tay (until Oct)
Senior Research Officer Frederic Sierro
Research Assistant Bharvi Maneck
Research Assistant Nicole Wood
Technical Officer Claire McGuffog
PhD Scholar Michelle Vo
Honours Student / Research Assistant David McDonald (from Nov)
Honours Student / Research Assistant Nicholas Meyer (from Dec)

RESEARCH HIGHLIGHT OF THE YEAR

In a study published in the *Journal of Hepatology*, our group was the first to identify the lymph nodes that specifically drain the mouse liver. Work performed in our group by a PhD scholar, Lauren Holz (now working at the NIH in the USA), has also clarified the signature of T cells activated in the liver and demonstrated that this signature is different from the signature of T cells activated in the lymph nodes.

This work, also published in the *Journal of Hepatology*, was highlighted by an editorial article in the same issue of the journal.

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

Liver Injury and Cancer

Placing the battle against liver disease in the public spotlight

STAFF

Assistant Director & Faculty
Geoff McCaughan
Associate Faculty Mark Gorrell
Associate Faculty Nick Shackel
Affiliate Member of the Faculty
Devanshi Seth
Senior Research Officer Fiona Warner
Research Officer
Alison Morgan (until Aug)
Research Officer Annette Maczurek
Research Officer Fiona Keane
Research Officer Jennifer Brockhausen
Research Officer Nicholas Sigglekow
Research Officer Thomas Tu (from Nov)
Research Assistant Alastair Duly
Research Assistant
Ana Julia Vieira de Ribeiro
Research Assistant
Bramilla Patkunanathan
Research Assistant Christine Yee
Research Assistant Sumayia Chowhury
Research Assistant Derrick Van Rooyen
PhD Scholar Aimei Lee
PhD Scholar Auvro Mridha (until Feb)
PhD Scholar Candice Grzelak
PhD Scholar Charlie Zheng (from Feb)
PhD Scholar Elizabeth Hamson
PhD Scholar Helen Vidot (from Sept)
PhD Scholar Hui (Emma) Zhang (from Mar)
PhD Scholar Margaret Gall (from Mar)
PhD Scholar Naveed Nadvi
PhD Scholar William D'Avigdor
PhD Scholar Yiqian Chen
Honours student Amanda Elaro
Honours student Bashar Alani (Mar – Oct)
Honours student Pok Fai Wong
Occupational Trainee
Marja Kornhuber (Aug – Oct)
Summer Research Scholar
Linda Ban (from Nov)
Work Experience Kaitlyn Preece

Overview

The liver is our largest solid organ. The size of a football in adults, it performs hundreds of essential tasks: the liver cleans blood of toxins; stores fats and sugars ready for rapid use; and is a factory for bile, clotting and immune factors. If the liver shuts down we would die within two days. However we work our livers hard and as a consequence serious liver diseases such as the hepatitis B and C viruses (HBV and HCV), affecting about half a million Australians, have increased. Unlike other cancers with unknown causes, 90% of liver cancer is due to serious liver disease, exacerbated by alcohol abuse, diabetes, obesity, and immune and genetic conditions. Liver disease therefore encompasses a whole spectrum of ages and etiologies. We aim to investigate and establish chronic liver disease and cancer as a priority for research and therapeutic development, with the vision to eradicate the disease.

— Geoff McCaughan

Research program

The molecular and cellular pathways implicated in liver injury

Our group studies the molecular and cellular pathways implicated in key liver diseases that ultimately predispose sufferers to primary liver cancer. We are studying chronic viral hepatitis, immune system disorders, alcoholic liver injury and diabetes related fatty liver disease. By understanding the mechanisms that trigger liver damage and the development of liver cancer, we can design targeted therapeutics to cure liver disease. We have a variety of key projects currently underway: we are studying the role of the hedgehog signalling pathway which has been implicated in cancer; identifying novel microRNAs in cirrhosis and hepatocellular carcinoma (HCC, the most common type of liver cancer); and characterising how molecules in the oligopeptidase family and CD147 cause fatty liver disease and cirrhosis.

Using our novel discoveries as liver health biomarkers

We are using our novel discoveries to develop biomarkers and diagnostics for the severity and progression of liver disease and HCC. Biomarkers are a measurable target for accurate diagnostics to ensure the timely initiation of treatment. We incorporate genomics and systems biology to understand chronic liver disease and HCC for the development of biomarkers, with two major ongoing biomarker projects. We are using serum levels of oligopeptidase protein family members to correlate with the stage of liver damage in chronic HCV, alcoholic liver disease and fatty liver disease. These markers, together with osteopontin, are also being used to predict outcome in advanced HCC. These projects are of extreme clinical significance with major implications for the development of superior diagnostics.

EMMPRIN: A promising diagnostic and biomarker for liver disease and cancer

We are investigating the role of the main liver cells, hepatocytes, during liver inflammation and scarring. Of particular interest is the CD 147 molecule (known as extracellular matrix metalloproteinase inducer, EMMPRIN) in scarring and the development of liver cancer. Our research has shown that serum CD 147 levels correlate with the severity of liver fibrosis in HCV and non-alcoholic fatty liver disease, and additionally predict worse outcomes in advanced HCC.

RESEARCH HIGHLIGHT OF THE YEAR

By knocking out the function of FAP and DPPIV, members of the oligopeptidase protein family, we were able to show an increase in the occurrence of fatty liver disease. This major finding indicates that these proteins are potential therapeutic targets for the fight against liver disease.

Novel therapeutics targeting FAP are already in place whilst DPPIV inhibitors are being pursued to treat human liver disease.

PhD Scholar, Candice Grzelak is shown here in the tissue culture room where she is researching to find the genes that are involved in healing the liver after injury.

RESEARCH HIGHLIGHT OF THE YEAR

Dr Jodie Ingles received the 2012 Rita and John Cornforth Medal, the highest award given to a University of Sydney PhD student for her research focused on optimizing the clinical care of families with genetic heart disease.

Her primary supervisor, Chris Semsarian, won the prestigious 2012 Cardiac Society of Australia and New Zealand RT Hall Research Prize in recognition of his research work on the genetic disease, hypertrophic cardiomyopathy, and for his role in establishing the first Genetic Heart Disease Clinic and Registry.

Professor Chris Semsarian and Dr Jodie Ingles studying the inheritance of a familial heart disease gene through the generations.

Molecular Cardiology

Getting to the heart of sudden death

Faculty, Professor Chris Semsarian, Molecular Cardiology

Overview

Cardiovascular diseases with genetic etiologies are the most common cause of sudden death in young people, including athletes. An example is the genetic disease hypertrophic cardiomyopathy (HCM). Affecting 1 in 500 people, HCM interferes with normal heart function, the symptoms tragically remaining silent in up to 50% who present with sudden death. Our group integrates basic science, clinical cardiology and public health strategies to investigate these genetic heart conditions to prevent complications of disease, including sudden death. To understand the clinical and genetic basis of inherited heart disease, we use several approaches including human gene discovery studies, cellular systems and animal models of human disease. The basis of all our genetic studies comes from our key clinical resources, including well phenotyped individual patients and families. By combining this clinical biology with population based psychosocial and public health studies we ensure we continue to target specific areas of unmet need in the community, strengthening our laboratory's focus on translational medicine.

— Chris Semsarian

Research program

Understanding HCM, the silent killer

The most common genetic heart disorder known is hypertrophic cardiomyopathy (HCM). HCM is characterized by marked thickening of the heart muscle and can affect even elite athletes. We have performed genetic studies using clinical information and DNA from over 600 HCM families involved with our program. This key clinical resource has allowed the development of two transgenic models of the genetic disease which, when combined with our cell culture models, have allowed in depth evaluation of the genes that are effected. This work will lead to diagnostic and therapeutic measures to treat patients suffering from HCM.

The genetics of sudden death

The unexpected death of an infant younger than 1 year of age from an apparently inexplicable cause is called sudden infant death syndrome (SIDS). It has been suggested that arrhythmia of the heart may be a possible cause of SIDS. Our group has identified a subset of genes affecting the membrane function of heart cells that are changed in some SIDS cases*. This and other studies in our group involving novel gene discovery, genetic diagnosis, and understanding disease progression, maximize our ability to develop strategies to reduce sudden death at all ages. Our research is already having an impact on the community, with patient education programs, new diagnostic approaches, and prevention of sudden death through family screening and genetic testing.
*http://www.ncbi.nlm.nih.gov/pubmed/23623143

Exciting times ahead

Our overarching vision for the next 35 years is to use advanced molecular and genetic approaches in both human patients and in animal models to address key clinical questions in genetic heart disease, with the ultimate goal to improve the cardiovascular health of our communities. We use state-of-the-art techniques such as whole exome sequencing, mRNA and microRNA profiling, which when combined with our laboratory models and clinical resources ensure we can develop better targeted, personalized therapy.

STAFF

Faculty Chris Semsarian
Research Officer Emily Tu (until Mar)
Research Officer Jodie Ingles
Research Officer Lien Lam (from Nov)
Research Officer Richard Bagnall
Research Officer Tatiana Tsoutsman
Research Assistant
Angharad Evans (until Nov)
Research Assistant
Erin Finch (May – Nov)
Research Assistant
Joanna Sweeting (from Nov)
Clinical Researcher Belinda Gray
Clinical Researcher Caroline Medi
PhD Scholar Jipin Das Kizhakkepatt
PhD Scholar Ratnasari Padang
PhD Scholar Rhian Shephard
PhD Scholar Sari Padang
Honours student Bianca Varney
Masters student
Maria Constantinou (from Nov)
Masters student
Renee Jonhson (from Nov)
Medical Student Jennifer Kozlovski
Registry Co-ordinator Tanya Sarina
Clinical Co-ordinator Laura Yeates
Work Experience
Andri Pujikurniawati (Mar – June)

Faculty, Associate Professor Pu Xia, Signal Transduction

Signal Transduction

Cell communication reveals new ways to treat human disease

STAFF

Faculty Pu Xia
Senior Research Officer
Carol Wadham
Research Officer Jinbiao Chen
Research Assistant
Dominik Kaczorovski
Research Assistant Jacob Qi
Senior Technical Officer
Lijun Wang (until Oct)
PhD Scholar Mei Li Ng
Masters Student
Dona Wethasinghe
Occupational Trainee Lan Dai

RESEARCH HIGHLIGHT OF THE YEAR

Diabetes is a serious global health problem. Currently more than one million Australians suffer from the disease and this number is expected to double by 2015.

Cell suicide causing the destruction of pancreatic beta cells is a fundamental pathogenic cause of diabetes. Our work has for the first time identified a new mechanism for protecting against beta cell death, providing a new strategy for the management of diabetes.

The results of these findings were published in the *Journal of Biological Chemistry*.

Overview

Our bodies are made of up to 75 trillion cells that communicate with each other extremely efficiently to ensure good health. Cells communicate using a unique language comprising of hundreds of thousands of specialised biochemical reactions. When these biochemical reactions, that is, cell communications, are disturbed by any conditions, disease will ultimately take place. Our aim is to investigate where and how these communication faults occur, by which we will be able to restore the normal communication and thus effectively treat and prevent diseases at their root. We have identified a critical signalling pathway built around a key enzyme, sphingosine kinase (SphK). SphK is overproduced by some cells when they become inflamed or cancerous. Blocking SphK with chemical or genetic inhibitors significantly reduces inflammation and delays or prevents cancer cell growth. We seek to explore the clinical implication of these findings and develop new therapeutic agents for the treatment of cancer, diabetes and inflammation-associated diseases.

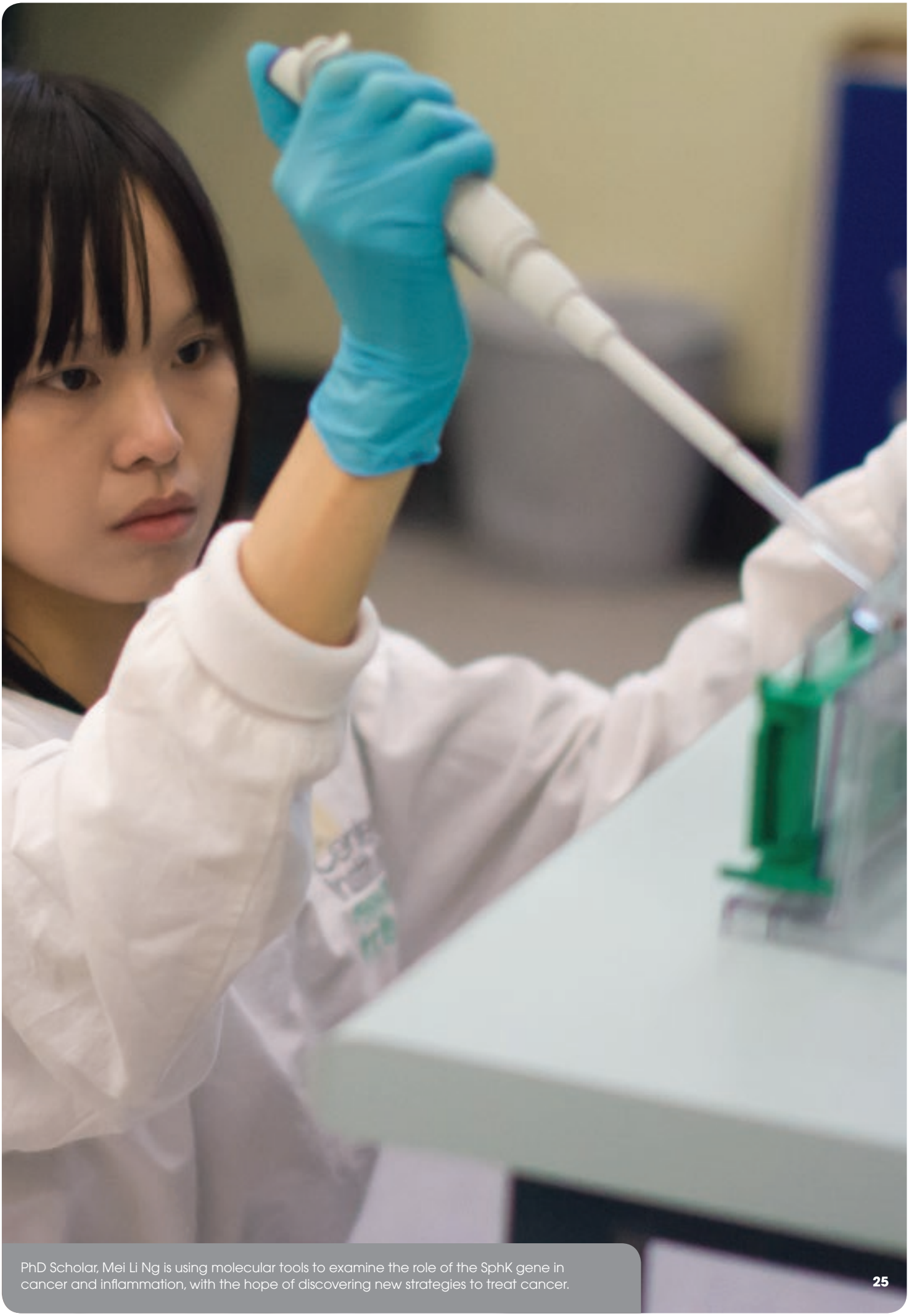
— Pu Xia

Research program

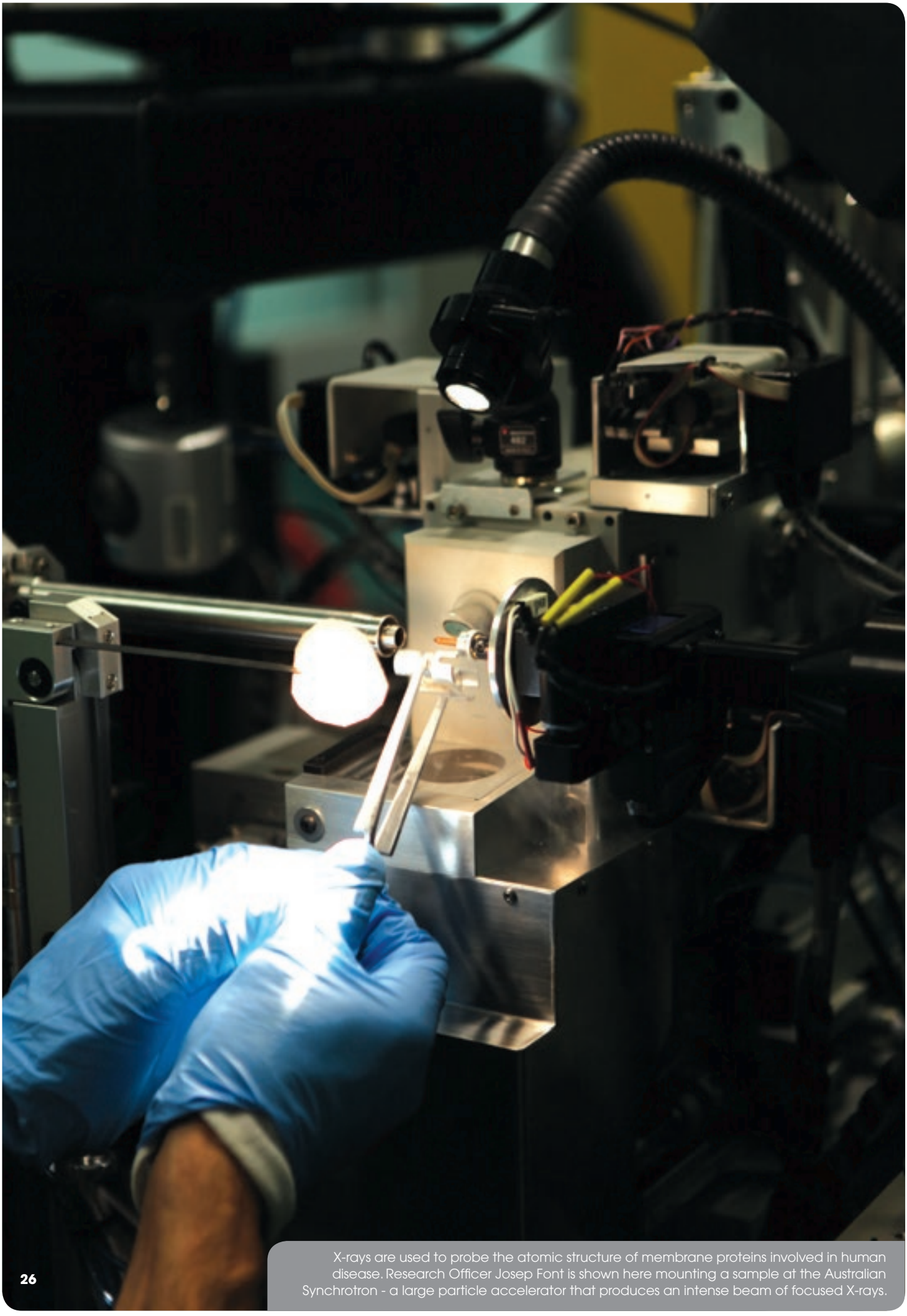
Saving pancreatic beta cells to treat diabetes
Type 1 and type 2 diabetes are both characterised by the death of pancreatic beta cells due to programmed cell death (cell suicide). Pancreatic beta cells are essential for health as their insulin secretory function allows sugar level regulation in our bodies. We have found a way to protect pancreatic beta cells from death - a new strategy for the management of diabetes. This study, while revealing a novel signalling pathway in promoting beta cell survival, may also provide a new drug target for prevention and treatment of diabetes.

Preventing insulin resistance in the liver
Obesity is often characterised by insulin resistance in the liver. This can lead to the development of diabetes and fatty liver disease. We have found for the first time that a specific isoform of SphK is an important signalling molecule, regulating the role of insulin in controlling sugar production by the liver. This information adds to our understanding of the molecular mechanisms of insulin resistance in the liver, paving a new path to fighting diabetes.

SphK inhibition for a healthy liver
A new animal model that mimics obesity-associated inflammation conditions in the human liver has become an invaluable tool for our group in investigating the role of SphK in liver health. We have discovered that SphK is a key signal node that promotes the process of chronic fatty liver disease to the development of liver cancer. Inhibition of SphK prevents fatty liver disease and cancer formation in our animal model. This is truly exciting and holds key potential to improve the health of sufferers of liver disease in the community.



PhD Scholar, Mei Li Ng is using molecular tools to examine the role of the SphK gene in cancer and inflammation, with the hope of discovering new strategies to treat cancer.



X-rays are used to probe the atomic structure of membrane proteins involved in human disease. Research Officer Josep Font is shown here mounting a sample at the Australian Synchrotron - a large particle accelerator that produces an intense beam of focused X-rays.

Structural Biology

3D protein structure may hold the key to designing better drugs

Faculty, Associate Professor Mika Jormakka, Structural Biology

Overview

The contents of every cell in our body are protected and held together by the cell membrane. The membrane is peppered with pumps and channels made of proteins acting as important cell checkpoints. Like passport control, they are the first barrier between the cell and a foreign atom, molecule, virus or bacteria. The impact of infection, disease or poisoning depends on what is allowed through the cell membranes. Proteins on the membrane that guard the cell thus play a critical role in normal cellular processes. Alterations in their function cause many human diseases, including diseases of iron metabolism and cancer progression. Each protein's function is determined by its unique three dimensional structure, without which it cannot function correctly. We aim to provide high resolution structures of critical proteins implicated in membrane diseases, in order to design a 'perfect' drug to fit. This will maximise treatment efficiency while minimising side effects.

— Mika Jormakka

Research program

Membrane protein anatomy for targeted drug development
A protein's function is determined by its structure and shape, and when this is disturbed it can have detrimental effects on the health of a cell. Hence, to fully understand the function of a protein, it is necessary to obtain a precise atomic model or 'blueprint' of how a protein is folded in space. To obtain this, we use synchrotron radiation (particle accelerators) and a technique known as X-ray crystallography. By understanding membrane protein structure and function, we hope to facilitate structure based drug discovery, enabling us to move away from trial and error to calculated methods of drug design. This 'lock and key' approach ensures high specificity with minimal side effects.

Toward drugs to modulate membrane proteins implicated in cancer
Cancer progression and development is often dependent on specific membrane proteins. For example the progression of prostate and breast cancer is dependent on an increasing amount of the amino-acid leucine, which is acquired through a specific type of membrane transporter called Linker of Activated T cells (LAT.) Determining the structure of LAT transporters will allow us to provide a scaffold for the development of drugs to 'tune' its function, providing a new method of cancer treatment.

Toward drugs for diseases of iron metabolism
Iron is an essential element which is acquired and distributed by a set of specific membrane proteins. In bacteria, the acquisition of iron is essential for successful colonization causing infection, while in humans the acquisition and distribution is required for a range of vital processes. Errors in the proteins involved in iron distribution can cause a range of diseases such as cancer, hemochromatosis and anemia. Our structure and function studies on the membrane proteins implicated in iron metabolism will provide a platform for designing drugs to regulate them.

STAFF

Faculty
Mika Jormakka

PhD Scholar
Amy Guilfoyle

Research Officer
Aaron McGrath

Research Officer
Chandrika Deshpande

Research Officer
Josep Font

RESEARCH HIGHLIGHT OF THE YEAR

We have made significant advances in understanding disease progression related to iron metabolism, but also on a more translational level, advances in characterising the effects of drug therapies in cancer.

We have provided new insight into disease causing iron acquisition through a particular iron transporter, and have characterised specific lead drug candidates targeting the LAT transporters in prostate cancer cells.

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

T cell Biology

Is our western lifestyle increasing chronic diseases such as asthma and diabetes?

STAFF

Faculty Barbara Fazekas de St Groth
Senior Research Officer Elena Shklovskaya
Research Assistant / Research Officer (from Sept) Holly Bolton
Research Assistant Cindy Zhu
Research Assistant Michelle Brownlee
Research Assistant Wendy Zhang
Research Assistant Yu Qing Rain Kwan
Research Officer Michael Kuligowski
PhD Scholar Alexandra Terry (from Mar)
PhD Scholar David Hancock
PhD Scholar Lauren McKnight
PhD Scholar Loretta Lee
PhD Scholar Nazri Mustaffa
PhD Scholar Suzanne Asad
PhD Scholar Thomas Guy
PhD Scholar Yik Wen Loh
Visiting Researcher Fan Wu (Mar – June)
Visiting Researcher Nick West (from Mar)
Visiting Researcher Peggy Horn (Mar – June)
Visiting Researcher Xiangguo Duan (until October)

Overview

Our environment and the lifestyles we lead can influence health more readily than genetic makeup. The western lifestyle has led to the rise of chronic diseases such as allergies and asthma, as well as other immune system disorders like type 1 diabetes, multiple sclerosis and psoriasis. Our immune system is central for health, acting as the security guard of our body. Made of a complex network of molecules, cells and organs, it provides layers of defense to remove disease-causing stimuli. Our group concentrates on the network managers of the immune system: regulatory T cells (T regs). We are investigating how T regs interact with other immune cells to prevent allergies and other immune disorders. Understanding the mechanism of action of T regs will ultimately lead to cures for sufferers of immune system mediated diseases.

— Barbara Fazekas de St Groth

Research program

Understanding how T regs manage the immune system
T regs are rare cells at the centre of the immune control network. They are absolutely crucial for the prevention of immune system mediated diseases. How regulatory T cells perform this vital function is a major focus of our research. We have developed a novel experimental model to study T regs, and have used this model to shed light on a major aspect of their function. We have discovered that T regs set the threshold for stimulation of the immune response, ensuring a healthy balance between protection against foreign pathogens and prevention of autoimmune disease – when the immune system starts to attack the body itself.

Teaching the immune system to control tumours
Harnessing the immune system in the fight against cancer is one of our major goals. Tumours survive and grow by evading immune system control. We are studying how different immune cell types interact with each other and the tumour. To make this possible, we use models in which we can track individual immune cell responses to molecules associated with the tumour. Our experiments have shown that T regs promote the survival of tumour cells, presenting a new target for cancer therapeutics.

T regs in human disease
We are studying T regs from patients suffering from immune-mediated diseases such as psoriasis, inflammatory bowel disease, systemic lupus erythematosis and asthma. Our bioinformatics capabilities make use of computerised analysis to accelerate our understanding of the key differences between T regs from these patients and healthy volunteers, providing insights into how they can influence disease progression, but more significantly how they can pre-dispose us to disease, potentially leading to cures not just treatments.

RESEARCH HIGHLIGHT OF THE YEAR

Dendritic cells are immune cells that detect and process information from foreign invaders in the body, and then communicate with other immune cells such as T cells. Our group showed how T regs prevent autoimmune disease by fine-tuning dendritic cells so that they can't stimulate autoimmune cells.

We have begun characterisation of the molecular machinery employed by T regs to achieve this vital function.

Research Officer Holly Bolton is working on a new approach to understanding how regulatory T cells prevent autoimmune diseases such as type 1 diabetes.

RESEARCH HIGHLIGHT OF THE YEAR

Our team of national and international researchers was awarded a Centre of Research Excellence (CRE) in TB. The CRE provides a unique opportunity for researchers at the Centenary and collaborators to strengthen existing research capability in TB and build world-leading research capacity.

The CRE brings together a unique combination of expertise in public health, epidemiology, basic science, ethics, law and clinical medicine, to effectively and practically address the complex public health problem that is TB.

Centenary's new PC3 laboratory was opened this year to help better understand and combat the killer mycobacteria that causes Tuberculosis.

Tuberculosis Research

Leading a global effort to combat tuberculosis

Assistant Director, Faculty,
Professor Warwick Britton, Tuberculosis Research

Overview

Tuberculosis (TB) remains a global health burden of staggering proportions. The World Health Organisation estimates that 1/3 of the world's population are infected by Mycobacterium tuberculosis, the bacteria that causes TB. In Australia TB infects around 1,300 people annually, and our nearest neighbour, Papua New Guinea, registered 14,000 new cases and almost 3,000 deaths in 2010. TB research is essential to assist the global fight against this deadly disease, but to combat the risk of drug-resistant TB entering Australia. Our group engages in national and international collaborations to address three major facets in the fight toward TB eradication. First, we are designing better tests for the diagnosis and monitoring of patients with TB; second, we aim to create a vaccine to provide lifelong TB immunity; and third, we are discovering the genetic and environmental factors that cause one individual to develop the disease while the other remains healthy.

— Warwick Britton

Research program

Designing better TB diagnostics

Current TB diagnosis is extremely slow and the current 6 month treatment is ineffective for 5-10 % of TB sufferers. Diagnosis is slow as the TB bacteria is extremely slow growing, and drug resistant forms of the disease are rising causing over half a million cases worldwide. New diagnostics, preferably blood-based, that identify active clinical disease and monitor therapy response would greatly assist TB control. In collaboration with local Sydney hospitals and the Ningxia Infectious Disease Hospital in China, we are testing the reliability of promising new blood-based markers of TB. If successful this test would enable rapid TB diagnosis in hours, not weeks.

Developing new TB vaccines

The current TB vaccine, BCG, protects children early in life, but fails to provide lifelong immunity to TB. The development of a new TB vaccine that is superior to BCG is critical for long-term control of TB. Our group is developing and testing novel vaccines based on the components of the TB bacterium that stimulate effective immune responses. Pre-clinical data indicate that these vaccines can protect against TB, resulting in the award of two NHMRC grants to improve their efficacy and to develop ways to deliver these to the lungs.

Genetic susceptibility to TB

It is well known that susceptibility to TB is influenced by our genetic makeup, environment and socio-economic risk factors. Understanding why relatively few individuals infected with TB develop the clinical disease is essential to dissect the relevant pathways involved in TB immunity. We are undertaking the first genome wide association study for TB in China using a large cohort comprising 2500 cases with matched healthy controls. This international collaboration between Australia, China and the UK will allow us to provide valuable insight into the protective and pathogenic mechanisms involved in TB susceptibility. This will identify novel drug and vaccine targets essential for long term TB control and ultimate global elimination.

STAFF

Faculty Warwick Britton
Associate Faculty
Bernadette Saunders
Associate Faculty Nick West (until June)
Affiliate Member of the Faculty
Jamie Triccas
Senior Research Officer Paul Reynolds
Research Officer
Amanda Brown (until Jun)
Research Officer Brian Chan
Research Officer Jennifer Huch
Research Officer Magda Ellis
Research Officer Manuela Florido
Research Officer
Rachel Pinto (from Aug)
Research Officer Shaun Walters (until Jul)
Research Assistant Angel Pang
Research Assistant Caitlin Gillis (until Aug)
Research Assistant Lisa Leotta (until Mar)
Research Assistant Theresa Corpuz
Research Assistant Tuyet Tran (until Feb)
Executive Officer
Gabriella Scandurra (from Nov)
Administration Officer
Lalita Narayan
PhD Scholar Anneliese Tyne (from Mar)
PhD Scholar Claudio Counoupas
PhD Scholar Erin Shanahan
PhD Scholar Gayathri Nagalingam
PhD Scholar Greg Fox
PhD Scholar
Mercedes Montelone (until June)
PhD Scholar Samantha Ellis
PhD Scholar Simone Barry
Honours student Edwina Chan
Honours student Roman Pillay
Visiting Researcher Carl Feng (from Aug)
Visiting Researcher
John Chan (Oct - Dec)

Faculty, Professor Jennifer Gamble, Vascular Biology

Vascular Biology

Targeting leaky blood vessels to find new therapeutics

STAFF

Faculty Jennifer Gamble
Faculty Mathew Vadas
Senior Research Officer Angelina Lay
Senior Research Officer Mai Tran
Research Officer Gabor Hutas
Research Officer Joshua Moses
Research Officer Ka Ka Ting
Research Officer Michael Lovelace
Research Officer Paul Coleman
Research Assistant Georgina Kalodimos (until Jul)
Research Assistant Jia Li
Research Assistant Julie Hunter
Research Assistant Ying Lu
Research Assistant Yue Zheng (from Apr)
Research Assistant Ann Formaz-Preston
Technical Officer Elena Zaporoshenko (until Jul)
Technical Officer Lutfun Khan (From Jul)
PhD Scholar Garry Chang
PhD Scholar Yang Zhao (from Sept)
Honours Student / Research Assistant Elizabeth Powter (from Nov)
MBBS Honours Student Ella Stephens (from Apr)
Visiting Researcher Peter Zhou (from Apr)
Work Experience Xin-Xin Hu (July)

Overview

An adult has 80 000 kilometres of blood vessels, transporting essential oxygen and nutrient rich blood to every region of the body. Blood vessels also transport critical infection fighting cells in blood, called inflammatory cells. Before they can combat infection, inflammatory cells must communicate with specialised cells lining the blood vessel surface, called endothelial cells. Endothelial cells are crucial for blood vessel integrity, preventing unnecessary blood and fluid leakage and controlling the passage of inflammatory cells from the blood to tissues. Endothelial cells are implicated when things go wrong, like in hardening of the arteries (atherosclerosis), complications associated with diabetes, and in ageing. They are also implicated in cancer: tumour cells need nourishment to survive, so endothelial cells are tricked into constructing new blood vessels that feed the tumour. By learning how endothelial cells function we can design new therapeutics that manipulate blood vessels as an avenue of disease control.

— Jennifer Gamble

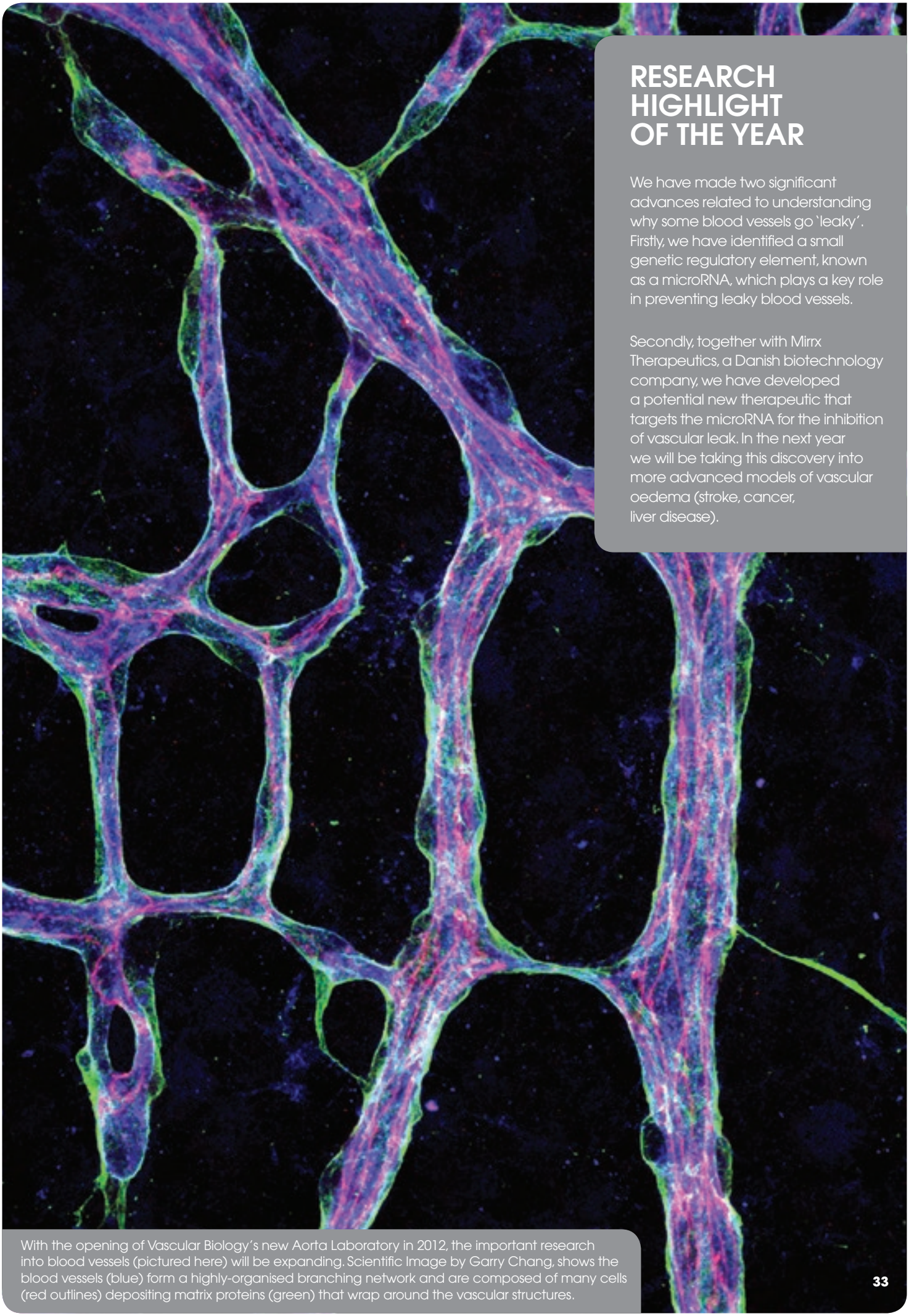
Research program

Preventing nourishment of cancerous tumour cells

A major role for the endothelial cells is in the process of new blood vessel formation, called angiogenesis. New vessels are needed during, for example, wound repair. However in cancer, the angiogenic response contributes to the growth of tumours leading to expansion in tumour mass. One of the hallmarks of blood vessels in tumours and in chronic inflammatory disease is that they are 'leaky' and this can contribute to much of the pathology of disease. We want to understand how the complex process of angiogenesis is orchestrated and how to maintain a non-leaky endothelial surface. We hope to identify new key molecules that could ultimately be used as therapeutic targets.

Ageing endothelial cells

With advancing age, endothelial cell function can be compromised, contributing to diseases primarily associated with age-cancer, cardiovascular disease and diabetes. We have identified a gene that signals the onset of ageing and decline in endothelial cell health, which we have called SENEX (gene name ARHGAP18). We aim to investigate the function of the SENEX/AHGAP18 protein. Specifically, we want to unravel its structure, the molecular events that govern its activity, regulation and interactions, and also define its role in regulating inflammation. These investigations will lead to more detailed understanding of the ageing endothelium and may elucidate new areas to target to maintain blood vessel health and strengthen the immune response to infection.



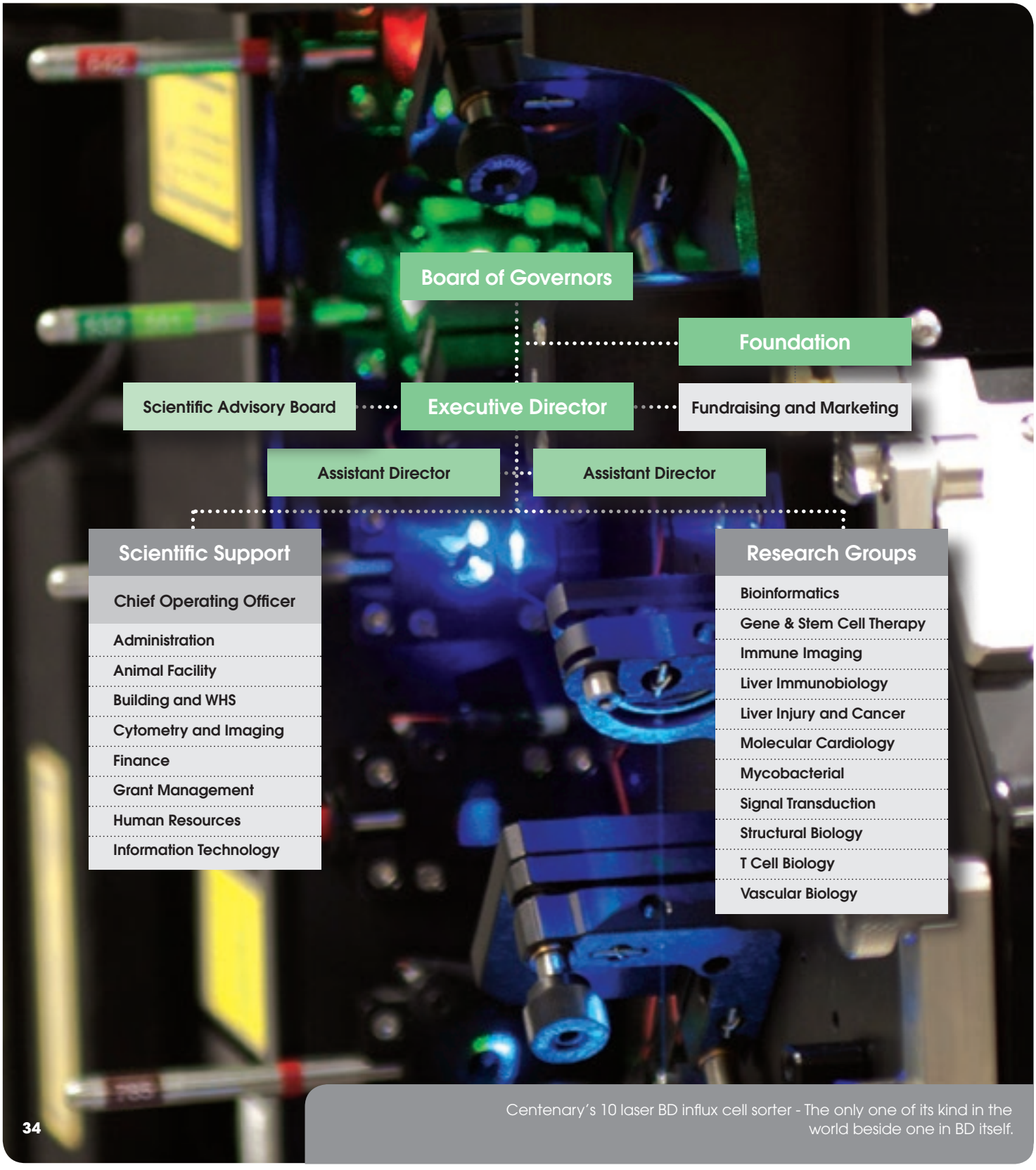
RESEARCH HIGHLIGHT OF THE YEAR

We have made two significant advances related to understanding why some blood vessels go 'leaky'. Firstly, we have identified a small genetic regulatory element, known as a microRNA, which plays a key role in preventing leaky blood vessels.

Secondly, together with Mirrx Therapeutics, a Danish biotechnology company, we have developed a potential new therapeutic that targets the microRNA for the inhibition of vascular leak. In the next year we will be taking this discovery into more advanced models of vascular oedema (stroke, cancer, liver disease).

With the opening of Vascular Biology's new Aorta Laboratory in 2012, the important research into blood vessels (pictured here) will be expanding. Scientific Image by Garry Chang, shows the blood vessels (blue) form a highly-organised branching network and are composed of many cells (red outlines) depositing matrix proteins (green) that wrap around the vascular structures.

Organisational Chart 2012



Centenary's 10 laser BD influx cell sorter - The only one of its kind in the world beside one in BD itself.

Dr Nick Pearce, Chief Operating Officer

Science Support

Working with researchers towards a common goal

STAFF

Administrative Assistant
Julie Langenberg (until Nov)
Administrative Assistant/Reception
Michael Greensmith
Administrative Assistant/Reception
Rachel Wolfenden
Animal Attendant Elizabeth Connolly
Animal Attendant Natalie Littlejohn
Animal Facility Assistant Victor Truong
Animal Facility Officer Marisa Henry
Animal Technician Carol Juaton
Animal Technician Danielle Moyes
Animal Technician David Herne
Animal Technician Leah Miller
Animal Technician Megan Kavazos
Animal Technician Michael Damjuncuk
Assistant Accountant Chelsea Wang
Building Services Assistant Bob Thorburn
Animal Facility Assistant Gary Black
Animal Facility Assistant
Rachel Barry (from Sept)
IT Support Nic Barker (until Jul)
Chief Operating Officer Nick Pearce
Cytometry and Imaging Support
Suat Dervish (from Feb)
Cytometry Technical Support
Frank Kao (from June)
Director's PA/Office Manager
Helen Warwick
Finance Manager Tim Neal
Finance Officer Willie Entona
Grants Manager Nick Keilar
HR Advisor Anna Slowiaczek
HR Assistant Julie Abalain (from Sept)
HR Manager Nan Herlihen
Imaging Support Specialist
Kristina Jahn (from Feb)
IT Helpdesk Owen Hoogvliet
IT Operations Manager
Daryl Hunt (from Nov)
Manager – Cytometry, Imaging and IT Adrian Smith
Systems Administrator Robert Middleton
Senior Technical Support Steve Allen
Veterinary Manager Maria Wynne
WHS and Operations Manager
Jeff Crosbie

It has been an immensely productive year with the entire scientific support team working hard in 2012 to provide the necessary resources for our bright researchers.

2012 saw the final expenditure on the 2006 Australian government grant to upgrade our building. The grant provided upgrades to all aspects of our infrastructure and the purchase of much needed equipment, including the purchase of the third multiphoton microscope.

The investment of several million dollars over a 6 year period has seen the number of cytometry and imaging machines in Centenary grow from six to seventeen. We are truly grateful to the Cancer Institute NSW, Perpetual Trustees, Ramaciotti Foundation and the Australian government for committing these funds to expand our cytometry and imaging facility – it is now considered one of the best in the country.

In 2012 three more scientific support staff joined the Cytometry and Imaging facility. The new staff have provided expert training, support, knowledge and new techniques to the researchers.

Professor Fazekas de St Groth's work on regulatory T cells using the Cytometry and Imaging facility has received enormous recognition. The T Cell Biology group's work has resulted in a number of highly cited publications and a patent for purifying regulatory T cells, which has been licensed.

With our important focus on translational bench to bedside research, it is wonderful to report that Professor Fazekas de St Groth's new approach to purify regulatory T cells is being used in clinical trials for children with recent-onset type 1 diabetes.

2012 also saw the implementation of a new finance system. This new system is much needed, with the predicted twenty percent growth of Centenary staff over the next three years as we expand into the Centenary-Lifehouse Cancer Research Centre based in Sydney University's Charles Perkins Centre.

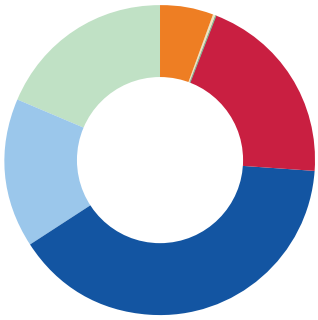
It would be neglect not to mention the strength of our grant applications in 2012. Centenary's Professor Warwick Britton was awarded funding to head up the new international Centre for Research Excellence for Tuberculosis Control (2012-2017). Importantly, our faculty heads continue to be awarded Australian Government grants (National Health and Medical Research Council and Australian Research Council), NSW Government grants and a wide variety of non-Governmental grants in recognition of their excellent work.

On behalf of all the researchers and support staff, many thanks to our supporters and key stakeholders 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 ongoing hard work. ☺

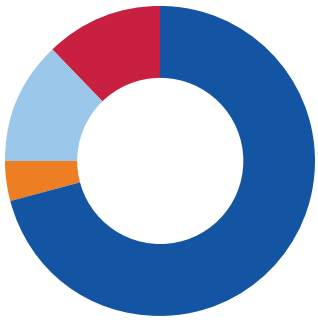
Financial Highlights

INCOME



- Fundraising – 5.83%
- Bequests – 0.14%
- Commercial – 0.03%
- Other – 20.14%
- Federal – NHMRC + ARC – 39.75%
- NSW Government – 15.67%
- Other Research Grants – 18.43%

EXPENDITURE



- Research Activities – 71%
- Fundraising – 4%
- Administration – 13%
- Building operations – 12%

	2012 in '000	2011 in '000	2010 in '000
INCOME			
Research Income			
Federal - NHMRC + ARC	6,923	7,086	5,989
NSW Government	2,729	1,050	1,331
Other Research Grants	3,209	4,566	3,999
Total research income	**12,861**	**12,702**	**11,319**
Fundraising			
Donations, events + other	1,016	1,082	1,198
Bequests	25	364	1,346
Total fundraising	**1,041**	**1,446**	**2,544**
Commercial	*6*	*13*	*3*
*Other**	*3,508*	*3,368*	*3,456*
	17,416	**17,529**	**17,351**
EXPENDITURE			
Research activities	14,221	12,694	12,625
Fundraising	805	898	870
Administration	2,588	1,699	1,606
Building operations	2,338	1,982	1,684
Total Expenditure	**19,952**	**17,273**	**16,785**

* The majority of '*Other*' revenue is from Facilities Agreements and Interest.

Successful Grant Recipients

Investigator/s*	Granting Body	Type
Saparna Pai	Australian Academy of Science	Travel (2012 - 2013)
Mark Gorrell	Australian Centre for HIV and Hepatitis Virology Research	Project (2012 - 2013)
Phillip Bird, **Wolfgang Weninger**	Australian Research Council	Project (2012 - 2014)
Wolfgang Weninger	Cancer Institute NSW	Fellowship (2012 - 2014)
Chris Semsarian & Ingrid Scheffer	CURE	Project (2012 - 2013)
Mark Gorrell, Oliver Schilling	DAAD	Travel (2012 - 2013)
Mark Gorrell	Diabetes Australia Research Trust	Project (2012 - 2012)
Jeff Holst	National Breast Cancer Foundation	Fellowship (2012 - 2015)
Chandrika Deshpande	National Breast Cancer Foundation	Fellowship (2012 - 2015)
Warwick Britton, Nick King, Georges Grau, **Wolfgang Weninger**, **Geoff McCaughan**, Barry Slobedman, **Bernadette Saunders, Nick West, Jamie Triccas**, Allison Abendroth, Valery Coombes, **David Bowen, Nick Shackel, Magda Ellis**	National Health & Medical Research Council	Equipment (2012 - 2012)
Jodie Ingles	National Health & Medical Research Council	Fellowship (2012 - 2015)
Mika Jormakka	National Health & Medical Research Council	Fellowship (2012 - 2015)
Warwick Britton, Barend Marais, Guy Marks, Vitali Sintchenko, Stephen Graham, **Jamie Triccas**, **Bernadette Saunders**, Ian Kerridge, Gwendolyn Gilbert, Belinda Bennett	National Health & Medical Research Council	Centre for Research Excellence (2012 - 2017)
Timothy Hughes, Deborah White, **John Rasko**	National Health & Medical Research Council	Project (2012 - 2014)
Joel Mackay, David Segal, **John Rasko**	National Health & Medical Research Council	Project (2012 - 2014)
Wolfgang Weninger	National Health & Medical Research Council	Project (2012 - 2014)
Wolfgang Weninger, **Arby Abtin**, Neville Firth	National Health & Medical Research Council	Project (2012 - 2014)
Paulus Mrass & Wolfgang Weninger	National Health & Medical Research Council	Project (2012 - 2014)
Chris Semsarian, Robert Weintraub, David Winlaw & **Richard Bagnall**	National Health & Medical Research Council	Project (2012 - 2014)
Magda Ellis, Adrian Hill & Yurong Yang	National Health & Medical Research Council	Project (2012 - 2014)
Jennifer Gamble & Mathew Vadas	National Heart Foundation	Project (2012 - 2013)
CJ Ertl Hildegund, John Wherry, **Wolfgang Weninger**, Louise Showe, Arlene Sharpe, **Barbara Fazekas**, Sarah Ratcliffe, Marcia Haigis, Gordon Freeman, Jan Erikson, Kenneth Schmader, Emily Lu	National Institutes of Health USA	Project (2012 - 2018)
Timothy Morgan, Chris Day, Paul Haber, Lawrence Lumeng, Bertrand Nalpas, **Devanshi Seth**, Felix Stickel, John Whitfield	National Institutes of Health USA	Project (2012 - 2016)
Nick Shackel	New South Wales Cancer Council	Project (2012 - 2013)
Nikolas Haass	Sydney Medical School Foundation	Project (2012 - 2012)
David Bowen	University of Sydney SU	Project (2012 - 2012)
Bernadette Saunders	University of Sydney SU	Project (2012 - 2012)
Michael Kuligowski	University of Sydney SU	Project (2012 - 2012)
Philip Tong	National Health & Medical Research Council	Scholarship (2012 - 2013)

**CIA is named first*

2012 Publications

Akladios FN, Nadvi NA, Park J, Hanrahan JR, Kapoor V, **Gorrell MD** & Church WB. 2012. Design and synthesis of novel inhibitors of human kynurenine aminotransferase-I. *Bioorganic & Medicinal Chemistry Letters*, 22, 1579-1581.

Arnold JC, Hone P, **Holland ML & Allen JD**. 2012. Cb2 And Trpv1 receptors mediate cannabinoid actions on mdr1 expression in multidrug resistant cells. *Pharmacological Reports*, 64, 751-757.

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Gracey D, Garsia RJ, **Britton WJ**, McKenzie P. 2012. Rapid recovery of renal function after pulse steroid therapy in an HIV-infected patient with glomerulo-nephritis. *Internal Med* J. 42:1363-5

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Harris TH, Banigan EJ, Christian DA, Konradt C, Wojno EDT, Norose K, Wilson EH, John B, **Weninger W**, Luster AD, Liu AJ & Hunter CA. 2012. Generalized levy walks and the role of chemokines in migration of effector CD8(+) T cells. *Nature*, 486, 545-8.

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2012 Publications

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Ritchie W, Gao DD & Rasko JEJ. 2012. Defining and providing robust controls for microrna prediction. *Bioinformatics*, 28, 1058-1061.

Ritchie W & Rasko JEJ. 2012. Integrated miRNA expression analysis and target prediction. *Methods in Molecular Biology*, 822, 289-93.

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Stacey KB, **Breen E** & Jefferies CA. 2012. Tyrosine phosphorylation of the e3 ubiquitin ligase trim21 positively regulates interaction with irf3 and hence trim21 activity. *PLoS One*, 7 (3):e34041.

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Tran AT, **West NP, Britton WJ** & Payne RJ. 2012. Elucidation of mycobacterium tuberculosis type ii dehydroquinase inhibitors using a fragment elaboration strategy. *Chemmedchem*, 7, 1031-1043.

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Postgraduate Training

Achieving excellence

Dr Bernadette Saunders, Postgraduate Coordinator and Associate Faculty, Tuberculous Research

Centenary's postgraduate training program continued to achieve excellence in 2012 with our PhD scholars and Honours students again achieving outstanding results.

Centenary is committed to creating an environment that nurtures and inspires innovative young minds to become Australia's next generation of brilliant scientists.

Students in the postgraduate program come from a wide range of academic and ethnic backgrounds to work with Australia's leading medical researchers at the Institute.

— Bernadette Saunders, Postgraduate Coordinator

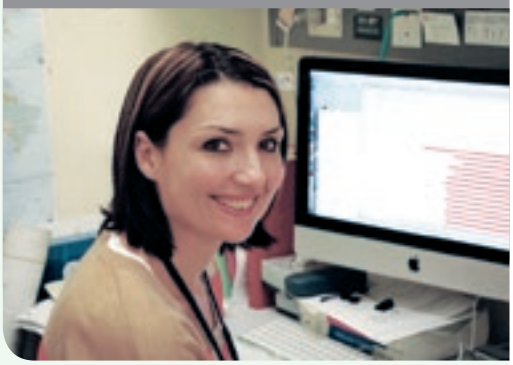
Centenary scholars Awarded in 2012

STUDENT	PRIMARY SUPERVISOR	LABORATORY GROUP
Doctor of Philosophy		
Elise Jackson	Nikolas Haass	Immune Imaging
Holly Bolton	Barbara Fazekas de St Groth	T cell Biology
Master of Philosophy		
Paula Rubim	Nikolas Haass	Immune Imaging
Honours		
Bashar Alani	Devanshi Seth	Liver Injury and Cancer
Bianca Varney	Chris Semsarian	Molecular Cardiology
*David McDonald	Patrick Bertolino	Liver Immunology
*Elizabeth Powter	Jennifer Gamble	Vascular Biology
Michelle Simmons	Jeff Holst	Gene and Stem Cell Therapy
Nicholas Meyer	Patrick Bertolino	Liver Immunology
Roman Pillay	Warwick Britton	Tuberculosis
Tim Durak	Chris Jolly	Immune Imaging

**Centenary Honours scholars awarded equal first place for the 2012 University of Sydney, Immunology and Infectious Disease Prize*

PHD SCHOLAR RECOGNISED

Dr Jodie Ingles in the Molecular Cardiology group was awarded the 2012 Rita and John Cornforth Medal for the top PhD across the University of Sydney at the Alumni Awards. Her important research showed that genetic testing is a cost effective approach to managing families with genetic heart disease.



2012 Invited Presentations

INTERNATIONAL

Bertolino P, How the liver kills killer cells, University College London, January 2012, London, UK

Bowen D, Recombinant adeno-associated virus vectors for the exploration of intrahepatic immune responses, Centre for Vaccines and Immunity, The Research Institute at Nationwide Children's Hospital, November 2012, Columbus, USA

Britton WJ, Assessing Memory T cell responses to live TB vaccines, NEWTBVAC ECF7 Consortium, January 2012, Les Diablerets, Switzerland

Britton WJ, Erythema Nodosum Leprosum, Mechanisms and challenges. New Leprosy and Tuberculosis vaccines: Challenges & possibilities, ENL Workshop, February 2012, Cebu, Phillipines

Britton WJ, Lessons from candidate TB vaccines, Stellenbosch University, June 2012, Cape Town, South Africa

Britton WJ, New Approaches to Tuberculosis Vaccine Design, 52nd ICAAC Conference, September 2012, San Francisco, USA

Britton WJ, Lessons from candidate TB vaccines, Duke Medical School, Month Year, Durham, USA

Gamble J, Consequence of Senescence in the Vasculature, Department of Biosciences, University of Milan, June 2012, Milan, Italy

Gamble J, Consequence of Senescence in the Vasculature, Kennedy Institute, June 2012, London, UK

Ingles J, The utility of genetic diagnosis for family members, Scientific Sessions of the American Heart Association, November 2012, Los Angeles, USA

Ingles J, Posttraumatic stress disorder following an implantable-cardioverter defibrillator shock in young patients with a genetic heart disease, Psychogenic Cardiovascular Disease Conference, September 2012, Prato, Italy

Ingles J, Genetic testing for inherited heart diseases: Longitudinal impact on health-related quality of life, Heart Rhythm Society's 33rd Annual Scientific Sessions, May 2012, Boston, USA

Jolly C, Cell cycle regulation of AID-induced DNA repair, American Association of Immunologists, May 2012, Boston, USA

Jolly C, Cell cycle regulation of AID-induced DNA repair, Harvard Medical School, May 2012, Boston, USA

Jormakka M, Molecular mechanism of bacterial iron transport, The 4th Membrane Protein Technologies Meeting (NIH Roadmap meeting), November 2012, San Francisco, USA

Lovelace M, Change In Functional Purinergic Signaling With Commitment To The Neuronal Lineage In Human Fetal Cortical Neural Precursor Cells, Purine, 2012 conference, May 2012, Fukuoka, Japan

McCaughan G, APASL Consensus statements fro HCV Diagnosis and Management, APASL, February 2012, Taiwan

McCaughan G, Management of Acute Liver Failure, TTS meeting, September 2012, Berlin, Germany

McCaughan G, Antiviral therapy for HCV Cirrhotic patients, Australasian Hepatitis Conference, September 2012, Auckland, New Zealand

McCaughan G, Overcoming Medical and Social impediments for Extended Criteria Liver Transplant Recipients, AASLD, November 2012, Boston, USA

McCaughan G, Cirrhosis: More then a liver Disease, St Louis University Visiting Professorship, Month Year, St Louis, USA

McCaughan G, Liver Tolerance_ T cells in and T cell out, St Louis University Visiting Professorship, Month Year, St Louis, USA

McCaughan G, HCV in liver transplantation: Interactions between the Virus and the Alloresponse, St Louis University Visiting Professorship, Month Year, St Louis, USA

McCaughan G, Liver Transplantation: Current Challenges, St Louis University Visiting Professorship, Month Year, St Louis, USA

Rasko J, Current landscape of iPS application for drug discovery within the Stem Cells for Drug Discovery Stream, World Stem Cells and Regenerative Medicine Congress Europe, May 2012, London, UK

Rasko J, Expanding Cells for tissue repair, 18th International Society for Cellular Therapies, June 2012, Seattle, USA

Rasko J, The future of Stem cells and Gene therapy, The 2nd International Seminar and Workshop on Stem Cell and Clinical Biology, November 2012, Indonesia

Rasko J, Haemopoiesis and stem cells: new views of the stem cell niche and mobilisation, The 2nd International Seminar and Workshop on Stem Cell and Clinical Biology, November 2012, Indonesia

Rasko J, Intron retention regulates normal white blood cell development, Cell symposia functional RNA's, December 2012, Siges, Spain

Rasko J, Intron retention coupled with nonsense-mediated decay determines protein expression and nuclear morphology in granulopoiesis, 54th ASH Annual Meeting, December 2012, Atlanta, USA

Semsarian C, Genetic testing in families with genetic heart disease, 5th Asia Pacific Heart Rhythm Society Semsarian C, Genetic testing in families with genetic heart disease, 5th Asia Pacific Heart Rhythm Society Meeting, October 2012, Taipei, Taiwan

Semsarian C, Genetic basis of sudden cardiac death in the young, 5th Asia Pacific Heart Rhythm Society Meeting, October 2012, Taipei, Taiwan

Semsarian C, Key role of the molecular autopsy in sudden unexplained death, 5th Asia Pacific Heart Rhythm Society Meeting, October 2012, Taipei, Taiwan

Semsarian C, SUDEP: Linking the heart and brain, Heart & Mind Meeting, September 2012, Prato, Italy

Semsarian C, Beyond DNA: transcriptomic and proteomic approaches in AF, Heart Rhythm Society Meeting, May 2012, Boston, USA

Semsarian C, Genetic basis of heart disease, Boston Scientific Annual General Meeting, February 2012, Queenstown, NZ

Weninger W, Imaging of T cell behaviour in the tumour microenvironment, 37th Japanese Society of Investigative Dermatology, December 2012, Okinawa, Japan

Weninger W, Visualising innate immune responses during skin infections, Centre for Molecular Medicine Seminar Series, December 2012, Vienna, Austria

Weninger W, Real-time imaging of antibacterial immunity in the skin, Institute of Science and Technology Seminar Series, December 2012, Vienna, Austria

NATIONAL

Bertolino P, How the liver kills killer cells, Prince of Wales Hospital, April 2012, Sydney

Bertolino P, The liver: a site of primary activation leading to tolerance? Annual meeting of the Brisbane Immunology Group (BIG), August 2012, Salt Beach Resort

Bertolino P, CD8 T cells and the liver: a love-kill relationship, Diamantina Research Institute, September 2012, Brisbane

Bertolino P, CD8 T cells and the liver: a love-kill relationship, QIMR, October 2012, Brisbane

Bertolino P, The liver: a site of primary T cell activation leading to tolerance? Department of Microbiology and Immunology, November 2012, Melbourne

Bowen D, Liver tolerance – novel pathways, Transplantation Society of Australia and New Zealand Postgraduate Course, June 2012, Canberra

Bowen D, Genetics and pathogenesis of primary biliary cirrhosis, Australian Liver Association Hepatology Masterclass, July 2012, Sydney

Bowen D, Use of recombinant adeno-associated viral vectors to study intrahepatic immunity, Virology Research Group, Prince of Wales Hospital, October 2012, Sydney

Bowen D, Immune responses to gene therapy vectors in the liver, Viertel Fellows Alumni Association Meeting, October 2012, Sydney

Bowen D, Advances in autoantibodies for the diagnosis of autoimmune liver diseases, Gastroenterological Society of Australia - Australian Gastroenterology Week, October 2012, Adelaide

Britton WJ, Biomarkers and Tuberculosis, Tuberculosis Research Symposium, Woolcock Institute for Medical Research, May 2012, Sydney

Britton WJ, Vaccines for Tuberculosis: the challenges and progress, Walter and Eliza Hall Institute, July 2012, Melbourne

Britton WJ, Tuberculosis: Challenges from the old enemy, Sydney Institute of Emerging Infections and Biosecurity Colloquium, October 2012, Sydney

Gamble J, Endothelial Cell Senescence and Regulation of Inflammation, Inflammation Conference, December 2012, Sydney

Holst JA, Title, Australian-Canadian Prostate Cancer Research Alliance Symposium, April 2012, Daydream Island

Holst JA, 13th Australasian Prostate Cancer Conference, August 2012, Melbourne

Holst JA, Speaker selected from Abstract, Sydney Cancer Conference, September 2012, Sydney

McCaughan G, Should treatment for HCV be deferred? Roche National Hepatitis Symposium, May 2012, Melbourne

McCaughan G, Advanced Liver Disease: Management and Pathogenesis, HAPT, August 2012, Sydney

2012 Invited Presentations

McCaughan G, The Intrahepatic Niche of the Hedgehog, UNSW Research Seminar, September 2012, Sydney

McCaughan G, Transplantation for Alcoholic Hepatitis, AGW, October 2012, Adelaide

Rasko J, New Developments in Cell and Gene Therapy, RCPA Pathology Update, March 2012, Sydney

Rasko J, RACP Future Directions In Health Congress, RACP Foundation 21st Anniversary Breakfast, May 2012, Brisbane

Rasko J, Regenerative medicine: resistance in futile, 3rd International NanoMedicine Conference, July 2012, Sydney

Rasko J, No fate but what we make - careers in gene cells, Combined Biological Sciences Meeting, August 2012, Sydney

Rasko J, HSANZ Symposium5: Haematopoietic Stem Cell Biology, HAA-APSTH 2012 Combined Annual Scientific Meeting, October 2012, Melbourne

Semsarian C, Approach to sudden unexplained death in the young, CSANZ Annual Scientific Meeting, August 2012, Brisbane

Semsarian C, Arrhythmogenic Genetics, National EP Fellows Weekend Symposium, March 2012, Sydney

Semsarian C, Australian Cardiac Health and Rehabilitation Association Annual Conference, November 2012, Sydney

Semsarian C, Can or will genetic testing guide management in cardiomyopathies? CSANZ Annual Scientific Meeting, August 2012, Brisbane

Semsarian C, Congenital LQTS case presentation: a hypothetical, HGSA 36th Annual Scientific Meeting, August 2012, Canberra

Semsarian C, Genetic basis of sudden cardiac death: latest technologies, Australasian Association of Clinical Biochemists, June 2012, Sydney

Semsarian C, Genetic research into cardiomyopathies and other cardiac conditions, Cardiomyopathy Australia Seminar: A Moving Picture, July 2012, Brisbane

Semsarian C, Genetics of heart disease, Masters of Genetic Counselling Course, May 2012, Sydney

Semsarian C, Getting to the heart of sudden death, Calvary Hospital Grand Rounds, June 2012, Canberra

Semsarian C, Getting to the heart of sudden death, SMS Foundation Council Meeting, University of Sydney, May 2012, Sydney

Semsarian C, Is it sudden cardiac death? Invited Neil Gollan Memorial Lecture, Launceston General Hospital, July 2012, Launceston

Semsarian C, MRI and cardiomyopathy, Cardiac MRI Masterclass, September 2012, Sydney

Semsarian C, Primary arrhythmogenic diseases and sudden death, Department of Anaesthetics, April 2012, Sydney

Semsarian C, Sudden cardiac death in the young, Invited 14th Dare Shott Public Lecture, University of Tasmania, July 2012, Launceston

Semsarian C, Sudden death – genetic screening and saving lives, Port Douglas Heart Meeting, June 2012, Port Douglas

Semsarian C, Sudden death in 2012, FRACP RPA BPT Revision Course, December 2012, Sydney

Semsarian C, Sudden unexplained death in children and babies, Heart Kids Education Day, October 2012, Brisbane

Semsarian C, The role of genetic testing in the setting of cardiomyopathies and sudden death, SA Cardiology Clinical Meeting, May 2012, Victor Harbor

Semsarian C, When is genetic testing appropriate in arrhythmia management? CSANZ Annual Scientific Meeting, August 2012, Brisbane

Vadas M, Pearls – Drawing value from networks and knowledge, Conference, March 2012, Location

Weninger W, Imaging innate immune responses in the skin in real time, Conjoint AWTRS- ASDR conference, May 2012, Sydney

Weninger W, Cell cycle imaging in melanoma, MMRI Stem Cell Symposium, May 2012, Brisbane

Weninger W, Imaging of bacterial skin infections, TLROZ 2012 conference, May 2012, Brisbane

Weninger W, Real time imaging of skin immune responses, Pathology Update, Annual Meeting of The Royal College of Pathologists, June 2012, Sydney

2012 Awards

2012 Australian Synchrotron Thesis Medal
Miriam Rose-Ash

2012 Rita and John Cornforth Medal, University of Sydney
Jodie Ingles

Allied Health and Technologist's Affiliate Prize, CSANZ
Jodie Ingles

2012 RT Hall Research Prize, CSANZ
Chris Semsarian

2012 Centenary Institute Lawrence Creative Prize, External award
Jian Yang

Best Oral Presentation Presented by an Honours Student, ASI NSW
David McDonald

Bosch Institute Advanced Microscopy Facility Micrograph of the Year (top 20 Finalist and 9th place prize winner)
Michael Lovelace

Brennan Prize Presentation, 33rd Australasian Dermatopathology Society Annual Meeting
Philip Tong

Early Career Researcher Poster Prize, Conjoint 3rd Australasian Wound & Tissue Repair Society Meeting and 9th Australasian Society for Dermatology Research Meeting
Philip Tong

Bright Sparks in ECImmunology 2012, Annual European Association of Immunology Meeting, (2nd prize)
Michelle Vo

High Achieving Young Investigator Award for the 6th Australian Association of Chinese Biomedical Scientists (3rd prize)
Hui (Emma) Zhang

Officer of the Order of Australia (AO), Queen's Birthday Honors' List for service to medical and biotechnological research, particularly in the area of human immunology, to higher education, and through contributions to professional organisations.
Mathew Vadas

Officer of the Order of Australia (AO), Queen's Birthday Honors' List for service to biomedical research in the field of gene and cell therapy, as a clinician, author, administrator and philanthropist.
John Rasko

Distinguished Fellow Award, The Royal College of Pathologists of Australasia.
John Rasko

Tied first place in the class of 2012 Immunology and Infectious Diseases Honours program, University of Sydney
Elizabeth Powter and David MacDonald

Scientific Image Prize, Centenary Institute
David Hancock, T cell Biology

Centenary Axel Ullrich Award (highest impact factor for a paper)
Wolfgang Weninger

Centenary Student Paper Award (highest impact factor for a student paper)
Jodie Ingles

Centenary Paper with Highest Citations Award published in the past five years
Chris Semsarian

Centenary Innovation Award
Barbara Fazekas de St Groth

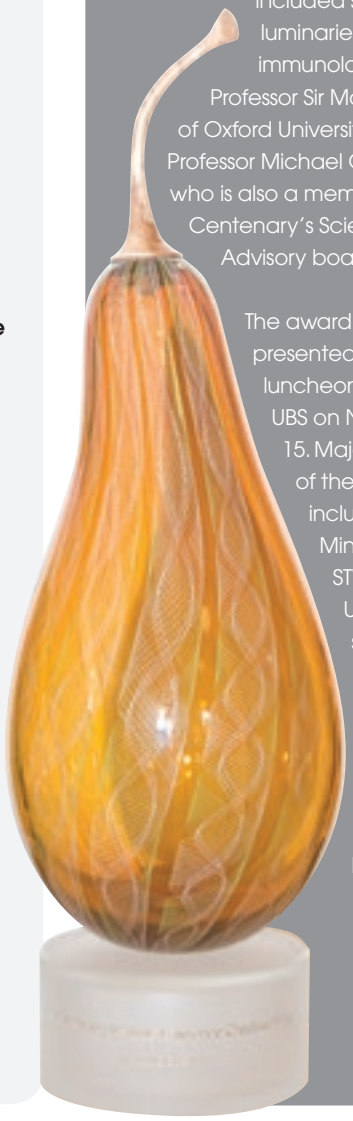
Centenary Outstanding Service Award
Bob Thornton

Centenary Institute Lawrence Creative Prize

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

Human genetics researcher, Dr Jian Yang, from the Diamantina Institute of the University of Queensland is the 2012 Lawrence Creative prize winner. He has solved one of the great puzzles of human genetics — why the genes typically implicated in inherited diseases like schizophrenia, obesity and diabetes only account for a small amount of their heritability.

The international judging panel included such luminaries as immunologists Professor Sir Marc Feldman of Oxford University and Professor Michael Goodman, who is also a member of Centenary's Scientific Advisory board.



The award was presented at a luncheon hosted by UBS on November 15. Major sponsors of the award included Mindshare, the STW group, UBS with supporting sponsors The Australian, Deloitte and Val Morgan Cinema Network.

Centenary Institute Collaborations 2012

Aarhus University Hospital, Aarhus, Denmark

Alavita Pharmaceuticals Inc, Mountain View, CA, USA

Anandaban Leprosy Hospital, Kathmandu, Nepal

ANU College of Medicine, Biology & Environment, Canberra, ACT

Archillion Pharmaceuticals Inc, New Haven, CT, USA

Austin Health, Melbourne, VIC

Australian Institute of Sport, Canberra, ACT

Australian Prostate Cancer Research Centre, Brisbane, QLD

Basil Hetzel Institute, Adelaide, SA

Bayer, Sydney, NSW

Brain and Mind Institute, Sydney, NSW

Bristol-Myers Squibb, Melbourne, VIC

Children's Medical Research Institute, Sydney, NSW

Colorado State University, Fort Collins, CO, USA

Columbia University, New York, NY, USA

Concord Hospital, Sydney, NSW

Dartmouth College, Hanover, NH, USA

Deakin University, Geelong, VIC

Department of Forensic Medicine, Sydney, NSW

European Molecular Biology Laboratory, Melbourne, VIC

Eskitis Institute, Brisbane, QLD

Flinders University, Adelaide, SA

Fudan University, Shanghai, China

Garvan Institute, Sydney, NSW

Gilead, Melbourne, VIC

GlaxoSmithKline, Melbourne, VIC

Griffith University, Brisbane, QLD

Harvard Medical School, Boston, MA, USA

Heart Research Institute, Sydney, NSW

ICGEB New Delhi, New Delhi, DL, India

Imperial College, London, UK

Institute of Human Genetics, Paris, France

The Jackson Laboratory, Bar Harbor, ME, USA

Janssen-Cilag, Sydney, NSW

Jiaotong University, Shanghai, China

The John Curtin School of Medical Research, Canberra, ACT

Juntendo University School of Medicine, Tokyo, Japan

La Trobe University, Melbourne, VIC

Louisiana State University, Baton Rouge, LA, USA

Macquarie University, Sydney, NSW

Malaghan Institute, Wellington, New Zealand

Mater Medical Research Institute, Brisbane, QLD

Max-Delbrück-Centre for Molecular Medicine, Berlin, Germany

Minnesota Heart Centre, Minneapolis, MN, USA

Monash Medical Centre, Melbourne, VIC

Monash Research Institute, Melbourne, VIC

Monash University, Melbourne, VIC

MRC Laboratory of Molecular Biology, Cambridge, UK

MSD, Sydney, NSW

National Centre for Asbestos Related Diseases, Perth, WA

National Centre in HIV Epidemiology and Clinical Research, Sydney, NSW

National Institutes of Health, Bethesda, MD, USA

National Lung Hospital, Hanoi, Vietnam

National Tuberculosis Program and National Hospital for Tuberculosis and Respiratory Diseases, Hanoi, Vietnam

Nationwide Children's Research Institute, Columbus, OH, USA

Newcastle University, Newcastle upon Tyne, UK

Ningxia Medical University, NHAR, China

Novartis, Sydney, NSW

Nuffield Department of Clinical Medicine, Oxford, UK

Peking Union Medical School Hospital, Beijing, China

Peter MacCallum Cancer Centre, Melbourne, VIC

Prince Henry's Institute of Medical Research, Melbourne, VIC

The Price of Wales Hospital, Sydney, NSW

Princeton University, Princeton, NJ, USA

Research Centre for Allergy and Immunology, Riken, Yokohama City, Japan

Royal Children's Hospital, Melbourne, VIC

Royal Prince Alfred Hospital, Sydney, NSW

SA Pathology, Adelaide, SA

Shenzhen-Hong Kong Infectious Diseases Research Institute, Hong Kong

St George Hospital, Sydney, NSW

St Jude Children's Research Hospital, Memphis, TN, USA

St Vincent's Hospital, Melbourne, VIC

St Vincent's Hospital, Sydney, NSW

St Vincent's Medical Research Institute, Melbourne, VIC

Statin Institute, Copenhagen, Denmark

Tokyo Medical and Dental University, Tokyo, Japan

The Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan

Tufts University, Boston, MA, USA

Università di Torino, Torino, Italy

University of Adelaide, Adelaide, SA

University of Antwerp, Antwerp, Belgium

University of Auckland, Auckland, New Zealand

University of British Columbia, Vancouver, BC, Canada

University of California, Berkeley, CA, USA

University of Freiburg, Freiburg, Germany

University of Massachusetts, Boston, MA, USA

University of Melbourne, Melbourne, VIC

University of Minnesota, Minneapolis, MN, USA

University of New South Wales, Sydney, NSW

University of Newcastle, Newcastle, NSW

University of Oxford, Oxford, UK

University of Pennsylvania, Philadelphia, PA, USA

University of Queensland, Brisbane, QLD

University of Sydney, Sydney, NSW

University of Technology Sydney, Sydney, NSW

University of Tokyo, Tokyo, Japan

University of Western Australia, Perth, WA

University of Wollongong, Wollongong, NSW

Victoria Genetics, Melbourne, VIC

Victorian Infectious Diseases Reference Laboratory, Melbourne, VIC

Victorian Institute of Forensic Medicine, Melbourne, VIC

Walter and Eliza Hall Institute of Medical Research, Melbourne, VIC

Washington University, St Louis, MO, USA

Wellcome Trust Sanger Institute, Cambridgeshire, UK

Western Australian Institute for Medical Research, Perth, WA

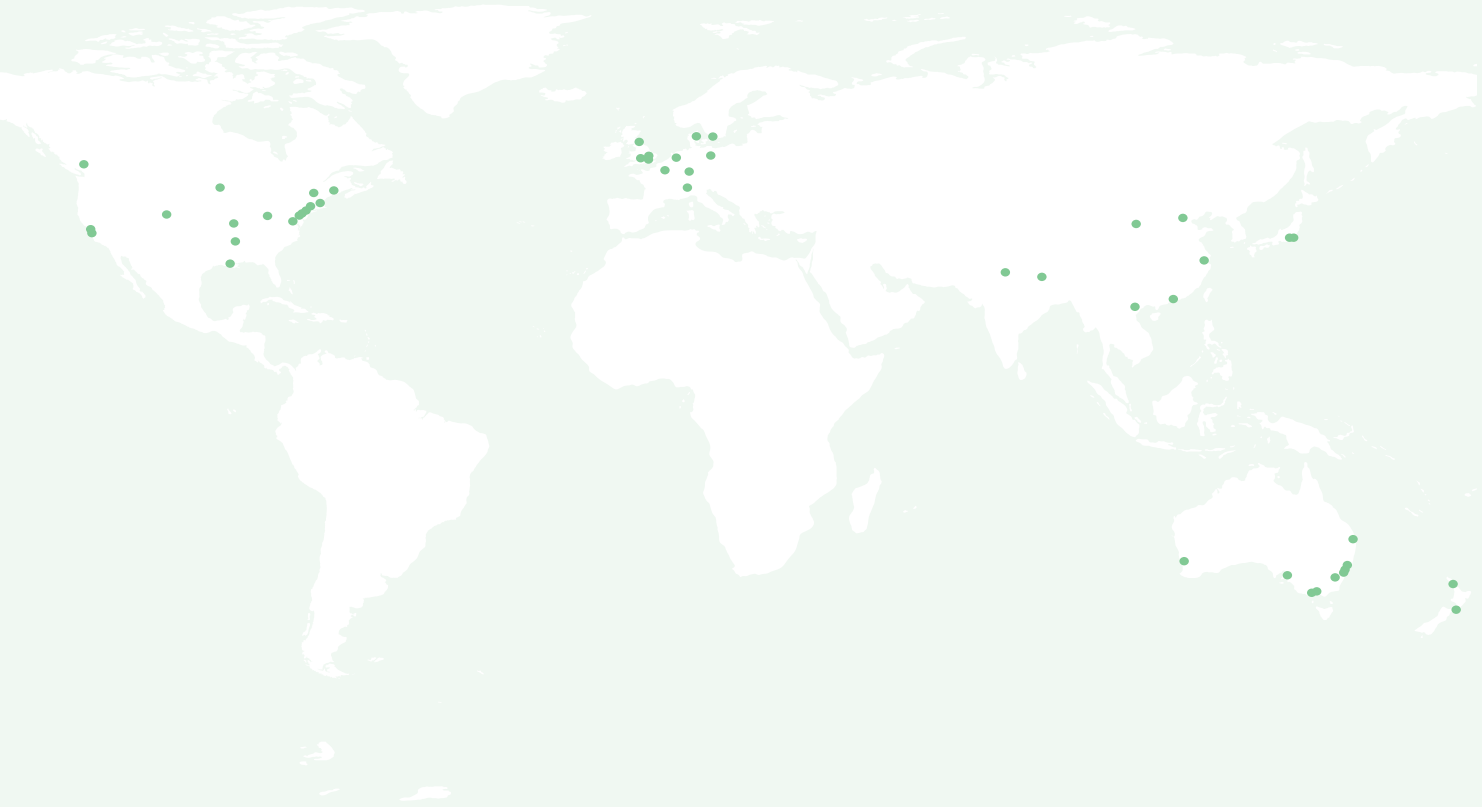
Westmead Hospital, Sydney, NSW

Westmead Millenium Institute for Medical Research, Sydney, NSW

Wistar Institute, Philadelphia, PA, USA

Woolcock Institute of Medical Research, Sydney, NSW

Yale University, New Haven, CT, USA



Centenary researcher, Patrick Bertolino Liver Immunology Group.

Centenary Institute research for life

The scientists and staff at Centenary wish to thank every one of our supporters for making 2012 such a successful year.

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Centenary Institute

A Locked Bag 6, Newtown NSW 2042
P +61 2 9565 6100
F +61 2 9565 6111
www.centenary.org.au

Centenary Institute research for life

Image front cover: Angelina Lay is a Research Officer in the Vascular Biology Group.